

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 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 September 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 001-36407

**ALNYLAM PHARMACEUTICALS, INC.**  
(Exact Name of Registrant as Specified in Its Charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

675 West Kendall Street,  
Henri A. Termeer Square  
Cambridge, MA  
(Address of Principal Executive Offices)

77-0602661  
(I.R.S. Employer  
Identification No.)

02142  
(Zip Code)

(617) 551-8200  
(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, \$0.01 par value per share	ALNY	The Nasdaq Stock Market LLC

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, a 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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

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 ☒

At October 22, 2021, the registrant had 119,601,177 shares of Common Stock, \$0.01 par value per share, outstanding.



**ALNYLAM PHARMACEUTICALS, INC.  
QUARTERLY REPORT ON FORM 10-Q**

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"Alnylam," ONPATTRO®, GIVLAARI®, OXLUMO® and Alnylam Act® are registered trademarks of Alnylam Pharmaceuticals, Inc. Our logo, trademarks and service marks are property of Alnylam. All other trademarks or service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective holders.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of the federal securities laws, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 and are including this statement for purposes of complying with those safe harbor provisions. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “could,” “expects,” “plans,” “intends,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- risks related to the direct or indirect impact of the COVID-19 global pandemic, emerging or future variants of COVID-19 or any future pandemic, such as the scope and duration of the pandemic, government actions and restrictive measures implemented in response, the effectiveness of vaccination campaigns, the necessity for and availability of booster vaccines, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by our products, or in patient enrollment in clinical trials, potential clinical trial, regulatory review and inspection or supply chain disruptions, and other potential impacts to our business, the effectiveness or timeliness of steps taken by us to mitigate the impact of the pandemic, our ability to execute business continuity plans to address disruptions caused by the COVID-19 or any future pandemic, and the success and effectiveness of our return to office initiatives;
- our views with respect to the potential for approved and investigational RNAi therapeutics, including ONPATTRO, GIVLAARI, OXLUMO, Leqvio® (inclisiran), vutrisiran and fitusiran;
- our plans for additional global regulatory filings and the continuing product launches of ONPATTRO, GIVLAARI, OXLUMO and our partner's plans with respect to Leqvio;
- our expectations regarding the regulatory review of vutrisiran and the advancement by our partner of inclisiran through United States, or U.S., regulatory review and toward the market;
- our expectations regarding potential market size for, and the successful commercialization of, ONPATTRO, GIVLAARI, OXLUMO, Leqvio or any future products, including vutrisiran;
- our ability to obtain and maintain regulatory approvals and pricing and reimbursement for ONPATTRO, GIVLAARI, OXLUMO or any future products, including vutrisiran, and our partners' ability with respect to Leqvio and fitusiran;
- the progress of our research and development programs;
- our current and anticipated clinical trials and expectations regarding the reporting of data from these trials;
- the timing of regulatory filings and interactions with or actions or advice of regulatory authorities, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing or the timing or likelihood of regulatory approvals;
- the status of our manufacturing operations and any delays, interruptions or failures in the manufacture and supply of ONPATTRO, GIVLAARI, OXLUMO, or any of our product candidates (or other products or product candidates being developed and commercialized by our partners) by our or their contract manufacturers or by us or our partners;
- our progress continuing to build and leverage global commercial infrastructure;
- our ability to successfully expand the indication for ONPATTRO in the future;
- the possible impact of any competing products on the commercial success of ONPATTRO, GIVLAARI, OXLUMO and Leqvio, as well as our product candidates, including vutrisiran, and, our, or with respect to Leqvio or fitusiran, our partners', ability to compete against such products;
- our ability to manage our growth and operating expenses;
- our views and plans with respect to our 5-year *Alnylam P<sup>5</sup>x25* strategy and our intentions to achieve the metrics associated with this strategy, including to become a top five biotech company in market capitalization by the end of 2025;
- our belief that the funding provided by our strategic financing collaboration with The Blackstone Group Inc., or Blackstone, and certain of its affiliates should enable us to achieve a self-sustainable profile without the need for future equity financing;
- our expectations regarding the length of time our current cash, cash equivalents and marketable securities will support our operations based on our current operating plan;

- our dependence on third parties for development, manufacture and distribution of products;
- our expectations regarding our corporate collaborations, including potential future licensing fees and milestone and royalty payments under existing or future agreements;
- obtaining, maintaining and protecting our intellectual property;
- our ability to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors;
- the outcome of litigation or other legal proceedings or of any current or future government investigation, including any investigation related to the subpoena received on or about April 9, 2021 pertaining to our marketing and promotion of ONPATTRO (patisiran) in the U.S.;
- regulatory developments in the U.S. and foreign countries;
- the impact of laws and regulations;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under the caption Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q.

The risks set forth above are not exhaustive. Other sections of this Quarterly Report on Form 10-Q may include additional factors that could adversely affect our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for management to predict all risk factors, nor can we assess the impact of all risk factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A, "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. 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. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

This Quarterly Report on Form 10-Q may include data that we obtained from industry publications and third-party research, surveys and studies. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. This Quarterly Report on Form 10-Q also may include data based on our own internal estimates and research, including estimates regarding the impact of the COVID-19 pandemic (or related pandemic caused by coronavirus variants) on our financial statements and business operations. Our internal estimates have not been verified by any independent source and, while we believe any data obtained from industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. Such third-party data, as well as our internal estimates and research, are subject to a high degree of uncertainty and risk due to a variety of factors, including those described in Part II, Item 1A, "Risk Factors" and elsewhere in this Quarterly Report on Form 10-Q. These and other factors could cause our results to differ materially from those expressed in this Quarterly Report on Form 10-Q.

## SUMMARY OF MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties that you should be aware of before making an investment decision, including those highlighted in the section entitled "Risk Factors." These risks include, but are not limited to, the following:

### Business Related Risks – Risks Related to Our Financial Results

- The current pandemic of the novel coronavirus, or COVID-19, and the future outbreak of other highly infectious or contagious diseases, could continue to have an adverse impact on our business, financial condition and results of operations, including our commercial operations and sales, clinical trials and pre-clinical studies.
- We are a young commercial company and the marketing and sale of ONPATTRO, GIVLAARI, OXLUMO or any future products, including vutrisiran, may be unsuccessful or less successful than anticipated.
- We have a history of losses and may never become and remain consistently profitable.
- We will require substantial funds to continue our research, development and commercialization activities.
- Although we sold a portion of the expected royalty stream and commercial milestones related to global sales of Leqvio by Novartis AG, or Novartis, we are entitled to retain the remaining portion of such future royalties and, if certain specified thresholds are met, to the remaining portion of commercial milestone payments, and any negative developments related to Leqvio could have a material adverse effect on the timing or amount of those payments.

### Risks Related to Our Dependence on Third Parties

- We may not be able to execute our business strategy if we are unable to maintain existing or enter into new alliances with other companies that can provide business and scientific capabilities and funds for the development and commercialization of certain of our product candidates.
- If any collaborator materially amends, terminates or fails to perform its obligations under agreements with us, the development and commercialization of certain of our product candidates could be delayed or terminated and we could suffer other economic harm.
- We have limited manufacturing experience and resources and we must incur significant costs to develop this expertise and/or rely on third parties to manufacture our products.
- We rely on third parties to conduct our clinical trials, and if they fail to fulfill their obligations, our development plans may be adversely affected.

### Risks Related to Managing Our Operations

- If we are unable to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors, our ability to implement our business plan may be adversely affected.
- We are currently embarking on our first CEO succession as a publicly traded company with commercial operations. Any leadership transition carries with it disruption risks that could have a negative impact on the execution of our *Alnylam P<sup>5</sup>x25* strategy. These risks include our ability to attract and retain qualified employees.
- We may have difficulty expanding our operations successfully as we continue our evolution from a U.S.- and Europe-based company primarily involved in discovery, pre-clinical testing and clinical development into a global company that develops and commercializes multiple drugs in multiple geographies including Asia, Latin America and the Middle East.
- We may experience computer system failures or unauthorized or inappropriate use of or access to our information systems or those of our contractors or collaborators, potentially resulting in substantial loss of data, business interruption or other harm.

### Industry Related Risks – Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates and the Commercialization of Our Approved Products

- Any product candidates we or our partners develop may fail in development or be delayed to a point where they do not become commercially viable.
- We or our partners may be unable to obtain U.S. or foreign regulatory approval for our or our partnered product candidates.
- Even if we or our partners obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight.

- Even if we receive regulatory approval to market our product candidates, and our collaborators receive regulatory approval to market product candidates discovered by us or developed with our technology, the market may not be receptive to such product candidates upon their commercial introduction, which could prevent us from becoming profitable.
- We are a multi-product commercial company and expect to continue to invest significant financial and management resources to continue to build our marketing, sales, market access and distribution capabilities and further establish our global commercial infrastructure, and our commercial efforts may not be successful.
- The patient populations suffering from hereditary transthyretin-mediated amyloidosis with polyneuropathy, acute hepatic porphyria and primary hyperoxaluria type 1 are small and have not been established with precision.
- We may incur significant liability if enforcement authorities allege or determine that we are engaging in commercial activities or promoting our commercially approved products in a way that violates applicable regulations.
- Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.
- Governments outside the U.S. may impose strict price controls, and the U.S. government may impose price controls or reference pricing, which may adversely affect our revenues.

#### **Risks Related to Patents, Licenses and Trade Secrets**

- If we are not able to obtain and enforce patent protection for our discoveries, our ability to develop and commercialize our product candidates will be harmed.
- We license patent rights from third-party owners. If such owners do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, our competitive position and business prospects may be harmed.
- Other companies or organizations may challenge our patent rights or may assert patent rights that prevent us from developing and commercializing our products.
- If we become involved in patent litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, substantial liability for damages or be required to stop our product development and commercialization efforts.
- If we fail to comply with our obligations under any licenses or related agreements, we may be required to pay damages and could lose license or other rights that are necessary for developing, commercializing and protecting our RNAi technology.

#### **Risks Related to Competition**

- The pharmaceutical market is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to commercialize successfully any drugs that we or our collaborators develop.
- We face competition from other companies that are working to develop novel drugs and technology platforms using technology similar to ours, as well as from companies utilizing emerging technologies, including gene therapy and gene editing.

#### **Risks Related to Our Common Stock**

- If our stock price fluctuates, purchasers of our common stock could incur substantial losses.
- We may incur significant costs from class action litigation.
- Future sales of shares of our common stock, including by our significant stockholders, us or our directors and officers, could cause the price of our common stock to decline.
- Regeneron's ownership of our common stock could delay or prevent a change in corporate control.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section entitled "Risk Factors" and the other information set forth in this Quarterly Report on Form 10-Q, including our consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

**PART I. FINANCIAL INFORMATION**  
**ITEM 1. FINANCIAL STATEMENTS (Unaudited)**

**ALNYLAM PHARMACEUTICALS, INC.**  
**CONDENSED CONSOLIDATED BALANCE SHEETS**  
(In thousands, except per share amounts)  
(Unaudited)

	September 30, 2021	December 31, 2020
<b>ASSETS</b>		
<b>Current assets:</b>		
Cash and cash equivalents	\$ 1,093,991	\$ 496,580
Marketable debt securities	1,161,324	1,333,182
Marketable equity securities	72,550	44,633
Accounts receivable, net	141,064	102,413
Inventory	97,899	75,202
Prepaid expenses and other current assets	108,534	62,767
Receivable related to the sale of future royalties	—	500,000
Total current assets	2,675,362	2,614,777
Property, plant and equipment, net	484,941	465,029
Operating lease right-of-use assets	235,853	241,485
Restricted investments	40,890	40,725
Other assets	35,267	45,045
Total assets	<u>\$ 3,472,313</u>	<u>\$ 3,407,061</u>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
<b>Current liabilities:</b>		
Accounts payable	\$ 40,048	\$ 51,966
Accrued expenses	388,576	355,909
Operating lease liability	40,612	36,872
Deferred revenue	115,044	127,207
Liability related to the sale of future royalties	26,376	13,316
Total current liabilities	610,656	585,270
Operating lease liability, net of current portion	286,030	293,039
Deferred revenue, net of current portion	177,123	225,094
Long-term debt	433,799	191,278
Liability related to the sale of future royalties, net of current portion	1,132,362	1,058,225
Other liabilities	76,450	37,908
Total liabilities	2,716,420	2,390,814
Commitments and contingencies (Note 14)		
<b>Stockholders' equity:</b>		
Preferred stock, \$0.01 par value per share, 5,000 shares authorized and no shares issued and outstanding as of September 30, 2021 and December 31, 2020	—	—
Common stock, \$0.01 par value per share, 250,000 shares authorized; 119,480 shares issued and outstanding as of September 30, 2021; 116,427 shares issued and outstanding as of December 31, 2020	1,195	1,164
Additional paid-in capital	5,968,661	5,644,074
Accumulated other comprehensive loss	(34,230)	(43,622)
Accumulated deficit	(5,179,733)	(4,585,369)
Total stockholders' equity	755,893	1,016,247
Total liabilities and stockholders' equity	<u>\$ 3,472,313</u>	<u>\$ 3,407,061</u>

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



**ALNYLAM PHARMACEUTICALS, INC.**  
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(In thousands, except per share amounts)  
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
<b>Statements of Operations</b>				
Revenues:				
Net product revenues	\$ 167,044	\$ 99,206	\$ 463,624	\$ 248,677
Net revenues from collaborations	20,136	26,647	121,328	80,614
Royalty revenue	453	—	800	—
Total revenues	187,633	125,853	585,752	329,291
Operating costs and expenses:				
Cost of goods sold	28,091	20,826	81,370	52,393
Cost of collaborations and royalties	4,572	971	21,110	2,635
Research and development	194,572	161,783	563,106	486,350
Selling, general and administrative	142,075	167,472	434,257	422,129
Total operating costs and expenses	369,310	351,052	1,099,843	963,507
Loss from operations	(181,677)	(225,199)	(514,091)	(634,216)
Other (expense) income:				
Interest expense	(40,274)	(28,731)	(106,205)	(55,979)
Interest income	225	2,072	1,084	10,717
Other (expense) income, net	17,490	(594)	27,370	67,477
Total other (expense) income, net	(22,559)	(27,253)	(77,751)	22,215
Loss before income taxes	(204,236)	(252,452)	(591,842)	(612,001)
Provision for income taxes	(278)	(839)	(2,522)	(2,740)
Net loss	\$ (204,514)	\$ (253,291)	\$ (594,364)	\$ (614,741)
Net loss per common share - basic and diluted	\$ (1.72)	\$ (2.18)	\$ (5.04)	\$ (5.37)
Weighted-average common shares used to compute basic and diluted net loss per common share	119,141	115,986	118,005	114,554
<b>Statements of Comprehensive Loss</b>				
Net loss	\$ (204,514)	\$ (253,291)	\$ (594,364)	\$ (614,741)
Other comprehensive income (loss):				
Unrealized (loss) gain on marketable securities	(64)	(1,481)	(312)	768
Foreign currency translation gain (loss)	1,857	(2,576)	9,530	(1,665)
Defined benefit pension plans, net of tax	58	76	174	222
Total other comprehensive income (loss)	1,851	(3,981)	9,392	(675)
Comprehensive loss	\$ (202,663)	\$ (257,272)	\$ (584,972)	\$ (615,416)

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

**ALNYLAM PHARMACEUTICALS, INC.**  
**CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
(In thousands)  
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balance as of December 31, 2020</b>	116,427	\$ 1,164	\$ 5,644,074	\$ (43,622)	\$ (4,585,369)	\$ 1,016,247
Exercise of common stock options, net of tax withholdings	614	6	47,028	—	—	47,034
Issuance of common stock under equity plans	280	3	(3)	—	—	—
Stock-based compensation expense	—	—	56,295	—	—	56,295
Other comprehensive income	—	—	—	6,905	—	6,905
Net loss	—	—	—	—	(200,291)	(200,291)
<b>Balance as of March 31, 2021</b>	117,321	1,173	5,747,394	(36,717)	(4,785,660)	926,190
Exercise of common stock options, net of tax withholdings	993	10	75,439	—	—	75,449
Issuance of common stock under equity plans	282	3	7,715	—	—	7,718
Stock-based compensation expense	—	—	32,928	—	—	32,928
Other comprehensive income	—	—	—	636	—	636
Net loss	—	—	—	—	(189,559)	(189,559)
<b>Balance as of June 30, 2021</b>	118,596	1,186	5,863,476	(36,081)	(4,975,219)	853,362
Exercise of common stock options, net of tax withholdings	883	9	71,490	—	—	71,499
Issuance of common stock under equity plans	1	—	—	—	—	—
Stock-based compensation expense	—	—	33,695	—	—	33,695
Other comprehensive income	—	—	—	1,851	—	1,851
Net loss	—	—	—	—	(204,514)	(204,514)
<b>Balance as of September 30, 2021</b>	119,480	\$ 1,195	\$ 5,968,661	\$ (34,230)	\$ (5,179,733)	\$ 755,893

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

**ALNYLAM PHARMACEUTICALS, INC.**  
**CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
(In thousands)  
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
<b>Balance as of December 31, 2019</b>	112,188	\$ 1,122	\$ 5,201,176	\$ (36,518)	\$ (3,727,088)	\$ 1,438,692
Exercise of common stock options, net of tax withholdings	976	9	54,212	—	—	54,221
Issuance of common stock under equity plans	4	—	—	—	—	—
Stock-based compensation expense	—	—	34,578	—	—	34,578
Other comprehensive income	—	—	—	4,459	—	4,459
Net loss	—	—	—	—	(182,221)	(182,221)
<b>Balance as of March 31, 2020</b>	113,168	1,131	5,289,966	(32,059)	(3,909,309)	1,349,729
Exercise of common stock options, net of tax withholdings	1,233	12	91,861	—	—	91,873
Issuance of common stock under equity plans	283	3	5,298	—	—	5,301
Issuance of common stock to strategic partners, net of closing costs	963	10	99,488	—	—	99,498
Stock-based compensation expense	—	—	33,707	—	—	33,707
Other comprehensive loss	—	—	—	(1,153)	—	(1,153)
Net loss	—	—	—	—	(179,229)	(179,229)
<b>Balance as of June 30, 2020</b>	115,647	1,156	5,520,320	(33,212)	(4,088,538)	1,399,726
Exercise of common stock options, net of tax withholdings	494	5	32,207	—	—	32,212
Issuance of common stock under equity plans	2	—	129	—	—	129
Issuance of common stock under benefit plans	—	—	—	—	—	—
Stock-based compensation expense	—	—	40,228	—	—	40,228
Other comprehensive loss	—	—	—	(3,981)	—	(3,981)
Net loss	—	—	—	—	(253,291)	(253,291)
<b>Balance as of September 30, 2020</b>	116,143	\$ 1,161	\$ 5,592,884	\$ (37,193)	\$ (4,341,829)	\$ 1,215,023

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

**ALNYLAM PHARMACEUTICALS, INC.**  
**CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(In thousands)  
(Unaudited)

	Nine Months Ended September 30,	
	2021	2020
<b>Cash flows from operating activities:</b>		
Net loss	\$ (594,364)	\$ (614,741)
Non-cash adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	36,192	24,386
Amortization and interest accretion related to operating leases	32,051	29,169
Non-cash interest expense on liability related to the sale of future royalties	87,197	55,979
Stock-based compensation	121,135	105,597
Realized and unrealized gain on marketable equity securities	(61,273)	(66,626)
Other	35,222	1,628
Changes in operating assets and liabilities:		
Accounts receivable, net	(42,350)	(35,070)
Inventory	(15,655)	(26,962)
Prepaid expenses and other assets	(48,765)	6,455
Accounts payable, accrued expenses and other liabilities	48,738	75,564
Deferred revenue	(60,094)	(15,924)
Operating lease liability	(29,586)	(31,272)
Net cash used in operating activities	(491,552)	(491,817)
<b>Cash flows from investing activities:</b>		
Purchases of property, plant and equipment	(54,486)	(48,693)
Purchases of marketable securities	(973,146)	(1,469,451)
Sales and maturities of marketable securities	1,172,100	1,190,714
Purchases of restricted investments	(26,140)	(9,900)
Proceeds from maturity of restricted investments	25,975	—
Other investing activities	(4,198)	(300)
Net cash provided by (used in) investing activities	140,105	(337,630)
<b>Cash flows from financing activities:</b>		
Proceeds from exercise of stock options and other types of equity, net	201,227	181,459
Proceeds from the sale of future royalties	500,000	500,000
Proceeds from development derivative	16,100	4,200
Proceeds from issuance of common stock to strategic partners, net of closing costs	—	99,498
Proceeds from term loan facility	250,000	—
Payment of transaction costs related to sale of future royalties and term loan facility	(12,500)	(8,128)
Net cash provided by financing activities	954,827	777,029
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(5,968)	1,946
Net increase (decrease) in cash, cash equivalents and restricted cash	597,412	(50,472)
Cash, cash equivalents and restricted cash, beginning of period	499,046	549,628
Cash, cash equivalents and restricted cash, end of period	\$ 1,096,458	\$ 499,156
<b>Supplemental disclosure of noncash investing and financing activities:</b>		
Capital expenditures included in accounts payable and accrued expenses	\$ 9,414	\$ 7,048
Lease liabilities arising from obtaining right-of-use assets	\$ 7,876	\$ 34,363
Receivable and liability related to the sale of future royalties	\$ —	\$ 500,000

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

**ALNYLAM PHARMACEUTICALS, INC.**  
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**  
**(Unaudited)**

## **1. NATURE OF BUSINESS**

Alnylam Pharmaceuticals, Inc. (also referred to as Alnylam, we, our or us) commenced operations on June 14, 2002 as a biopharmaceutical company seeking to develop and commercialize novel therapeutics based on ribonucleic acid interference, or RNAi. We are committed to the advancement of our company strategy of building a multi-product, global, commercial biopharmaceutical company with a deep and sustainable clinical pipeline of RNAi therapeutics for future growth and a robust, organic research engine for sustainable innovation and great potential for patient impact. Since inception, we have focused on discovering, developing and commercializing RNAi therapeutics by establishing and maintaining a strong intellectual property position in the RNAi field, establishing strategic alliances with leading pharmaceutical and life sciences companies, generating revenues through licensing agreements, and ultimately developing and commercializing RNAi therapeutics globally, either independently or with our strategic partners. We have devoted substantially all of our efforts to business planning, research, development, manufacturing and early commercial efforts, acquiring, filing and expanding intellectual property rights, recruiting management and technical staff, and raising capital.

In early 2021, we launched our *Alnylam P<sup>5</sup>x25* strategy, which focuses on our planned transition to a top five biotech company, as measured by market capitalization, by the end of 2025. With *Alnylam P<sup>5</sup>x25*, we aim to deliver transformative rare and prevalent disease medicines for patients around the world through sustainable innovation, delivering exceptional financial performance and driving profitability.

As of September 30, 2021, we have four products that have received marketing approval, including one partnered product, and six late-stage investigational programs advancing towards potential commercialization. We currently generate worldwide product revenues from three commercialized products, ONPATTRO, GIVLAARI and OXLUMO, primarily in the U.S., Europe and Japan.

## **2. BASIS OF PRESENTATION AND PRINCIPLES OF CONSOLIDATION**

The accompanying condensed consolidated financial statements of Alnylam are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP, applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to state fairly the results of operations for the reported periods. Our condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, our audited consolidated financial statements for the year ended December 31, 2020, which were included in our Annual Report on Form 10-K that was filed with the Securities and Exchange Commission on February 11, 2021. The year-end condensed consolidated balance sheet data was derived from our audited financial statements but does not include all disclosures required by GAAP. The results of our operations for any interim period are not necessarily indicative of the results of our operations for any other interim period or for a full fiscal year.

The accompanying condensed consolidated financial statements reflect the operations of Alnylam and our wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated.

Our significant accounting policies are described in Note 2 of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2020.

### ***Reclassification***

Certain prior period amounts in the condensed consolidated financial statements have been reclassified to conform to the current period presentation.

### ***Use of Estimates***

The preparation of 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 condensed consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. In our condensed consolidated financial statements, we use estimates and assumptions related to our inventory valuation and related reserves, liability related to the sale of future royalties, development derivative liability, income taxes, revenue recognition, research and development expenses, and stock-based compensation. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable. Actual results could differ from those estimates.

The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including sales, expenses, reserves and allowances, the supply of our products and product candidates, clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and variants thereof, and the actions taken to contain or treat it or vaccinate against it, as well as the economic impact on local, regional, national and international customers and markets.

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We have made estimates of the impact of COVID-19 within our financial statements and there may be changes to those estimates in future periods. Actual results may differ from these estimates.

**Liquidity**

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of September 30, 2021, together with the cash we expect to generate from product sales and under our current alliances, in addition to our strategic financing collaboration with The Blackstone Group Inc. and certain of its affiliates, will be sufficient to enable us to advance our *Alnylam P<sup>5</sup>x25* strategy for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q.

**3. NET PRODUCT REVENUES**

Net product revenues consist of the following:

(In thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
<b>ONPATTRO</b>				
United States	\$ 51,247	\$ 39,027	\$ 153,109	\$ 108,491
Europe	51,019	30,478	136,576	74,664
Rest of World (primarily Japan)	18,051	13,011	46,422	32,560
Total	\$ 120,317	\$ 82,516	\$ 336,107	\$ 215,715
<b>GIVLAARI</b>				
United States	\$ 22,372	\$ 12,108	\$ 62,502	\$ 26,043
Europe	7,568	4,582	22,461	6,919
Rest of World (primarily Japan)	1,893	—	2,173	—
Total	\$ 31,833	\$ 16,690	\$ 87,136	\$ 32,962
<b>OXLUMO</b>				
United States	\$ 5,236	\$ —	\$ 13,156	\$ —
Europe	9,658	—	27,225	—
Total	\$ 14,894	\$ —	\$ 40,381	\$ —
Total net product revenues	\$ 167,044	\$ 99,206	\$ 463,624	\$ 248,677

The following table presents the balance of our receivables related to our net product revenues:

(In thousands)	As of September 30, 2021	As of December 31, 2020
Receivables included in “Accounts receivable, net”	\$ 116,872	\$ 68,871

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#### 4. NET REVENUES FROM COLLABORATIONS

Net revenues from collaborations consist of the following:

(In thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Regeneron Pharmaceuticals	\$ 14,161	\$ 14,874	\$ 90,908	\$ 49,790
Novartis AG	4,160	1,091	21,179	6,029
Vir Biotechnology	1,233	8,512	8,033	21,476
Other	582	2,170	1,208	3,319
Total	\$ 20,136	\$ 26,647	\$ 121,328	\$ 80,614

The following table presents the balance of our receivables and contract liabilities related to our collaboration agreements:

(In thousands)	As of September 30, 2021		As of December 31, 2020	
Receivables included in “Accounts receivable, net”	\$	23,584	\$	33,542
Contract liabilities included in “Deferred revenue”	\$	76,452	\$	120,021

We recognized revenue of \$12.7 million and \$65.2 million in the three and nine months ended September 30, 2021, respectively, and revenue of \$19.2 million and \$50.7 million in the three and nine months ended September 30, 2020, respectively, that in each case was included in the contract liability balance at the beginning of the respective period.

In order to determine revenue recognized in the period from contract liabilities, we first allocate revenue to the individual contract liability balance outstanding at the beginning of the period until the revenue exceeds that balance. 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 a portion applying to the new consideration for the period.

The following table provides research and development expenses incurred by type, for which we recognize net revenue, that are directly attributable to our collaboration agreements, by collaboration partner:

(In thousands)	Three Months Ended September 30,					
	2021			2020		
	Clinical Trial and Manufacturing	External Services	Other	Clinical Trial and Manufacturing	External Services	Other
Regeneron Pharmaceuticals	\$ 3,152	\$ 285	\$ 10,964	\$ 3,355	\$ 43	\$ 9,167
Vir Biotechnology	519	37	546	1,379	277	3,247
Other	53	—	182	513	17	546
Total	\$ 3,724	\$ 322	\$ 11,692	\$ 5,247	\$ 337	\$ 12,960

(In thousands)	Nine Months Ended September 30,					
	2021			2020		
	Clinical Trial and Manufacturing	External Services	Other	Clinical Trial and Manufacturing	External Services	Other
Regeneron Pharmaceuticals	\$ 17,343	\$ 547	\$ 34,082	\$ 10,751	\$ 67	\$ 33,290
Vir Biotechnology	2,234	693	2,599	2,757	486	8,539
Other	742	52	1,245	1,710	46	1,486
Total	\$ 20,319	\$ 1,292	\$ 37,926	\$ 15,218	\$ 599	\$ 43,315

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The research and development expenses incurred for each agreement listed in the table above consist of costs incurred for (i) clinical expenses, including manufacturing of clinical product, (ii) external services including consulting services and lab supplies and services, and (iii) other expenses, including professional services, facilities and overhead allocations, and a reasonable estimate of compensation and related costs as billed to our counterparties, for which we recognize net revenue from collaborations. For the three and nine months ended September 30, 2021 and 2020, we did not incur material selling, general and administrative expenses related to our collaboration agreements.

In addition, we recognized a reduction to our research and development expenses of \$3.3 million and \$12.7 million for the three and nine months ended September 30, 2021, respectively, and of \$3.2 million and \$8.4 million for the three and nine months ended September 30, 2020, respectively, from cost reimbursement due under certain of our collaboration agreements accounted for under ASC 808.

**Product Alliances**

*Regeneron Pharmaceuticals, Inc.*

In April 2019, we entered into a global, strategic collaboration with Regeneron Pharmaceuticals, Inc., or Regeneron, to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic targets expressed in the eye and central nervous system, or CNS, in addition to a select number of targets expressed in the liver, which we refer to as the Regeneron Collaboration. The Regeneron Collaboration is governed by a Master Agreement, referred to as the Regeneron Master Agreement, which became effective on May 21, 2019. In connection with the Regeneron Master Agreement, we and Regeneron entered into (i) a binding co-co collaboration term sheet covering the continued development of cemdisiran, our C5 small interfering RNA, or siRNA, currently in Phase 2 development for C5 complement-mediated diseases, as a monotherapy and (ii) a binding license term sheet to evaluate anti-C5 antibody-siRNA combinations for C5 complement-mediated diseases including evaluating the combination of Regeneron's pozelimab (REGN3918), currently in Phase 2 development, and cemdisiran. The C5 co-co collaboration and license agreements were executed in August 2019.

Under the terms of the Regeneron Collaboration, we are working exclusively with Regeneron to discover RNAi therapeutics for eye and CNS diseases for an initial five-year research period, which we refer to as the Initial Research Term. Regeneron has an option to extend the Initial Research Term (referred to as the Research Term Extension Period, and together with the Initial Research Term, the Research Term) for up to an additional five years, for a research term extension fee of up to \$400.0 million. The Regeneron Collaboration also covers a select number of RNAi therapeutic programs designed to target genes expressed in the liver, including our previously announced collaboration with Regeneron to identify RNAi therapeutics for the chronic liver disease nonalcoholic steatohepatitis. We retain broad global rights to all of our other unpartnered liver-directed clinical and pre-clinical pipeline programs. The Regeneron Collaboration is governed by a joint steering committee that is comprised of an equal number of representatives from each party.

Regeneron will lead development and commercialization for all programs targeting eye diseases (subject to limited exceptions), entitling us to certain potential milestone and royalty payments pursuant to the terms of a license agreement, the form of which has been agreed upon by the parties. We and Regeneron will alternate leadership on CNS and liver programs covered by the Regeneron Collaboration, with the lead party retaining global development and commercial responsibility. For such CNS and liver programs, both we and Regeneron will have the option at lead candidate selection to enter into a co-co collaboration agreement, the form of which has been agreed upon by the parties, whereby both companies will share equally all costs of, and profits from, all development and commercialization activities under the program. If the non-lead party elects to not enter into a co-co collaboration agreement with respect to a given CNS or liver program, we and Regeneron will enter into a license agreement with respect to such program and the lead party will be the "Licensee" for the purposes of the license agreement. If the lead party for a CNS or liver program elects to not enter into the co-co collaboration agreement, then we and Regeneron will enter into a license agreement with respect to such program and leadership of the program will transfer to the other party and the former non-lead party will be the "Licensee" for the purposes of the license agreement.

With respect to the programs directed to C5 complement-mediated diseases, we retain control of cemdisiran monotherapy development, and Regeneron is leading combination product development. Under the C5 co-co collaboration agreement, we and Regeneron equally share costs and potential future profits on any monotherapy program. Under the C5 license agreement, for cemdisiran to be used as part of a combination product, Regeneron is solely responsible for all development and commercialization costs and we will receive low double-digit royalties and commercial milestones of up to \$325.0 million on any potential combination product sales. The C5 co-co collaboration agreement, the C5 license agreement, and the Master Agreement have been combined for accounting purposes and treated as a single agreement.

In connection with the Regeneron Master Agreement, Regeneron made an upfront payment of \$400.0 million. We are also eligible to receive up to an additional \$200.0 million in milestone payments upon achievement of certain criteria during early clinical development for eye and CNS programs. We and Regeneron plan to advance programs directed to up to 30 targets under the Regeneron Collaboration during the Initial Research Term. For each program, Regeneron will provide us with \$2.5



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million in funding at program initiation and an additional \$2.5 million at lead candidate identification, with the potential for approximately \$30.0 million in annual discovery funding to us as the Regeneron Collaboration reaches steady state.

Regeneron has the right to terminate the Regeneron Master Agreement for convenience upon ninety days' notice. The termination of the Regeneron Master Agreement does not affect the term of any license agreement or co-co collaboration agreement then in effect. In addition, either party may terminate the Regeneron Master Agreement for a material breach by, or insolvency of, the other party. Unless earlier terminated pursuant to its terms, the Regeneron Master Agreement will remain in effect with respect to each program until (a) such program becomes a terminated program or (b) the parties enter into a license agreement or co-co collaboration agreement with respect to such program. The Regeneron Master Agreement includes various representations, warranties, covenants, dispute escalation and resolution mechanisms, indemnities and other provisions customary for transactions of this nature.

For any license agreement subsequently entered into, the licensee will generally be responsible for its own costs and expenses incurred in connection with the development and commercialization of the collaboration products. The licensee will pay to the licensor certain development and/or commercialization milestone payments totaling up to \$150.0 million for each collaboration product. In addition, following the first commercial sale of the applicable collaboration product under a license agreement, the licensee is required to make certain tiered royalty payments, ranging from low double-digits up to 20%, to the licensor based on the aggregate annual net sales of the collaboration product, subject to customary reductions.

For any co-co collaboration agreement subsequently entered into, we and Regeneron will share equally all costs of, and profits from, development and commercialization activities. Reimbursement of our share of costs will be recognized as a reduction to research and development expense in the condensed consolidated statements of operations and comprehensive loss. In the event that a party exercises its opt-out right, the lead party will be responsible for all costs and expenses incurred in connection with the development and commercialization of the collaboration products under the applicable co-co collaboration agreement, subject to continued sharing of costs through defined points. If a party exercises its opt-out right, following the first commercial sale of the applicable collaboration product under a co-co collaboration agreement, the lead party is required to make certain tiered royalty payments, ranging from low double-digits up to 20%, to the other party based on the aggregate annual net sales of the collaboration product and the timing of the exercise of the opt-out right, subject to customary reductions and a reduction for opt-out transition costs.

Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Regeneron under the Regeneron Master Agreement, the C5 license agreement, or any future license agreement, or under any co-co collaboration agreement in the event we exercise our opt-out right.

Our obligations under the Regeneron Collaboration include: (i) a research license and research services, collectively referred to as the Research Services Obligation; (ii) a worldwide license to cemdisiran for combination therapies, and manufacturing and supply, and development service obligations, collectively referred to as the C5 License Obligation; and (iii) development, manufacturing and commercialization activities for cemdisiran monotherapies, referred to as the C5 Co-Co Obligation.

The research license is not distinct from the research services primarily as a result of Regeneron being unable to benefit on its own or with other resources reasonably available, as the license is providing access to specialized expertise, particularly as it relates to RNAi technology that is not available in the marketplace. Similarly, the worldwide license to cemdisiran for combination therapies is not distinct from the manufacturing and supply, and development service obligations, as Regeneron cannot benefit on its own from the value of the license without receipt of supply.

Separately, the cemdisiran monotherapy co-co collaboration agreement is under the scope of ASC 808 as we and Regeneron are both active participants in the development and manufacturing activities and are exposed to significant risks and rewards that are dependent on commercial success of the activities of the arrangement. The development and manufacturing activities are a combined unit of account under the scope of ASC 808 and are not deliverables under ASC 606.

The total transaction price is comprised of the \$400.0 million upfront payment and additional variable consideration related to research, development, manufacturing and supply activities related to the Research Services Obligation and the C5 License Obligation. We utilized the expected value method to determine the amount of reimbursement for these activities. We determined that any variable consideration related to sales-based royalties and milestones related to the worldwide license to cemdisiran for combination therapies is deemed to be constrained and therefore has been excluded from the transaction price. In addition, we are eligible to receive future milestones upon the achievement of certain criteria during early clinical development for the eye and CNS programs. We are also eligible to receive royalties on future commercial sales for certain eye, CNS or liver targets, if any; however, these amounts are excluded from variable consideration under the Regeneron Collaboration as we are only eligible to receive such amounts if, after a drug candidate is identified, the form of license agreement is subsequently

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executed resulting in a license that is granted to Regeneron. Any such subsequently granted license would represent a separate transaction under ASC 606.

We allocated the initial transaction price to each unit of account based on the applicable accounting guidance as follows, in thousands:

Performance Obligations	Standalone Selling Price	Transaction Price Allocated	Accounting Guidance
Research Services Obligation	\$ 130,700	\$ 183,100	ASC 606
C5 License Obligation	97,600	92,500	ASC 606
C5 Co-Co Obligation	364,600	246,000	ASC 808
		<u>\$ 521,600</u>	

The transaction price was allocated to the obligations based on the relative estimated standalone selling prices of each obligation, over which management has applied significant judgment. We developed the estimated standalone selling price for the licenses included in the Research Services Obligation and the C5 License Obligation primarily based on the probability-weighted present value of expected future cash flows associated with each license related to each specific program. In developing such estimate, we applied judgment in the determination of the forecasted revenues, taking into consideration the applicable market conditions and relevant entity-specific factors, the expected number of targets or indications expected to be pursued under each license, the probability of success, the time needed to develop a product candidate pursuant to the associated license and the discount rate. We developed the estimated standalone selling price for the services and/or manufacturing and supply included in each of the obligations, as applicable, primarily based on the nature of the services to be performed and/or goods to be manufactured and estimates of the associated costs. The estimated standalone selling price of the C5 Co-Co Obligation was developed by estimating the present value of expected future cash flows that Regeneron is entitled to receive. In developing such estimate, we applied judgment in determining the indications that will be pursued, the forecasted revenues for such indications, the probability of success and the discount rate.

For the Research Services Obligation and the C5 License Obligation accounted for under ASC 606, we measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for each of the identified obligations, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the transaction price allocated to each obligation. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch up. We re-evaluate the transaction price as of the end of each reporting period and as of September 30, 2021, the total transaction price was \$539.7 million, an increase of \$7.9 million from December 31, 2020. As of September 30, 2021, the transaction price is comprised of the upfront payment and variable consideration related to development, manufacture and supply activities. For the C5 Co-Co Obligation accounted for under ASC 808, the transaction price allocated to this obligation is recognized using a proportional performance method. Revenue recognized under this agreement, inclusive of the amount allocated to the C5 Co-Co Obligation, is accounted for as collaboration revenue.

The following tables provide a summary of the transaction price allocated to each unit of account based on the applicable accounting guidance, in addition to revenue activity during the period, in thousands:

Performance Obligations	Transaction Price Allocated	Deferred Revenue			Accounting Guidance
	As of September 30, 2021	As of September 30, 2021	As of December 31, 2020		
Research Services Obligation	\$ 200,700	\$ 41,000	\$ 54,900		ASC 606
C5 License Obligation	93,000	28,300	58,700		ASC 606
C5 Co-Co Obligation	246,000	215,000	231,400		ASC 808
	<u>\$ 539,700</u>	<u>\$ 284,300</u>	<u>\$ 345,000</u>		

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Performance Obligations	Revenue Recognized During				Accounting Guidance
	Three Months Ended September 30, 2021	Three Months Ended September 30, 2020	Nine Months Ended September 30, 2021	Nine Months Ended September 30, 2020	
Research Services Obligation	\$ 8,900	\$ 10,700	\$ 28,900	\$ 33,300	ASC 606
C5 License Obligation	1,200	—	30,400	—	ASC 606
C5 Co-Co Obligation	2,500	2,400	16,400	9,500	ASC 808
	<u>\$ 12,600</u>	<u>\$ 13,100</u>	<u>\$ 75,700</u>	<u>\$ 42,800</u>	

As of September 30, 2021, the aggregate amount of the transaction price allocated to the remaining Research Services Obligation and C5 License Obligation that was unsatisfied was \$161.5 million, which is expected to be recognized through the term of the Regeneron Collaboration as the services are performed. This amount excludes the transaction price allocated to the C5 Co-Co Obligation accounted for under ASC 808. Deferred revenue related to the Regeneron Collaboration is classified as either current or non-current in the condensed consolidated balance sheets based on the period the revenue is expected to be recognized.

*Novartis AG*

In February 2013, we and The Medicines Company, or MDCO, entered into a license and collaboration agreement pursuant to which we granted to MDCO an exclusive, worldwide license to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9, or PCSK9, for the treatment of hypercholesterolemia and other human diseases, including inclisiran. We refer to this agreement, as amended through the date hereof, as the MDCO License Agreement. On January 6, 2020, Novartis completed its acquisition of MDCO, and assumed all rights and obligations under the MDCO License Agreement.

As of September 30, 2021, we have earned \$45.0 million of milestones and upon achievement of certain events, we will be entitled to receive additional milestones, up to an aggregate of \$135.0 million, including \$25.0 million associated with the U.S. regulatory approval milestone, \$10.0 million in other specified regulatory milestones and \$100.0 million in specified commercialization milestones. In addition, we are entitled to royalties ranging from 10% up to 20% based on annual worldwide net sales of licensed products by Novartis, its affiliates and sublicensees, subject to reduction under specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments under the MDCO License Agreement.

Unless terminated earlier in accordance with the terms of the agreement, the MDCO License Agreement expires on a licensed product-by-licensed product and country-by-country basis upon expiration of the last royalty term for any licensed product in any country, where a royalty term is defined as the latest to occur of (1) the expiration of the last valid claim of patent rights covering a licensed product, (2) the expiration of the Regulatory Exclusivity, as defined in the MDCO License Agreement, and (3) the twelfth anniversary of the first commercial sale of the licensed product in such country. We estimate that our fundamental RNAi patents covering licensed products under the MDCO License Agreement will expire both in and outside of the U.S. generally by 2028. We also estimate that our inclisiran product-specific patents covering licensed products under the MDCO License Agreement will expire in the U.S., Europe, China, Japan and elsewhere between 2033 and 2036. Certain of these patent rights are subject to potential patent term extensions and/or supplemental protection certificates extending such terms in countries where such extensions may become available due to regulatory delay. In addition, more patent filings relating to the collaboration may be made in the future.

Either party may terminate the MDCO License Agreement in the event the other party fails to cure a material breach or upon patent-related challenges by the other party. In addition, Novartis has the right to terminate the agreement without cause at any time upon four months' prior written notice.

During the term of the MDCO License Agreement, neither party will, alone or with an affiliate or third party, research, develop or commercialize, or grant a license to any third party to research, develop or commercialize, in any country, any siRNA product directed to the PCSK9 gene, other than a licensed product, without the prior written agreement of the other party, subject to the terms of the MDCO License Agreement.

We evaluated the MDCO License Agreement and concluded that Novartis meets the definition of a customer and that the MDCO License Agreement is a contract. During 2018, we completed the performance obligations identified in the MDCO License Agreement. However, we continue to receive additional orders for supply of certain material. Given Novartis now has the ability to manufacture on its own through its own vendors, such orders will be treated as separate agreements and any associated revenue will be recognized upon transfer of control.

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*Vir Biotechnology, Inc.*

In October 2017, we and Vir Biotechnology, Inc., or Vir, entered into a collaboration and license agreement, or the Vir Agreement, for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic hepatitis B virus, or HBV, infection.

Pursuant to the Vir Agreement, we granted to Vir an exclusive license to develop, manufacture and commercialize ALN-HBV02 (VIR-2218), for all uses and purposes other than certain excluded fields, as set forth in the Vir Agreement. In addition, we granted Vir an exclusive option for up to four additional RNAi therapeutic programs for the treatment of infectious diseases. Under the terms of the Vir Agreement, for each product arising from the HBV program, including ALN-HBV02, we retained the right to opt into a profit-sharing arrangement prior to the start of a Phase 3 clinical trial. In addition, we have the right on a product-by-product basis with respect to each additional infectious disease program that Vir elects to pursue, to opt into a profit-sharing arrangement for each such product at any time during a specified period prior to the initiation of a Phase 3 clinical trial for each such product.

Pursuant to the Vir Agreement, Vir paid us an upfront fee of \$10.0 million and issued to us 1,111,111 shares of its common stock. Under the Vir Agreement, we may also receive milestone payments upon the achievement of certain development, regulatory and commercial milestones, as well as royalties on the net sales of licensed products ranging from high-single-digit to sub-teen double-digit percentages. In March 2020, we achieved a development milestone relating to ALN-HBV02 and earned a \$15.0 million cash milestone and 1,111,111 shares of Vir's common stock, which were received in the second quarter of 2020. In June 2020, we earned and received a \$10.0 million payment from Vir related to Vir's sublicense for ALN-HBV02 in China. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or any royalty payments under the Vir Agreement.

In March and April 2020, we entered into amendments to the Vir Agreement to expand our collaboration to include the development and commercialization of RNAi therapeutics targeting SARS-CoV-2, the virus that causes the disease COVID-19, along with three additional targets focused on human host factors for SARS-CoV-2, including angiotensin converting enzyme-2 and transmembrane protease, serine 2 and potentially a third mutually selected host factor target.

In December 2020, we signed a letter agreement to amend the Vir Agreement such that we would be solely responsible for conducting pre-clinical research activities under the pre-clinical development plan related to the COVID-19 activities in the March and April 2020 amendments, at our discretion and sole expense, and effective as of July 1, 2020, we were responsible for all pre-clinical development costs incurred under such plan for such COVID-19 related activities. In July 2021, we notified Vir that we have elected to discontinue ALN-COV, in development for the treatment of COVID-19, and all other COVID-19 research and development activities, based on a portfolio prioritization decision in view of the availability of highly effective vaccines and alternative treatment options, in accordance with our rights under the letter agreement with Vir. Following such discontinuation of COVID-19 related activities, we have no further obligations to work on the COVID-related targets and Vir will have no further rights to such targets under the Vir Agreement.

Unless terminated earlier in accordance with the terms of the agreement, the Vir Agreement expires on a licensed product-by-product and country-by-country basis upon expiration of all royalty payment obligations under the agreement. If Vir does not exercise its option for an infectious disease program, the Vir Agreement will expire upon the expiration of the applicable option period with respect to such program. However, if we exercise our profit-sharing option for any product, the term of the agreement will continue until the expiration of the profit-sharing arrangement for such product.

Either party may terminate the agreement in the event the other party fails to cure a material breach, or upon patent-related challenges by the other party. In addition, Vir has the right to terminate the agreement on a program-by-program basis or in its entirety for any reason on 90 days' written notice.

We identified one performance obligation under the Vir Agreement, as amended, comprised of: i) the exclusive license to develop, manufacture and commercialize RNAi therapeutics (including ALN-HBV02); ii) the obligation to deliver four additional development candidates and supply product for each such RNAi therapeutic program; and iii) the obligation to deliver up to four development candidates and supply product for RNAi therapeutic programs targeting SARS-CoV-2. The license is not distinct from the services, including the obligation to deliver development candidates and supply product, as Vir cannot benefit on its own from the value of the license without receipt of such services and supply.

We measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for the identified performance obligation, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the total transaction price. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch up. As of September 30, 2021, the total transaction price was determined to be \$110.8 million, and is comprised of the upfront payment, fair value of non-cash equity consideration at contract inception, milestones achieved and variable consideration related to development, manufacture and supply activities. We utilized the

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expected value method to determine the amount of reimbursement for these activities. The total transaction price is allocated entirely to the single performance obligation. We determined any variable consideration related to sales-based royalties and milestones related to the exclusive license to be constrained and therefore excluded such consideration from the transaction price.

As of September 30, 2021, the aggregate amount of the transaction price allocated to the performance obligation that was unsatisfied was \$44.4 million, which is expected to be recognized through the term of the Vir Agreement as the services are performed.

***Other Strategic License Agreements***

*PeptiDream, Inc.*

In July 2021, we entered into a license and collaboration agreement with PeptiDream, Inc., or PeptiDream, to discover and develop peptide-siRNA conjugates to create multiple opportunities to deliver RNAi therapeutics to tissues outside the liver. Through this collaboration, the companies will collaborate to select and optimize peptides for targeted delivery of small siRNA molecules to a wide range of cell types and tissues via specific interactions with receptors expressed on the target cells. Under the terms of the agreement, PeptiDream received an upfront payment from us of \$10.0 million and we will provide research and development funding over the term of the research collaboration, according to the terms of the PeptiDream agreement. Due to the early stage of these assets, we recorded research and development expense for the upfront payment of \$10.0 million during the third quarter of 2021. PeptiDream may also receive payments based on the achievement of specified development, regulatory, and commercial milestones potentially totaling up to \$247.0 million for each product developed by us that utilizes PeptiDream's technology, as well as low-to-mid single digit royalties on sales, if any, of any such products.

**5. LIABILITY RELATED TO THE SALE OF FUTURE ROYALTIES**

In April 2020, we entered into a purchase and sale agreement, or Purchase Agreement, with BX Bodyguard Royalties L.P. (an affiliate of The Blackstone Group Inc.), or Blackstone Royalties, under which Blackstone Royalties acquired 50% of royalties payable, or Royalty Interest, with respect to net sales by MDCO, its affiliates or sublicensees of inclisiran and any other licensed products under the MDCO License Agreement, and 75% of the commercial milestone payments payable under the MDCO License Agreement, together with the Royalty Interest, the Purchased Interest. If Blackstone Royalties does not receive payments in respect of the Royalty Interest by December 31, 2029, equaling at least \$1.00 billion, Blackstone Royalties will receive 55% of the Royalty Interest beginning on January 1, 2030. In consideration for the sale of the Purchased Interest, Blackstone Royalties paid us \$500.0 million in April 2020 and \$500.0 million in September 2021.

We continue to own or control all inclisiran intellectual property rights and are responsible for certain ongoing manufacturing and supply obligations related to the generation of the Purchased Interest. Due to our continuing involvement, we will continue to account for any royalties and commercial milestones due to us under the MDCO License Agreement as revenue on our condensed consolidated statement of operations and comprehensive loss and record the proceeds from this transaction as a liability, net of closing costs, on our condensed consolidated balance sheet.

In order to determine the amortization of the liability related to the sale of future royalties, we are required to estimate the total amount of future payments to Blackstone Royalties over the life of the Purchase Agreement. The \$1.00 billion liability, recorded at execution of the agreement, will be accreted to the total of these royalty and commercial milestone payments as interest expense over the life of the Purchase Agreement. At execution, our estimate of this total interest expense resulted in an effective annual interest rate of 11%. This estimate contains assumptions that impact both the amount recorded at execution and the interest expense that will be recognized in future periods.

As payments are made to Blackstone Royalties, the balance of the liability will be effectively repaid over the life of the Purchase Agreement. The exact timing and amount of repayment is likely to change each reporting period. A significant increase or decrease in net sales of inclisiran will materially impact the liability related to the sale of future royalties, interest expense and the time period for repayment. We will periodically assess the expected payments to Blackstone Royalties and to the extent the amount or timing of such payments is materially different than our initial estimates, we will prospectively adjust the amortization of the liability related to the sale of future royalties and the related interest expense.

As of September 30, 2021, the carrying value of the liability related to the sale of future royalties was \$1.16 billion, net of closing costs of \$12.0 million. The carrying value of the liability related to the sale of future royalties approximates fair value as of September 30, 2021 and is based on our current estimates of future royalties and commercial milestones expected to be paid to Blackstone Royalties over the life of the arrangement, which are considered Level 3 inputs.

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The following table shows the activity with respect to the liability related to the sale of future royalties, in thousands:

Carrying value of liability related to sale of future royalties as of December 31, 2020	\$ 1,071,541
Interest expense recognized	87,349
Payments	(152)
Carrying value of liability related to sale of future royalties as of September 30, 2021	<u>\$ 1,158,738</u>

## 6. FAIR VALUE MEASUREMENTS

The following tables present information about our financial assets and liabilities that are measured at fair value on a recurring basis and indicate the fair value hierarchy of the valuation techniques we utilized to determine such fair value:

(In thousands)	As of September 30, 2021	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Financial assets</b>				
Cash equivalents:				
Money market funds	\$ 341,315	\$ 341,315	\$ —	\$ —
U.S. treasury securities	10,000	—	10,000	—
Marketable debt securities:				
U.S. treasury securities	769,224	—	769,224	—
Corporate notes	167,888	—	167,888	—
U.S. government-sponsored enterprise securities	128,161	—	128,161	—
Commercial paper	87,523	—	87,523	—
Certificates of deposit	7,502	—	7,502	—
Municipal securities	1,026	—	1,026	—
Marketable equity securities	72,550	72,550	—	—
Restricted cash (money market funds)	1,483	1,483	—	—
Total financial assets	<u>\$ 1,586,672</u>	<u>\$ 415,348</u>	<u>\$ 1,171,324</u>	<u>\$ —</u>
<b>Financial liabilities</b>				
Development derivative liability	<u>\$ 61,340</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 61,340</u>
(In thousands)	As of December 31, 2020	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Financial assets</b>				
Cash equivalents:				
Money market funds	\$ 75,726	\$ 75,726	\$ —	\$ —
U.S. treasury securities	20,000	—	20,000	—
Marketable debt securities:				
U.S. treasury securities	1,087,968	—	1,087,968	—
U.S. government-sponsored enterprise securities	245,214	—	245,214	—
Marketable equity securities	44,633	44,633	—	—
Restricted cash (money market funds)	1,483	1,483	—	—
Total financial assets	<u>\$ 1,475,024</u>	<u>\$ 121,842</u>	<u>\$ 1,353,182</u>	<u>\$ —</u>
<b>Financial liabilities</b>				
Development derivative liability	<u>\$ 25,585</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 25,585</u>

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The carrying amounts reflected on our condensed consolidated balance sheets for cash, accounts receivable, net, other current assets, accounts payable and accrued expenses approximate fair value due to their short-term maturities. The carrying amount of our debt as of September 30, 2021 approximates fair value.

## 7. MARKETABLE DEBT SECURITIES

We invest our excess cash balances in marketable debt securities and at each balance sheet date presented, we classify all of our investments in debt securities as available-for-sale and as current assets as they represent the investment of funds available for current operations. We did not record any impairment charges related to our marketable debt securities during the three and nine months ended September 30, 2021 or 2020.

The following tables summarize our marketable debt securities:

(In thousands)	As of September 30, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	\$ 779,163	\$ 96	\$ (35)	\$ 779,224
Corporate notes	167,938	20	(70)	167,888
U.S. government-sponsored enterprise securities	128,136	30	(5)	128,161
Commercial paper	87,523	—	—	87,523
Certificates of deposit	7,502	—	—	7,502
Municipal securities	1,026	—	—	1,026
Total	<u>\$ 1,171,288</u>	<u>\$ 146</u>	<u>\$ (110)</u>	<u>\$ 1,171,324</u>

(In thousands)	As of December 31, 2020			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	\$ 1,107,721	\$ 328	\$ (81)	\$ 1,107,968
U.S. government-sponsored enterprise securities	245,113	135	(34)	245,214
Total	<u>\$ 1,352,834</u>	<u>\$ 463</u>	<u>\$ (115)</u>	<u>\$ 1,353,182</u>

The fair values of our marketable debt securities by classification in the condensed consolidated balance sheets were as follows:

(In thousands)	As of September 30, 2021	As of December 31, 2020
Marketable debt securities	\$ 1,161,324	\$ 1,333,182
Cash and cash equivalents	10,000	20,000
Total	<u>\$ 1,171,324</u>	<u>\$ 1,353,182</u>



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## 8. OTHER BALANCE SHEET DETAILS

### *Inventory*

The components of inventory are summarized as follows:

(In thousands)	As of September 30, 2021	As of December 31, 2020
Raw materials	\$ 65,158	\$ 63,460
Work in progress	33,124	16,149
Finished goods	12,667	12,693
Total	<u>\$ 110,949</u>	<u>\$ 92,302</u>

As of September 30, 2021 and December 31, 2020, we held \$13.1 million and \$17.1 million of long-term inventory, respectively, included within other assets in our condensed consolidated balance sheet as we anticipate it being consumed beyond our normal operating cycle. As of September 30, 2021, we hold \$7.1 million of capitalized inventory produced for commercial sale for products awaiting regulatory approval. As of December 31, 2020, there was no capitalized inventory for products awaiting regulatory approval.

### *Cash, Cash Equivalents and Restricted Cash*

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

(In thousands)	As of September 30,	
	2021	2020
Cash and cash equivalents	\$ 1,093,991	\$ 496,704
Total restricted cash included in other assets	2,467	2,452
Total cash, cash equivalents, and restricted cash shown in the condensed consolidated statements of cash flows	\$ 1,096,458	\$ 499,156

### *Accumulated Other Comprehensive (Loss) Income*

The following tables summarize the changes in accumulated other comprehensive loss, by component:

(In thousands)	Loss on Investment in Joint Venture	Defined Benefit Pension Plans	Unrealized Gains (Losses) from Debt Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Loss
Balance as of December 31, 2020	\$ (32,792)	\$ (3,754)	\$ 348	\$ (7,424)	\$ (43,622)
Other comprehensive income before reclassifications	—	—	(219)	9,530	9,311
Amounts reclassified from other comprehensive income	—	174	(93)	—	81
Net other comprehensive income (loss)	—	174	(312)	9,530	9,392
Balance as of September 30, 2021	<u>\$ (32,792)</u>	<u>\$ (3,580)</u>	<u>\$ 36</u>	<u>\$ 2,106</u>	<u>\$ (34,230)</u>



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(In thousands)	Loss on Investment in Joint Venture	Defined Benefit Pension Plans	Unrealized Gains from Debt Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Loss
Balance as of December 31, 2019	\$ (32,792)	\$ (3,520)	\$ 137	\$ (343)	\$ (36,518)
Other comprehensive income before reclassifications	—	—	7	(1,665)	(1,658)
Amounts reclassified from other comprehensive income	—	222	761	—	983
Net other comprehensive income	—	222	768	(1,665)	(675)
Balance as of September 30, 2020	\$ (32,792)	\$ (3,298)	\$ 905	\$ (2,008)	\$ (37,193)

Amounts reclassified out of accumulated other comprehensive loss relate to settlements of marketable equity securities and amortization of our pension obligation which are recorded as interest income and other income, respectively, in the condensed consolidated statements of operations and comprehensive loss.

## 9. CREDIT AGREEMENT

In April 2020, we entered into a credit agreement, or Credit Agreement, among us, certain of our subsidiaries (such subsidiaries, together with us, the Loan Parties), funds or accounts managed or advised by GSO Capital Partners LP (now Blackstone Alternative Credit Advisors LP) and certain other affiliates of The Blackstone Group Inc., and the other lenders from time to time parties thereto, collectively, the Lenders, and Wilmington Trust, National Association, as the administrative agent for the Lenders. The Credit Agreement provides for a senior secured delayed draw term loan facility, referred to as the Term Loans, which consists of three tranches providing funding up to \$700.0 million. The Tranche 1 Loan of \$200.0 million and the Tranche 2 Loan of \$250.0 million were drawn as of December 31, 2020 and June 30, 2021, respectively, and are included in long-term debt in the condensed consolidated balance sheets as of September 30, 2021. The remaining tranche, the Tranche 3 Loan of \$250.0 million, will be requested no later than December 31, 2021. In addition, we may request an increase in respect of the unfunded commitments in an amount not to exceed \$50.0 million on terms to be agreed and subject to the consent of the Lenders providing such increase.

The Tranche 3 Loan is subject to customary terms and conditions, including either (a) the first sale of inclisiran in the U.S. for end use or consumption after FDA regulatory approval thereof or (b) revenue attributable to ONPATTRO and GIVLAARI equal to or greater than \$300.0 million as of the last day of the most recently ended twelve month period, referred to as the Subsequent Borrowing Conditions. The Subsequent Borrowing Conditions were satisfied as of September 30, 2021. The Term Loans mature in December 2027. We can elect an interest rate of either LIBOR plus 7% subject to a floor of 1%, referred to as the LIBOR Rate, or a base rate plus 6%, subject to a floor of 2%. We may, at our option, pay interest in kind on interest due through 2023 at a rate that is 1% higher than the interest rate otherwise applicable to such Term Loan. As of September 30, 2021, we drew the Tranche 1 Loan and the Tranche 2 Loan, elected a LIBOR Rate plus 7%, and paid a \$5.0 million and \$6.3 million funding fee, respectively, in connection with such Term Loans. On the date the Tranche 3 Loan is funded, we will pay a funding fee equal to 2.5% of the principal amount of the Term Loans funded on such date. In addition, we will pay an exit fee equal to 1% of the commitments in respect of the Term Loans, payable upon any repayment of the Term Loans or termination of the unfunded Term Loan commitments. Our interest rate was 8% as of September 30, 2021 and December 31, 2020.

We are obligated to pay interest due on the Term Loans from 2021 through 2022 which will be calculated without regard to the Term Loans being prepaid or an unfunded tranche being terminated during this period (in whole or in part). Any prepayments of Term Loans or terminations of unfunded tranches that occur between 2023 and 2025 are subject to a fee of up to 5% of the loan principal that is prepaid or the amount of the unfunded tranche that is terminated.

All obligations under the Credit Agreement are secured, subject to certain exceptions, by security interests in the following assets: (i) intellectual property owned by us relating to ONPATTRO, GIVLAARI, and vutrisiran, (ii) the equity interests held by the Loan Parties in their subsidiaries, (iii) all of our ownership of the inclisiran royalty remaining after the royalty purchase under the Purchase Agreement, and (iv) material real property, and certain personal property, including, without limitation, cash held in certain deposit accounts of the Loan Parties and equipment.

The Credit Agreement contains negative covenants that, among other things and subject to certain exceptions, could restrict our ability to, incur additional liens, incur additional indebtedness, make investments, including acquisitions, engage in fundamental changes, sell or dispose of assets that constitute collateral, including certain intellectual property, pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests, amend, modify or waive certain material

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agreements or organizational documents and make payments of certain subordinated indebtedness. Additionally, the Credit Agreement contains certain customary representations and warranties, affirmative covenants and provisions relating to events of default, including nonpayment of principal, interest and other amounts; failure to comply with covenants; the rendering of judgments or orders of default by us in respect of other material indebtedness; and certain insolvency and ERISA events. The Credit Agreement also requires us to have consolidated liquidity of at least \$100.0 million as of the last day of each fiscal quarter. As of September 30, 2021, we were in compliance with the applicable terms and conditions of the covenants under the Credit Agreement.

#### **10. DEVELOPMENT DERIVATIVE LIABILITY**

In August 2020, we entered into a co-development agreement, referred to as the Funding Agreement, with BXLS V Bodyguard – PCP L.P. and BXLS Family Investment Partnership V – ESC L.P., collectively referred to as Blackstone Life Sciences, pursuant to which Blackstone Life Sciences will provide up to \$150.0 million in funding for the clinical development of vutrisiran and zilebesiran (formerly ALN-AGT), two of our cardiometabolic programs. With respect to vutrisiran, Blackstone Life Sciences has committed to provide up to \$70.0 million to fund development costs related to the HELIOS-B Phase 3 clinical trial. In addition, Blackstone Life Sciences has the right, but is not obligated, to fund up to \$26.0 million for development costs related to a Phase 2 clinical trial of zilebesiran and up to \$54.0 million for development costs related to a Phase 3 clinical trial of zilebesiran. The amount of funding ultimately provided by Blackstone Life Sciences is dependent on us achieving specified development milestones with respect to each clinical trial. We retain sole responsibility for the development and commercialization of both vutrisiran and zilebesiran.

As consideration for Blackstone Life Sciences' funding for vutrisiran clinical development costs, we have agreed to pay Blackstone Life Sciences a 1% royalty on net sales of vutrisiran for a 10-year term beginning upon the first commercial sale following regulatory approval of vutrisiran for ATTR-cardiomyopathy, as well as fixed payments of up to 2.5 times their investment over a two-year period upon regulatory approval of vutrisiran for ATTR-cardiomyopathy in specified countries, unless it is later withdrawn from the market following a mandatory recall. As consideration for Blackstone Life Sciences' funding for Phase 2 clinical development costs of zilebesiran, we have agreed to pay Blackstone Life Sciences fixed payments of up to 3.25 times their Phase 2 investment over a four-year period upon the successful completion of the zilebesiran Phase 2 clinical trial, unless certain regulatory events affecting the continued development of zilebesiran occur. As consideration for Blackstone Life Sciences' funding for Phase 3 clinical development costs of zilebesiran, we have agreed to pay Blackstone Life Sciences fixed payments of up to 4.5 times their Phase 3 investment over a four-year period upon regulatory approval of zilebesiran in specified countries, unless it is later withdrawn from the market following a mandatory recall.

Our payment obligations under the Funding Agreement will be secured, subject to certain exceptions, by security interests in intellectual property owned by us relating to vutrisiran and zilebesiran, as well as in our bank account in which the funding deposits will be made.

We and Blackstone Life Sciences each have the right to terminate the Funding Agreement in its entirety in the event of the other party's bankruptcy or similar proceedings. We and Blackstone Life Sciences may each terminate the Funding Agreement in its entirety or with respect to either product in the event of an uncured material breach by the other party, or with respect to a product for certain patient health and safety reasons, or if regulatory approval in specified major market countries is not obtained for the product following the completion of clinical trials for the product. In addition, Blackstone Life Sciences has the right to terminate the Funding Agreement in its entirety upon the occurrence of certain events affecting our ability to make payments under the agreement or to develop or commercialize the products, or upon a change of control of us. Blackstone Life Sciences may also terminate the Funding Agreement with respect to a product if the joint steering committee elects to terminate the development program for that product in its entirety, if certain clinical endpoints are not achieved for that product or, with respect to vutrisiran only, if our right to develop or commercialize vutrisiran is enjoined in a specified major market as a result of an alleged patent infringement. In certain termination circumstances, we will be obligated to pay Blackstone Life Sciences an amount that is equal to, or a multiplier of, the development funding received from Blackstone Life Sciences, and we may remain obligated under certain circumstances to make the payments to Blackstone Life Sciences described above, or the royalty described above in the case of vutrisiran, should we obtain regulatory approval for vutrisiran or zilebesiran following termination.

We account for the Funding Agreement under ASC 815 as a derivative liability, measured at fair value, within other liabilities on our condensed consolidated balance sheets. The change in fair value due to the remeasurement of the development derivative liability is recorded as other expense on our condensed consolidated statements of operations and comprehensive loss.

As of September 30, 2021, the derivative liability is classified as a Level 3 financial liability in the fair value hierarchy. The valuation method incorporates certain unobservable Level 3 key inputs including (i) the probability and timing of achieving stated development milestones to receive payments from Blackstone Life Sciences, (ii) the probability and timing of achieving

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regulatory approval and payments to Blackstone Life Sciences, (iii) an estimate of the amount and timing of the royalty payable on net sales of vutrisiran, assuming regulatory approval, (iv) our cost of borrowing (15%), and (v) Blackstone Life Sciences' cost of borrowing (4%).

The following table presents the activity with respect to the development derivative liability, in thousands:

Development derivative liability as of December 31, 2020	\$ 25,585
Amount received under the Funding Agreement	16,100
Loss recorded from remeasurement of development derivative liability	19,655
Development derivative liability as of September 30, 2021	<u>\$ 61,340</u>

## 11. EQUITY

### *Blackstone Equity Placement*

In April 2020, we entered into a stock purchase agreement, or Investors SPA, with certain affiliates of The Blackstone Group Inc., or Investors, pursuant to which we sold 963,486 shares of our common stock to the Investors for aggregate cash consideration of \$100.0 million, or \$103.79 per share, as part of the broad strategic financing collaboration with The Blackstone Group Inc. The Investors SPA contains customary representations, warranties, and covenants of each of the parties thereto.

## 12. STOCK-BASED COMPENSATION

The following table summarizes stock-based compensation expenses included in operating costs and expenses:

(In thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Research and development	\$ 12,417	\$ 13,703	\$ 49,878	\$ 45,542
Selling, general and administrative	20,950	23,561	71,257	60,055
Total	<u>\$ 33,367</u>	<u>\$ 37,264</u>	<u>\$ 121,135</u>	<u>\$ 105,597</u>

## 13. NET LOSS PER COMMON SHARE

We compute basic net loss per common share by dividing net loss by the weighted-average number of common shares outstanding during the period. We compute diluted net loss per common share by dividing net loss by the weighted-average number of common shares and dilutive potential common share equivalents outstanding during the period. Potential common shares consist of shares issuable upon the exercise of stock options (the proceeds of which are then assumed to have been used to repurchase outstanding shares using the treasury stock method). Because the inclusion of potential common shares would be anti-dilutive for all periods presented, diluted net loss per common share is the same as basic net loss per common share.

The following common share equivalents were excluded from the calculation of net loss per common share because their inclusion would be anti-dilutive:

(In thousands)	As of September 30,	
	2021	2020
Options to purchase common stock	11,715	11,856
Unvested restricted common stock	1,246	1,145
Total	<u>12,961</u>	<u>13,001</u>

## 14. COMMITMENTS AND CONTINGENCIES

### *Legal Matters*

From time to time, we may be a party to litigation, arbitration or other legal proceedings in the course of our business, including the matters described below. The claims and legal proceedings in which we could be involved include challenges to the scope, validity or enforceability of patents relating to our products or product candidates, and challenges by us to the scope,

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validity or enforceability of the patents held by others. These include claims by third parties that we infringe their patents or breach our license or other agreements with such third parties. The outcome of any such legal proceedings, regardless of the merits, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in other activities. If we were unable to prevail in any such legal proceedings, our business, results of operations, liquidity and financial condition could be adversely affected. Our accounting policy for accrual of legal costs is to recognize such expenses as incurred.

*Securities Litigation*

On September 12, 2019, the Chester County Employees Retirement Fund, individually and on behalf of all others similarly situated, filed a purported securities class action complaint for violation of federal securities laws against us, certain of our current and former directors and officers, and the underwriters of our November 14, 2017 public stock offering, in the Supreme Court of the State of New York, New York County. On November 7, 2019, plaintiff filed an amended complaint, or the New York Complaint. The New York Complaint is brought on behalf of an alleged class of those who purchased our securities pursuant and/or traceable to our November 14, 2017 public stock offering. The New York Complaint purports to allege claims arising under Sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended, and generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning the results of our APOLLO Phase 3 clinical trial of patisiran. The plaintiff seeks, among other things, the designation of the action as a class action, an award of unspecified compensatory damages, rescissory damages, interest, costs and expenses, including counsel fees and expert fees, and other relief as the court deems appropriate. All defendants filed a joint motion to dismiss the New York Complaint in its entirety on December 20, 2019. On November 2, 2020, the Supreme Court of the State of New York entered a Decision and Order denying defendants' motion to dismiss. In November 2020, defendants filed a notice of appeal of the Supreme Court's decision to the Appellate Division of the Supreme Court of the State of New York for the First Department. In April 2021, the First Department entered a Decision and Order affirming in part and reversing in part the Supreme Court's decision. In June 2021, defendants filed a motion in the First Department seeking reargument or, in the alternative, for leave to appeal to the New York Court of Appeals. In August 2021, the parties reached an agreement in principle to resolve the matter. Proceedings in the First Department are adjourned until February 2022 pending final approval of any settlement.

*Government Investigation*

We have previously disclosed that, on or about April 9, 2021, we received a subpoena from the U.S. Department of Justice, U.S. Attorney's Office for the District of Massachusetts, requiring production of documents pertaining to our marketing and promotion of ONPATTRO (patisiran) in the U.S. We are cooperating with the U.S. Attorney's Office and producing documents in response to the subpoena. Current and former officers and employees also have received subpoenas in connection with the preservation and production of related materials. Given the ongoing nature of the investigation, it is possible that the U.S. Attorney's Office for the District of Massachusetts or other government entities may request other information from, or issue other subpoenas, findings or similar documents to, us, our related entities and their respective directors, officers and employees. In light of the relatively early stage and ongoing nature of the investigation, no determination has been made that a loss, if any, arising from this matter is probable or that the amount of any such loss, or range of loss, is reasonably estimable. We also previously disclosed that since learning of this federal government investigation, our nominating and corporate governance committee is directing our review of and response to the matter.

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

### Overview

We are a global commercial-stage biopharmaceutical company developing novel therapeutics based on ribonucleic acid interference, or RNAi. RNAi is a naturally occurring biological pathway within cells for sequence-specific silencing and regulation of gene expression. By harnessing the RNAi pathway, we have developed a new class of innovative medicines, known as RNAi therapeutics. RNAi therapeutics are comprised of small interfering RNA, or siRNA, and function upstream of conventional medicines by potently silencing messenger RNA, or mRNA, that encode for disease-causing proteins, thus preventing them from being made. We believe this is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases. To date, our efforts to advance this revolutionary approach have yielded the approval of four first-in-class RNAi-based medicines, ONPATPRO® (patisiran), GIVLAARI® (givosiran), OXLUMO® (lumasiran) and Leqvio® (inclisiran).

Our research and development strategy is to target genetically validated genes that have been implicated in the cause or pathway of human disease. We utilize a N-acetylgalactosamine (GalNAc) conjugate or lipid nanoparticle (LNP) approach to enable hepatic delivery of siRNAs. For delivery to the central nervous system, or CNS, and the eye (ocular delivery), we are utilizing alternative conjugate approaches. We are also advancing approaches for delivery of siRNAs to lung and other tissue types. Our focus is on clinical indications where there is a high unmet need, early biomarkers for the assessment of clinical activity in Phase 1 clinical studies, and a definable path for drug development, regulatory approval, patient access and commercialization.

In early 2021, we launched our *Alnylam P<sup>5</sup>x25* strategy, which focuses on our planned transition to a top five biotech company, as measured by market capitalization, by the end of 2025. With *Alnylam P<sup>5</sup>x25*, we aim to deliver transformative rare and prevalent disease medicines for patients around the world through sustainable innovation, delivering exceptional financial performance and driving profitability. On October 28, 2021, we announced a leadership transition pursuant to which our current long-time Chief Executive Officer, John M. Maraganore, Ph.D., will depart on December 31, 2021, and Yvonne L. Greenstreet, MBChB, MBA, our current President and Chief Operating Officer, will transition to the role of Chief Executive Officer.

We currently have four marketed products and 12 clinical programs, including six in late-stage development, across four Strategic Therapeutic Areas, or "STArS:" Genetic Medicines; Cardio-Metabolic Diseases; Hepatic Infectious Diseases; and CNS/Ocular Diseases. Three of our marketed products are within the Genetic Medicines STAr, ONPATPRO, GIVLAARI and OXLUMO. ONPATPRO is approved in the United States, or U.S., by the United States Food and Drug Administration, or FDA, for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis, or hATTR amyloidosis, in adults and has also been approved in the European Union, or EU, for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, in Japan for the treatment of transthyretin, or TTR, type familial amyloidosis with polyneuropathy, and in several additional countries, including Brazil. Regulatory filings in other territories are pending and additional filings are planned for 2022 and beyond. GIVLAARI is approved in the U.S. by the FDA for the treatment of adults with acute hepatic porphyria, or AHP, in the EU for the treatment of AHP in adults and adolescents aged 12 years and older, and in several additional countries, including Brazil, Canada and Japan. We have also filed for regulatory approval for givosiran (the non-branded drug name for GIVLAARI) in Switzerland and additional regulatory filings are pending or planned for 2021 and beyond. In November 2020, we received regulatory approval for OXLUMO in the U.S. and EU for the treatment of primary hyperoxaluria type 1, or PH1, in all age groups. In June 2021, we received marketing authorization approval for OXLUMO in Brazil for the treatment of PH1 in both children and adult patients. Regulatory filings in other territories are pending and additional filings are planned for 2021 and beyond.

Our fourth product, Leqvio (inclisiran), is being developed and commercialized by our partner Novartis AG, or Novartis, and in December 2020 received marketing authorization from the European Commission, or EC, for the treatment of adults with hypercholesterolemia or mixed dyslipidemia and is in the Cardio-Metabolic Diseases STAr. With respect to regulatory review by the FDA of the New Drug Application, or NDA, filed with the FDA for inclisiran, the FDA issued a complete response letter in December 2020, due to unresolved facility inspection-related conditions at a third-party manufacturing facility in Europe. In July 2021, Novartis announced that the resubmission to the FDA for the inclisiran NDA to address the complete response letter was filed with an action date of January 1, 2022 under the Prescription Drug User Fee Act, or PDUFA. Novartis listed its own site in Schaffhausen, Austria, as the manufacturing location for the final finished product within its NDA resubmission. Novartis reported that the transfer of the manufacturing location for the final finished product to its Schaffhausen site was planned and initiated in 2020, prior to the receipt of the complete response letter.

In addition to our marketed products, we have six late-stage investigational programs, advancing toward potential commercialization. These programs include our wholly owned programs: givosiran (the non-branded name for GIVLAARI) for the treatment of adolescent patients with AHP; lumasiran for the treatment of PH1 and recurrent renal stones; patisiran (the non-branded drug name for ONPATPRO) for the treatment of transthyretin amyloidosis, or ATTR amyloidosis, with cardiomyopathy; and vutrisiran for the treatment of ATTR amyloidosis. In addition, inclisiran (the non-branded name for Leqvio) for the treatment of hypercholesterolemia and atherosclerotic cardiovascular disease, or ASCVD, is being advanced by

our partner Novartis, and fitusiran for the treatment of hemophilia, is being advanced by our partner Sanofi Genzyme, the specialty care global business unit of Sanofi.

In January 2021, we reported positive topline results from our HELIOS-A Phase 3 study of vutrisiran in patients with hATTR amyloidosis with polyneuropathy, and in April 2021, based on the positive HELIOS-A data, we submitted an NDA for vutrisiran, which was accepted by the FDA. The FDA has set an action date of April 14, 2022 under the PDUFA, and indicated that they were not currently planning an advisory committee meeting as part of the NDA review. In September 2021, we presented additional 9-month data from the HELIOS-A Phase 3 study of vutrisiran, and submitted a marketing authorisation application, or MAA, in the EU with the European Medicines Agency, or EMA. In October 2021, we reported positive topline results for 18-month endpoints and safety from the HELIOS-A Phase 3 study of vutrisiran.

Based on our expertise in RNAi therapeutics and broad intellectual property estate, we have formed alliances with leading pharmaceutical and life sciences companies to support our development and commercialization efforts, including Regeneron Pharmaceuticals, Inc., or Regeneron, Novartis (which acquired our partner The Medicines Company, or MDCO, in 2020), Sanofi Genzyme, Vir Biotechnology, Inc., or Vir, and Dicerna Pharmaceuticals, Inc., or Dicerna.

We have incurred significant losses since we commenced operations in 2002 and expect such losses to continue for the foreseeable future. As of September 30, 2021, we had an accumulated deficit of \$5.18 billion. Historically, we have generated losses principally from costs associated with the establishment of late-stage clinical and commercial capabilities, including global commercial operations, research and development activities, acquiring, filing and expanding intellectual property rights, and selling, general and administrative costs. While we believe 2019 was our peak net loss year, and believe the funding provided by our strategic financing collaboration with The Blackstone Group Inc., or Blackstone, should enable us to achieve a self-sustainable financial profile without the need for future equity financing, we expect to continue to incur annual net operating losses for the foreseeable future as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We also anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods.

We currently have programs focused on a number of therapeutic areas and as of September 30, 2021, we are generating net revenue from product sales for three marketed products, ONPATTRO, GIVLAARI and OXLUMO. However, our ongoing development efforts may not be successful and we may not be able to commence sales of any other products and/or successfully market and sell ONPATTRO, GIVLAARI, OXLUMO or any other approved products in the future. A substantial portion of our total revenues in recent years has been derived from collaboration revenues from strategic alliances with Regeneron, Novartis and Vir. In addition to revenues from the commercial sales of ONPATTRO, GIVLAARI, OXLUMO and potentially from sales of future products, including vutrisiran, we expect our sources of potential funding for the next several years to continue to be derived in part from existing and new strategic alliances, which may include license and other fees, funded research and development, milestone payments and royalties on product sales by our licensees, as well as funding due or available to us under our strategic financing collaboration with Blackstone.

#### ***The COVID-19 Pandemic***

In March 2020, the World Health Organization declared the outbreak of a novel strain of coronavirus, or COVID-19, as a pandemic, which continues to spread throughout the U.S. and worldwide. More recently, other, potentially more infectious, variants of COVID-19 have been identified. We could be materially and adversely affected by the risks, or the public perception of the risks, related to an epidemic, pandemic, outbreak, or other public health crisis, such as the current COVID-19 pandemic. Since the onset of the global pandemic in 2020 and throughout 2021, we have been closely monitoring the spread of COVID-19 and its variants, and plan to continue taking steps to identify and mitigate the adverse impacts on, and risks to, our business posed by its spread and actions taken by governmental and health authorities to address the COVID-19 pandemic. The spread of COVID-19 caused us to modify our business practices, including implementing a temporary global work from home policy in March 2020 for all employees who were able to perform their duties remotely and temporarily restricting all nonessential business travel, and we expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees, the patients we serve and other business partners in light of COVID-19 and variants thereof. Where and to the extent permitted to be open under local regulations, our office sites are operational with appropriate safety precautions based on COVID-19 infection rates, vaccination rates and local guidance, and in October 2021, we formally re-opened our offices in the U.S., following openings in other territories, to those employees who have been fully vaccinated. The effects of the COVID-19 pandemic continue to evolve and, at this time, we cannot predict when certain restrictions that remain in place to protect our employees, customers and patients will no longer be needed. Recognizing that local conditions vary for our offices around the world and that the trajectory of the virus continues to be uncertain, we may adjust our plans for employees returning to our offices as deemed necessary. Since early 2021, global vaccination efforts have been underway to control the pandemic. However, due to the speed and fluidity with which the COVID-19 pandemic continues to evolve, and the emergence of highly contagious variants, we do not yet know the full extent of the impact of COVID-19 on our business operations. The ultimate extent of the impact of any epidemic, pandemic, outbreak, or other public health crisis on our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of such epidemic, pandemic, outbreak, or other public health crisis and actions taken to contain or prevent the further spread, including the effectiveness of vaccination.



campaigns, among others. Accordingly, we cannot predict the extent to which our business, financial condition and results of operations will be affected. We remain focused on maintaining a strong balance sheet, liquidity and financial flexibility and continue to monitor developments as we deal with the disruptions and uncertainties from a business and financial perspective relating to COVID-19 and variants thereof. We will continue to work diligently with our partners and stakeholders to support patient access to our approved medicines, advance our product candidates under regulatory review as well as in our clinical studies to the extent safe to do so for patients, caregivers and healthcare practitioners, and ensure the continuity of our manufacturing and supply chain. For additional information related to the actual or potential impacts of COVID-19 on our business, please read Part II, Item 1A, “Risk Factors” of this Quarterly Report on Form 10-Q.




### Research and Development

Since our inception, we have focused on drug discovery and development programs. Research and development expenses represent a substantial percentage of our total operating expenses, as reflected by our broad pipeline of clinical development programs, which includes multiple programs in late-stage development.

### Our Product Pipeline

Our broad pipeline, including four approved products and multiple late and early-stage investigational RNAi therapeutics, is focused in four STArS: Genetic Medicines; Cardio-Metabolic Diseases; Hepatic Infectious Diseases; and CNS/Ocular Diseases.

The chart below is a summary of our commercial products and late- and early-stage development programs as of October 2021. It identifies those programs for which we have received marketing approval, the stage of our programs and our commercial rights to such programs:

Alnylam Clinical Development Pipeline		Focused in 4 Strategic Therapeutic Areas (STArS):			
		Genetic Medicines		Cardio-Metabolic Diseases	
		Infectious Diseases		CNS/Ocular Diseases	
		EARLY/MID-STAGE (IND/CTA Filed/Phase 2)		LATE STAGE (Phase 2-Phase 3)	
		REGISTRATION/ COMMERCIAL <sup>1</sup> (OLE/Phase 4/III/registries)		COMMERCIAL RIGHTS	
	hATTR Amyloidosis-PN <sup>2</sup>				Global
	Acute Hepatic Porphyria <sup>3</sup>				Global
	Primary Hyperoxaluria Type 1 <sup>4</sup>				Global
Leqvio® (inclisiran)	Hypercholesterolemia				Milestones & up to 20% Royalties <sup>5</sup>
Vutrisiran*	hATTR Amyloidosis-PN				Global
Patisiran	ATTR Amyloidosis				Global
Vutrisiran*	ATTR Amyloidosis				Global
Fitusiran*	Hemophilia				15-30% Royalties
Lumasiran	Severe PH1 Recurrent Renal Stones				Global
Cemdisiran*	Complement-Mediated Diseases				50-50
Cemdisiran/Pozelimab Combo <sup>6</sup>	Complement-Mediated Diseases				Milestone/Royalty
Belcesiran <sup>7</sup>	Alpha-1 Liver Disease				Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218) <sup>8</sup>	Hepatitis B Virus Infection				50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	Hypertension				Global
ALN-HSD*	NASH				50-50

<sup>1</sup> Includes marketing application submissions; <sup>2</sup> Approved in the U.S. and Canada for the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; <sup>3</sup> Approved in the U.S., Brazil and Canada for the treatment of adults with acute hepatic porphyria (AHP), and in the EU and Japan for the treatment of AHP in adults and adolescents aged 12 years and older; <sup>4</sup> Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; <sup>5</sup> Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; <sup>6</sup> Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; <sup>7</sup> Dicerna is leading and funding development of Belcesiran; <sup>8</sup> Vir is leading and funding development of ALN-HBV02; \* Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

During the third quarter of 2021 and recent period, we reported the following updates from our commercially approved products and our late-stage clinical programs:

### Commercial

#### ONPATTRO

- We achieved ONPATTRO global net product revenues for the third quarter of 2021 of \$120.3 million.

#### GIVLAARI

- We achieved GIVLAARI global net product revenues for the third quarter of 2021 of \$31.8 million, and continued geographic expansion for GIVLAARI with pricing and reimbursement approvals in Spain, the United Kingdom, France and Japan.

## **OXLUMO**

- We achieved OXLUMO global net product revenues for the third quarter of 2021 of \$14.9 million, and continued planned geographic expansion for OXLUMO with ongoing pricing and reimbursement discussions in many European countries.

## **Leqvio**

- We earned royalty revenues of \$0.5 million from our partner, Novartis, based on Leqvio global net product revenues in the third quarter of 2021.
- Novartis announced a commercial agreement with the NHS in England as part of a collaboration to pioneer a first-of-its-kind population health management approach to address elevated LDL-C in eligible patients with ASCVD across England.

### ***Late-Stage Clinical Development***

- We continued to advance vutrisiran, a subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis:
  - Reported positive topline results for 18-month endpoints and safety from the HELIOS-A Phase 3 study in hATTR amyloidosis patients with polyneuropathy;
  - Completed enrollment in the HELIOS-B Phase 3 study in ATTR amyloidosis patients with cardiomyopathy, ahead of schedule; and
  - Submitted an MAA to the EMA, ahead of schedule, and an NDA to ANVISA in Brazil for the treatment of hATTR amyloidosis in adult patients with polyneuropathy.
- We continued to advance lumasiran for the treatment of PH1:
  - Reported positive topline results from the ILLUMINATE-C Phase 3 study in patients with advanced PH1.
- Our partner, Sanofi Genzyme, continued advancement of the ATLAS Phase 3 program for fitusiran in patients with hemophilia A or B with and without inhibitors:
  - Announced that a potential filing date for fitusiran has been moved to 2024 due to the introduction of a lower dose cohort in the ongoing phase 3 studies.

There is a risk that any drug discovery or development program may not produce revenue for a variety of reasons, including the possibility that we will not be able to adequately demonstrate the safety and effectiveness of the product candidate. Moreover, there are uncertainties specific to any new field of drug discovery, including RNAi. The success of ONPATTRO, GIVLAARI, OXLUMO or any other product candidate we develop, including vutrisiran, is highly uncertain. Due to the numerous risks associated with developing drugs, including those risks associated with the COVID-19 pandemic, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts necessary to complete the development of any potential product candidate or indication, or the period, if any, in which material net cash inflows will commence from any approved product or indication. Any failure to complete any stage of the development of any potential products or any approved product for an expanded indication in a timely manner or successfully launch, market and sell any of our commercially approved products, could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with completing our research and development programs within the planned timeline, or at all, and the potential consequences of failing to do so, are set forth in Part II, Item 1A below under the heading “Risk Factors.”

### ***Strategic Alliances***

Our business strategy is to develop and commercialize a broad pipeline of RNAi therapeutic products directed towards our four STArS. As part of this strategy, we have entered into, and expect to enter into additional, collaboration and licensing agreements as a means of obtaining resources, capabilities and funding to advance our investigational RNAi therapeutic programs.

Our collaboration strategy is to form alliances that create significant value for ourselves and our collaborators in the advancement of RNAi therapeutics as a new class of innovative medicines. Specifically, with respect to our CNS/Ocular Disease pipeline, in April 2019, we entered into a global, strategic collaboration with Regeneron to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing disease targets expressed in the eye and CNS, in addition to a select number of targets expressed in the liver.



With respect to our Cardio-Metabolic pipeline, in March 2013, we entered into an exclusive, worldwide license with MDCO (acquired by Novartis AG in January 2020) pursuant to which MDCO was granted the right to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9, or PCSK9, for the treatment of hypercholesterolemia and other human diseases, including inclisiran. In March 2018, we entered into a discovery collaboration with Regeneron to identify RNAi therapeutics for nonalcoholic steatohepatitis, or NASH, and potentially other related diseases, and in November 2018, we and Regeneron entered into a separate, fifty-fifty collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts. In April 2020, we entered into a development and commercialization collaboration with Dicerna to advance investigational RNAi therapeutics for the treatment of alpha-1 antitrypsin deficiency-associated liver disease, or alpha-1 liver disease.

With respect to our Hepatic Infectious Disease pipeline, in October 2017, we announced an exclusive licensing agreement with Vir for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic hepatitis B virus, or HBV, infection. In March 2020, we announced an expansion of our exclusive licensing agreement with Vir to include the development and commercialization of RNAi therapeutics targeting SARS-CoV-2, the virus that causes the disease COVID-19. In April 2020, we further expanded our broad multi-target existing collaboration for the development and commercialization of RNAi therapeutics for infectious diseases to include up to three additional targets focused on host factors for SARS-CoV-2, including angiotensin converting enzyme-2, and transmembrane protease, serine 2, and potentially a third mutually selected host factor target. In July 2021, we notified Vir that we elected to discontinue ALN-COV, in development for the treatment of COVID-19, and all other COVID-19 research and development activities, based on a portfolio prioritization in view of the availability of highly effective vaccines and alternative treatment options. Following such discontinuation of COVID-19 related activities, we have no further obligations to work on the COVID-related targets and Vir will have no further rights to such targets under our exclusive licensing agreement.

With respect to our Genetic Medicine pipeline, we formed a broad strategic alliance with Sanofi Genzyme in 2014. In January 2018, we and Sanofi Genzyme amended our 2014 collaboration and entered into the Exclusive License Agreement, referred to as the Exclusive TTR License, under which we have the exclusive right to pursue the further global development and commercialization of all TTR products, including ONPATTRO, vutrisiran and any back-up products, and the ALN-AT3 Global License Terms, referred to as the AT3 License Terms, under which Sanofi Genzyme has the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products. In April 2019, we and Sanofi Genzyme agreed to further amend the 2014 Sanofi Genzyme collaboration to conclude the research and option phase and to amend and restate the AT3 License Terms to modify certain of the business terms.

We also have entered into license agreements to obtain rights to intellectual property in the field of RNAi. In addition, because delivery of RNAi therapeutics has historically been an important objective of our research activities, we have entered into various collaboration and licensing arrangements with other companies and academic institutions to gain access to delivery technologies, including various LNP delivery technologies, and we may enter into such agreements in the future to gain access to products or technologies.

### **Critical Accounting Policies and Estimates**

Our critical accounting policies are described in the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of our Annual Report on Form 10-K for the year ended December 31, 2020, which we filed with the SEC on February 11, 2021. There have been no significant changes to our critical accounting policies since the beginning of this fiscal year.

## Results of Operations

The following data summarizes the results of our operations:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Total revenues	\$ 187,633	\$ 125,853	\$ 61,780	49 %	\$ 585,752	\$ 329,291	\$ 256,461	78 %
Operating costs and expenses	\$ 369,310	\$ 351,052	\$ 18,258	5 %	\$ 1,099,843	\$ 963,507	\$ 136,336	14 %
Loss from operations	\$ (181,677)	\$ (225,199)	\$ 43,522	(19)%	\$ (514,091)	\$ (634,216)	\$ 120,125	(19)%
Total other (expense) income, net	\$ (22,559)	\$ (27,253)	\$ 4,694	(17)%	\$ (77,751)	\$ 22,215	\$ (99,966)	(450)%
Net loss	\$ (204,514)	\$ (253,291)	\$ 48,777	(19)%	\$ (594,364)	\$ (614,741)	\$ 20,377	(3)%

## Discussion of Results of Operations

### Revenues

Total revenues consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Net product revenues	\$ 167,044	\$ 99,206	\$ 67,838	68 %	\$ 463,624	\$ 248,677	\$ 214,947	86 %
Net revenues from collaborations	20,136	26,647	(6,511)	(24)%	121,328	80,614	40,714	51 %
Royalty revenue	453	—	453	N/A	800	—	800	N/A
Total	<u>\$ 187,633</u>	<u>\$ 125,853</u>	<u>\$ 61,780</u>	<u>49 %</u>	<u>\$ 585,752</u>	<u>\$ 329,291</u>	<u>\$ 256,461</u>	<u>78 %</u>

### Net product revenues

Net product revenues consist of the following, by product and region:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
<b>ONPATTRO</b>								
United States	\$ 51,247	\$ 39,027	\$ 12,220	31 %	\$ 153,109	\$ 108,491	\$ 44,618	41 %
Europe	51,019	30,478	20,541	67 %	136,576	74,664	61,912	83 %
Rest of World (primarily Japan)	18,051	13,011	5,040	39 %	46,422	32,560	13,862	43 %
Total	\$ 120,317	\$ 82,516	\$ 37,801	46 %	\$ 336,107	\$ 215,715	\$ 120,392	56 %
<b>GIVLAARI</b>								
United States	\$ 22,372	\$ 12,108	\$ 10,264	85 %	\$ 62,502	\$ 26,043	\$ 36,459	140 %
Europe	7,568	4,582	2,986	65 %	22,461	6,919	15,542	225 %
Rest of World (primarily Japan)	1,893	—	1,893	N/A	2,173	—	2,173	N/A
Total	\$ 31,833	\$ 16,690	\$ 15,143	91 %	\$ 87,136	\$ 32,962	\$ 54,174	164 %
<b>OXLUMO</b>								
United States	\$ 5,236	\$ —	\$ 5,236	N/A	\$ 13,156	\$ —	\$ 13,156	N/A
Europe	9,658	—	9,658	N/A	27,225	—	27,225	N/A
Total	\$ 14,894	\$ —	\$ 14,894	N/A	\$ 40,381	\$ —	\$ 40,381	N/A
Total net product revenues	\$ 167,044	\$ 99,206	\$ 67,838	68 %	\$ 463,624	\$ 248,677	\$ 214,947	86 %

Net product revenues increased during the three and nine months ended September 30, 2021, as compared to the same periods in the prior year, as a result of the continued, global expansion of ONPATTRO and GIVLAARI into additional major markets and increased patients on therapy, in addition to sales generated from our third commercial product, OXLUMO, following regulatory approvals in the fourth quarter of 2020.

We expect net product revenues to increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, as we continue to add new patients onto our approved, commercial products, as well as launch our approved products into additional markets, assuming regulatory approvals.

### Net revenues from collaborations

Net revenues from collaborations consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Regeneron Pharmaceuticals	\$ 14,161	\$ 14,874	\$ (713)	(5)%	\$ 90,908	\$ 49,790	\$ 41,118	83 %
Novartis AG	4,160	1,091	3,069	281 %	21,179	6,029	15,150	251 %
Vir Biotechnology	1,233	8,512	(7,279)	(86)%	8,033	21,476	(13,443)	(63)%
Other	582	2,170	(1,588)	(73)%	1,208	3,319	(2,111)	(64)%
Total	\$ 20,136	\$ 26,647	\$ (6,511)	(24)%	\$ 121,328	\$ 80,614	\$ 40,714	51 %

Net revenues from collaborations decreased during the three months ended September 30, 2021, as compared to the same period in the prior year, primarily due to a decrease in revenue recognized in connection with our collaboration agreement with Vir. Net revenues from collaborations increased during the nine months ended September 30, 2021, as compared to the same period in the prior year, primarily due to an increase in revenue recognized in connection with our collaboration agreements with Regeneron as a result of increased activities under the C5 collaboration.

We expect net revenues from collaborations to increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, primarily due to increased activities under our collaborations with Regeneron and Novartis.

### **Royalty revenue**

We earn royalty revenue from global net sales of Leqvio by our collaborator, Novartis. We expect royalty revenue to increase for the remainder of 2021 as Novartis continues to execute on its launch of Leqvio in Europe and potentially other geographies, assuming regulatory approvals.

### **Operating Costs and Expenses**

Operating costs and expenses consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Cost of goods sold	\$ 28,091	\$ 20,826	\$ 7,265	35 %	\$ 81,370	\$ 52,393	\$ 28,977	55 %
Cost of collaborations and royalties	4,572	971	3,601	N/A	21,110	2,635	18,475	N/A
Research and development	194,572	161,783	32,789	20 %	563,106	486,350	76,756	16 %
Selling, general and administrative	142,075	167,472	(25,397)	(15)%	434,257	422,129	12,128	3 %
Total	\$ 369,310	\$ 351,052	\$ 18,258	5 %	\$ 1,099,843	\$ 963,507	\$ 136,336	14 %

### **Cost of goods sold.**

Cost of goods sold increased during the three and nine months ended September 30, 2021, as compared to the same periods in the prior year, due to the increase in third-party royalties and sales of capitalized inventory.

We anticipate variability in our cost of goods sold as a percentage of net product revenues due to the timing of manufacturing runs and utilization and the depletion of zero-cost inventories, as well as future product launches. We expect cost of goods sold will increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, primarily as a result of an expected increase in net product sales as well as the sale of capitalized inventory.

### **Cost of collaborations and royalties.**

Cost of collaborations and royalties includes costs we incur in connection with providing commercial drug supplies, such as GalNAc, for collaborators, in addition to royalties we owe to third parties on the net sales of licensed products by Novartis.

We expect cost of collaborations and royalties will increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, as we continue to supply material to Novartis to support the manufacturing of Leqvio as Novartis executes on the product launch in Europe and prepares for other potential market approvals.

### **Research and development.**

Research and development expenses consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Clinical trial and manufacturing	\$ 75,639	\$ 54,705	\$ 20,934	38 %	\$ 217,683	\$ 155,757	\$ 61,926	40 %
Compensation and related	47,168	47,982	(814)	(2)%	142,547	145,459	(2,912)	(2)%
External services	27,982	17,512	10,470	60 %	58,734	53,450	5,284	10 %
Facilities-related	19,928	18,256	1,672	9 %	59,932	51,658	8,274	16 %
Stock-based compensation	12,417	13,703	(1,286)	(9)%	49,878	45,542	4,336	10 %
Lab supplies, materials and other	11,275	9,625	1,650	17 %	32,952	32,071	881	3 %
License Fees	163	—	163	N/A	1,380	2,413	(1,033)	(43)%
Total	\$ 194,572	\$ 161,783	\$ 32,789	20 %	\$ 563,106	\$ 486,350	\$ 76,756	16 %

For the three and nine months ended September 30, 2021, the increase in research and development expenses, as compared to the same period in the prior year, was primarily related to increased expenses associated with activities related to the advancement of our early- and late-stage programs.

During the three and nine months ended September 30, 2021 and 2020, in connection with advancing activities under our collaboration agreements, we incurred research and development expenses, primarily related to external development and clinical expenses, including manufacturing of clinical product.

The following table summarizes research and development expenses incurred, for which we recognize net revenue, that are directly attributable to our collaboration agreements, by collaboration partner:

(In thousands)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Regeneron Pharmaceuticals	\$ 14,401	\$ 12,565	\$ 51,972	\$ 44,108
Vir Biotechnology	1,102	4,903	5,526	11,782
Other	235	1,076	2,039	3,242
Total	\$ 15,738	\$ 18,544	\$ 59,537	\$ 59,132

***Selling, general and administrative.***

Selling, general and administrative expenses consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Compensation and related	\$ 52,075	\$ 53,532	\$ (1,457)	(3)%	\$ 162,516	\$ 148,502	\$ 14,014	9 %
Consulting and professional services	45,622	40,008	5,614	14 %	129,887	120,318	9,569	8 %
Stock-based compensation	20,950	23,561	(2,611)	(11)%	71,257	60,055	11,202	19 %
Facilities-related	10,343	11,299	(956)	(8)%	33,944	32,695	1,249	4 %
Other	13,085	39,072	(25,987)	(67)%	36,653	60,559	(23,906)	(39)%
Total	\$ 142,075	\$ 167,472	\$ (25,397)	(15)%	\$ 434,257	\$ 422,129	\$ 12,128	3 %

For the three months ended September 30, 2021, the decrease in selling, general and administrative expenses, as compared to the same periods in the prior year, was primarily due to a change in an estimate of contingent liabilities related to our arbitration with Ionis Pharmaceuticals, Inc. in 2020.

For the nine months ended September 30, 2021, the increase in selling, general and administrative expenses, as compared to the same periods in the prior year, was primarily related to increases in compensation and related expenses and stock-based compensation expense as a result of increased headcount to support our *Alnylam P<sup>5</sup>x25* strategy, offset by a change in an estimate of contingent liabilities related to our arbitration with Ionis Pharmaceuticals, Inc. in 2020.

We expect that research and development expenses combined with selling, general and administrative expenses will increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, as we continue to develop our pipeline, advance our product candidates, including partnered programs, into later-stage development, prepare regulatory submissions and build-out of our global commercial infrastructure and field team to support ONPATTRO, GIVLAARI, OXLUMO and potentially additional product launches, including vutrisiran. However, we expect that certain expenses will be variable depending on the timing of manufacturing batches, clinical trial enrollment and results, regulatory review of our product candidates and programs, and stock-based compensation expenses due to our determination regarding the probability of vesting for performance-based awards.

### Other (Expense) Income.

Other (expense) income consists of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2021	2020	\$ Change	% Change	2021	2020	\$ Change	% Change
Interest expense	\$ (40,274)	\$ (28,731)	\$ (11,543)	40 %	\$ (106,205)	\$ (55,979)	\$ (50,226)	90 %
Interest income	225	2,072	(1,847)	(89)%	1,084	10,717	(9,633)	(90)%
Other (expense) income, net								
Realized and unrealized gains (losses) on marketable equity securities	18,691	(3,017)	21,708	(720)%	61,273	66,626	(5,353)	(8)%
Change in fair value of development derivative liability	3,188	(1,229)	4,417	N/A	(19,655)	(1,229)	(18,426)	N/A
Other	(4,389)	3,652	(8,041)	(220)%	(14,248)	2,080	(16,328)	(785)%
Total	<u>\$ (22,559)</u>	<u>\$ (27,253)</u>	<u>\$ 4,694</u>	<u>(17)%</u>	<u>\$ (77,751)</u>	<u>\$ 22,215</u>	<u>\$ (99,966)</u>	<u>(450)%</u>

For the three months ended September 30, 2021, total other expense, net, decreased, as compared to the same period in the prior year, primarily due to realized and unrealized gains on marketable equity securities offset by increases in interest expense associated with the sale of future royalties and the drawdown of our credit facility beginning in December 2020.

For the nine months ended September 30, 2021, total other expense, net, increased, as compared to total other income, net, in the same period in the prior year, primarily due to increases in interest expense associated with the sale of future royalties and the drawdown of our credit facility beginning in December 2020.

We expect total other expense, net, will increase for the twelve-month period ending December 31, 2021, as compared to the same period in 2020, as we continue to incur interest expense on our long-term debt and sale of future royalties.

### Liquidity and Capital Resources

The following table summarizes our cash flow activities:

(In thousands)	Nine Months Ended September 30,	
	2021	2020
Net loss	\$ (594,364)	\$ (614,741)
Non-cash adjustments to reconcile net loss to net cash used in operating activities:	250,524	150,133
Changes in operating assets and liabilities	(147,712)	(27,209)
Net cash used in operating activities	(491,552)	(491,817)
Net cash provided by (used in) investing activities	140,105	(337,630)
Net cash provided by financing activities	954,827	777,029
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(5,968)	1,946
Net increase (decrease) in cash, cash equivalents and restricted cash	597,412	(50,472)
Cash, cash equivalents and restricted cash, beginning of period	499,046	549,628
Cash, cash equivalents and restricted cash, end of period	<u>\$ 1,096,458</u>	<u>\$ 499,156</u>

Since we commenced operations in 2002, we have generated significant losses. As of September 30, 2021, we had an accumulated deficit of \$5.18 billion. As of September 30, 2021, we had cash, cash equivalents and marketable securities of \$2.33 billion, compared to \$1.87 billion as of December 31, 2020.

### Operating activities

Net cash used in operating activities was relatively consistent during the nine months ended September 30, 2021, compared to the same period in 2020, as stronger cash receipts from increased product sales were largely offset by cash disbursements related to working capital receipts and payments.

### **Investing activities**

Net cash provided by investing activities increased during the nine months ended September 30, 2021, compared to the same period in the prior year, reflecting timing differences related to purchases, sales, and maturities of debt securities and changes in our portfolio-mix.

### **Financing activities**

Net cash provided by financing activities increased during the nine months ended September 30, 2021, compared to the same period in the prior year, primarily due to proceeds of \$250.0 million in connection with the second drawdown on our credit agreement, received in June 2021.

### **Operating Capital Requirements**

We currently have programs focused on a number of therapeutic areas and, as of September 30, 2021, have received regulatory approval and commercially launched three products: ONPATTRO, GIVLAARI and OXLUMO. In early 2021, we announced our *Alnylam P<sup>5</sup>x25* strategy, which is aimed at our planned transition to a top 5 biotech in market capitalization. With *Alnylam P<sup>5</sup>x25*, we aim to deliver transformative rare and prevalent disease medicines for patients around the world through sustainable innovation, delivering exceptional financial performance and driving profitability. However, our ongoing development efforts may not be successful and we may not be able to commence sales of any other products in the future. In addition, we anticipate that we will continue to generate losses as a result of planned expenditures for research and development activities relating to our research platform, our drug development programs, including clinical trial and manufacturing costs, the establishment of late-stage clinical, manufacturing and commercial capabilities, including global operations, continued management and growth of our intellectual property including our patent portfolio, collaborations and general corporate activities.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of September 30, 2021, together with the cash we expect to generate from product sales and under our current alliances, in addition to our strategic financing collaboration with The Blackstone Group Inc. and certain of its affiliates, will be sufficient to enable us to advance our long-term strategic goals for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q. However, due to numerous factors described in more detail under the caption Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q, we may require significant additional funds earlier than we currently expect in order to continue to commercialize ONPATTRO, GIVLAARI and OXLUMO, and to develop, conduct clinical trials for, manufacture and, if approved, commercialize additional product candidates, including vutrisiran.

### **Contractual Obligations and Commitments**

The disclosure of our contractual obligations and commitments is set forth under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations" in our Annual Report on Form 10-K for the year ended December 31, 2020. There have been no material changes in our contractual obligations and commitments since December 31, 2020.

## **ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Financial market risks related to interest rates are described in our Annual Report on Form 10-K for the year ended December 31, 2020. As of September 30, 2021, there have been no significant changes to the financial market risks described as of December 31, 2020. We do not currently anticipate any other near-term changes in the nature of our financial market risk exposures or in management's objectives and strategies with respect to managing such exposures.

## **ITEM 4. CONTROLS AND PROCEDURES**

### **Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer (principal executive officer) and executive vice president, Chief Financial Officer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2021. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment

in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2021, our Chief Executive Officer and executive vice president, Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

**Changes in Internal Control**

There were no changes in our internal control over financial reporting during the quarter ended September 30, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.



## PART II. OTHER INFORMATION

### ITEM 1. LEGAL PROCEEDINGS

For a discussion of material pending legal proceedings, please read Note 14, Commitments and Contingencies – Legal Matters, to our condensed consolidated financial statements included in Part I, Item I, “Financial Statements (Unaudited),” of this Quarterly Report on Form 10-Q, which is incorporated into this item by reference.

### ITEM 1A. RISK FACTORS

#### Risks Related to Our Business

##### Risks Related to Our Financial Results

***The current pandemic of COVID-19 and the future outbreak of other highly infectious or contagious diseases, could continue to have an adverse impact on our business, financial condition and results of operations, including our commercial operations and sales, clinical trials and pre-clinical studies.***

The novel coronavirus identified in late 2019, SARS-CoV-2, which causes the disease known as COVID-19, has led to an ongoing global pandemic that continues to evolve and the ultimate impact of this pandemic remains highly uncertain. To date, the COVID-19 pandemic has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. COVID-19 has and may continue to impact our operations and those of our third-party partners and the ultimate impact on our business and financial results remains uncertain and cannot be predicted with confidence, and will depend on many factors, including the scope, severity, duration and any recurrence of the COVID-19 pandemic, including through any new variant strains of the underlying virus, the actions taken to contain the pandemic or mitigate its impact, the direct and indirect economic effects of the pandemic and containment measures, the effectiveness of vaccination campaigns, and the necessity for and availability of booster vaccines, among others. The continued development and fluidity of the COVID-19 pandemic precludes any prediction as to its full impact on our business.

In response to the spread of COVID-19, we took, and have continued to take, both temporary and ongoing precautionary measures, intended to help minimize the risk of the virus to our employees and their families, including implementing a global work from home policy in early March 2020 for nearly all employees who were able to perform their duties remotely. Where and to the extent permitted to be open under local regulations, our office sites are operational with appropriate safety precautions based on COVID-19 infection rates, vaccination rates and local guidance, and in October 2021, we formally re-opened our U.S. offices to those employees who have been fully vaccinated. Working arrangements for many of our employees differ from the arrangements before the COVID-19 pandemic, and we expect a number of employees to continue to work in a remote capacity or a hybrid of in-person and remote work. We may face several challenges or disruptions as a result of our return to the workplace, including re-integration challenges for our employees, and our hybrid of in-person and remote work option may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. Compliance with governmental measures imposed in response to COVID-19 has caused and will continue to cause us to incur additional costs, and any inability to comply with such measures can subject us to restrictions on our business activities, fines, and other penalties, any of which can adversely affect our business. We cannot predict when certain restrictions that are in place to protect our employees can be further reduced or will no longer be needed. In addition, the increase in certain of our employees working remotely has amplified certain risks to our business, including increased demand on our information technology resources and systems, increased phishing and other cybersecurity attacks, and any failure to effectively manage these risks, including to timely identify and appropriately respond to any cyberattacks, could adversely impact our business operations.

As the pandemic continues, and if conditions worsen or if the duration of the pandemic extends significantly, we may experience disruptions that could severely impact our business and operations, including our ability to successfully commercialize our approved products, ONPATTRO, GIVLAARI and OXLUMO, and due to the current pandemic, we may not be able to meet expectations with respect to commercial sales. For example, due to the impact of the COVID-19 pandemic, product revenues in the second quarter of 2020 for ONPATTRO were less than originally forecast. In addition, we may also experience decreased patient demand for our approved products if current or potential patients decide to delay treatment as a result of the COVID-19 or a future pandemic. For example, in the second quarter of 2020, we experienced a decrease in patient demand in the U.S. due to reduced adherence as some patients skipped doses or experienced dose delays while moving to new sites of care, and additionally experienced reduced requests for genetic testing through our third party genetic testing program resulting in delays in diagnoses of the rare diseases our medicines are approved to treat. In addition, business interruptions from the current or future pandemics, including staffing shortages, production slowdowns and disruptions in delivery systems, may also adversely impact the third parties we or our partners rely on in the U.S. and abroad to sufficiently manufacture our approved products and to produce product candidates in quantities we require, which may impair our commercialization efforts, our research and development activities and the potential commercialization of our product candidates.

Additionally, timely completion of pre-clinical activities and initiation of planned clinical trials is dependent upon the availability of, for example, pre-clinical and clinical trial sites, researchers and investigators, patients or healthy volunteer subjects available for recruitment and enrollment, and regulatory agency personnel, which may be adversely affected by global

health matters, such as the COVID-19 pandemic. We are conducting and plan to continue to conduct pre-clinical activities and clinical trials for our drug product candidates in geographies which have been and continue to be affected by COVID-19, and believe that the COVID-19 pandemic will have an impact on various aspects of our ongoing clinical trials and on the clinical trials and pre-clinical studies we expect to initiate during the remainder of 2021 or potentially in early 2022. For example, certain trial sites in some of our ongoing clinical trials were restricted temporarily by the institutions where they are located from scheduling patient visits or permitting onsite monitoring due to the COVID-19 pandemic, and in some of our ongoing trials, delayed or missed doses of study drug have been reported. In addition, due to the impact of the COVID-19 pandemic, enrollment delays in our APOLLO-B Phase 3 study of patisiran for the treatment of ATTR amyloidosis with cardiomyopathy resulted in a shift in the enrollment completion date from late 2020 into early 2021. Any business interruptions caused by the COVID-19 pandemic could also delay necessary interactions with local regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors, which could adversely impact the clinical trials of our product candidates.

Health regulatory agencies globally may also experience disruptions in their operations as a result of the COVID-19 pandemic, which may impact review, inspection and approval timelines. Since March 2020, when foreign and domestic inspections of facilities 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 determining when and where it is safest to conduct prioritized domestic inspections. As of May 2021, certain inspections, such as foreign preapproval, surveillance, and for-cause inspections that are not deemed mission-critical, remain temporarily postponed. 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 and in May 2021 announced plans to continue progress toward resuming standard operational levels. Should the FDA determine that an inspection is necessary for approval of a marketing application 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 adequate, the FDA has stated that it generally intends to issue a complete response letter or defer action on the application until an inspection can be completed. For example, in December 2020, the FDA issued a complete response letter regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the PDUFA action date due to unresolved facility inspection-related conditions. 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.

Some factors from the COVID-19 pandemic that may delay or otherwise adversely affect enrollment in and the conduct of the clinical trials of our product candidates, as well as adversely impact our business generally, include:

- the diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the availability of materials necessary to conduct our clinical trials;
- limitations on travel that could interrupt 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 will impact the ability or willingness of patients, employees or contractors to travel to our research, manufacturing and clinical trial sites or secure visas or entry permissions, any of which could delay or adversely impact the conduct or progress of our clinical trials; and
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations, or CMOs, due to staffing shortages, production slowdowns, raw material or other supply shortages, or stoppages and disruptions in delivery systems.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19 or could return to countries where the pandemic has been partially contained, 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. In addition, a recession, depression or other sustained adverse market event resulting from the COVID-19 pandemic could materially and adversely affect our business and the value of our common stock.

***We are a young commercial company and the marketing and sale of ONPATTRO, GIVLAARI, OXLUMO or any future products may be unsuccessful or less successful than anticipated.***

In 2018, our first commercial product, ONPATTRO, was approved by the FDA and EMA, and we have since received approval and launched ONPATTRO in several additional territories. In 2019, the FDA approved our second product, GIVLAARI, which was also approved by the EMA and has since received approval in several additional territories, and in November 2020, the FDA and EMA approved our third product, OXLUMO. While we have commercially launched ONPATTRO, GIVLAARI and OXLUMO, we have limited experience as a commercial company and there is limited information about our ability to successfully overcome many of the risks and uncertainties encountered by companies commercializing products in the biopharmaceutical industry. We also have several product candidates in late-stage clinical development, including vutrisiran, which is under review by the FDA. To execute our business plan of building a profitable, top 5 biotech company, as measured by market capitalization, over the next 5 years and achieving our *Alynxam P<sup>3</sup>x25* strategy and

the metrics associated with such strategy, in addition to successfully marketing and selling our approved products we will need to successfully:

- execute product development activities and continue to leverage new technologies related to both RNAi and to the delivery of siRNAs to the relevant tissues and cells, including the liver, CNS, eye and lung;
- successfully execute our planned leadership transition;
- build and maintain a strong intellectual property portfolio;
- gain regulatory acceptance for the development and commercialization of our product candidates and market success for our approved products, as well as any other products we commercialize;
- attract and retain customers for our products;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing the objectives set forth above, we may not be able to develop product candidates, successfully commercialize our approved products or any future products, raise capital, if needed, repay the debt we incurred in 2020 and 2021 and plan to incur in the future, expand our business, achieve financial self-sustainability or continue our operations.

***We have a history of losses and may never become and remain consistently profitable.***

We have experienced significant operating losses since our inception. As of September 30, 2021, we had an accumulated deficit of \$5.18 billion. Although to date we have launched three products in the U.S., EU and various other countries globally, and expect to launch our commercially approved products in additional countries during the remainder of 2021 and beyond, we may never attain profitability or positive cash flow from operations. For the three months ended September 30, 2021, we recognized \$167.0 million in net product revenues from sales of ONPATTRO, GIVLAARI and OXLUMO. While our full year 2020 operating loss improved relative to the prior year, marking 2019 as our peak operating loss year, we expect to continue to incur annual net operating losses, and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics, and aim to achieve self-sustainability by the end of 2025. While we believe the funding provided by our strategic financing collaboration with Blackstone should enable us to achieve a self-sustainable profile without the need for future equity financing, we will depend on our ability to generate revenues to achieve this goal. In addition to revenues derived from sales of our current and future, if any, commercially approved products, we anticipate that a portion of any revenues we generate over the next several years will continue to be from alliances with pharmaceutical and biotechnology companies. We cannot be certain that we will be able to maintain our existing alliances, secure and maintain new alliances, meet the obligations, or achieve any milestones that we may be required to meet or achieve to receive payments under our existing or new alliances.

We believe that to become and remain consistently profitable, we must succeed in discovering, developing and commercializing novel drugs with significant market potential. This will require us to build upon the success we have had in a range of challenging activities, including pre-clinical testing and clinical trial stages of development, obtaining regulatory approval and reimbursement for these novel drugs and manufacturing, marketing and selling them. We may never succeed as a commercial company, and may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we cannot become and remain consistently profitable, the market price of our common stock could decline. In addition, we may be unable to raise capital, expand our business, develop additional product candidates or continue our operations.

***We will require substantial funds to continue our research, development and commercialization activities and if the funds we require are greater than what we have estimated, we may need to critically limit or significantly scale back or cease our operations.***

We have used substantial funds to develop our RNAi technologies and will require substantial funds to conduct further research and development, including pre-clinical testing and clinical trials of our product candidates, and to manufacture, market and sell our three approved products and any other products that are approved for commercial sale. Because the length of time or activities associated with successful development of our product candidates, including vutrisiran, may be greater than we anticipate, we are unable to estimate the actual funds we will require to develop and commercialize them.

We believe 2019 was our peak operating loss year, and believe that our strategic financing collaboration with Blackstone will enable us to achieve a self-sustainable financial profile without need for future equity financing. However, our future capital requirements and the period for which we expect our existing resources to support our operations may vary from what we expect. We have based our expectations on a number of factors, many of which are difficult to predict or are outside of our control, including:

- progress in our research and development programs, as well as what may be required by regulatory bodies to advance these programs;
- the timing, receipt and amount of milestone and other payments, if any, from present and future collaborators, if any, including milestone payments related to Leqvio, which is being developed and commercialized by our partner, Novartis;
- our ability to maintain and establish additional collaborative arrangements and/or new business initiatives;
- the resources, time and costs required to successfully initiate and complete our pre-clinical and clinical studies, obtain regulatory approvals, prepare for global commercialization of our product candidates and obtain and maintain licenses to third-party intellectual property;
- our ability to establish, maintain and operate our own manufacturing facilities in a timely and cost-effective manner;
- our ability to manufacture, or contract with third parties for the manufacture of, our product candidates for clinical testing and commercial sale;
- the impact of COVID-19 on the initiation or completion of pre-clinical studies or clinical trials and the supply of our products or product candidates;
- the resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;
- the costs associated with legal activities, including litigation and government investigations, arising in the course of our business activities and our ability to prevail or reach a satisfactory result in any such legal disputes and investigations;
- the timing, receipt and amount of sales and royalties, if any, from our approved products and our potential products, if and when approved; and
- the outcome of the regulatory review process and commercial success of drug products for which we are entitled to receive royalties, including Leqvio.

If our estimates, predictions and financial guidance relating to these factors are incorrect, we may need to modify our operating plan and may be required to seek additional funding in the future. We may do so through either collaborative arrangements, public or private equity offerings or debt financings, royalty or other monetization transactions or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all.

In April 2020, we entered into a credit agreement, or Credit Agreement, for up to \$750.0 million among us, certain of our subsidiaries (together with us, the Loan Parties), funds or accounts managed or advised by GSO Capital Partners LP (now Blackstone Alternative Credit Advisors LP) and certain other affiliates of Blackstone, and the other lenders from time to time party thereto and Wilmington Trust, National Association, as the administrative agent for the lenders. The Credit Agreement provides for a senior secured delayed draw term loan facility to be funded in three tranches, or Term Loans, each tranche to be requested by certain dates specified in the Credit Agreement, and subject to customary terms and conditions in the case of each tranche. The Term Loans mature seven years from the date of the first draw, and bear interest at a variable rate. All obligations under the Credit Agreement are secured, subject to certain exceptions, by security interests in certain assets, including the intellectual property owned by us relating to ONPATTRO, GIVLAARI and vutrisiran, the equity interests held by the Loan Parties in their subsidiaries, all of our ownership of the inclisiran royalty remaining after the royalty purchase and material real property, and certain personal property, including, without limitation, cash held in certain deposit accounts of the Loan Parties and equipment. The Credit Agreement contains negative covenants that, among other things and subject to certain exceptions, could restrict our ability to, incur additional liens, incur additional indebtedness, make investments, including acquisitions, engage in fundamental changes, sell or dispose of assets that constitute collateral, including certain intellectual property, pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests, amend, modify or waive certain material agreements or organizational documents and make payments of certain subordinated indebtedness. The Credit Agreement also requires us to have consolidated liquidity of at least \$100.0 million as of the last day of each fiscal quarter. Additionally, the Credit Agreement contains certain customary representations and warranties, affirmative covenants and provisions relating to events of default. In August 2020, in connection with execution of the funding agreement for the clinical development of vutrisiran and zilebesiran (formerly ALN-AGT), or Funding Agreement, we entered into the First Amendment to the Credit Agreement. The First Amendment added certain intellectual property owned by us relating to zilebesiran as collateral under the Credit Agreement, as amended, and made certain other amendments related thereto and the Funding Agreement. In December 2020, we drew down the first tranche of \$200.0 million and in June 2021, we drew down the second tranche of \$250.0 million under the Credit Agreement, as amended. Our ability to satisfy our obligations under the Credit Agreement, as amended, and meet our debt service obligations will depend upon our future performance, which will be subject to financial, business and other factors affecting our operations, many of which are beyond our control. If we are unable to secure future borrowings under the term loan facility, we may not be able to replace the financing commitment on favorable terms, or at all.

The terms of any financing we may be required to pursue in the future notwithstanding the funds due or available to us from Blackstone may adversely affect the holdings or the rights of our stockholders. If we raise additional funds by issuing equity securities, further dilution to our existing stockholders will result. In addition, as a condition to providing additional funding to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. For example, pursuant to our stock purchase agreement with Blackstone, we agreed to register the resale of the shares purchased on a registration statement within 60 days of April 10, 2020, and on June 5, 2020, such registration statement was filed with the SEC. In addition, subject to certain conditions, Blackstone will be entitled to participate in registered underwritten public offerings by us if other selling stockholders are included in the registration.

If we are unable to obtain additional funding on a timely basis, we may be required to significantly delay or curtail one or more of our research or development programs, or delay or curtail the further development of our global commercial infrastructure, and our ability to achieve our long-term strategic goals may be delayed or diminished. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products that we would otherwise pursue on our own.

***Although we sold a portion of the expected royalty stream and commercial milestones from the global sales of Leqvio by our collaborator, Novartis, we are entitled to retain the remaining portion of future royalties from the global sales of Leqvio and, if certain specified thresholds are met, to the remaining portion of commercial milestone payments, and any negative developments related to Leqvio could have a material adverse effect on our receipt of those payments.***

In April 2020, we sold to Blackstone 50% of the royalties payable to us with respect to net sales by Novartis, its affiliates or sublicensees of Leqvio and 75% of the commercial milestone payments payable to us under the MDCO agreement. If Blackstone does not receive royalty payments in respect of global sales of Leqvio equaling at least \$1.00 billion by December 31, 2029, Blackstone's royalty interest will increase to 55% effective January 1, 2030. Our receipt of future royalty payments and a portion of commercial milestone payments may be negatively impacted if the Leqvio royalty stream and commercial milestones payments are insufficient to meet the specified thresholds. For example, in December 2020, the FDA issued a complete response letter regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the PDUFA action date due to unresolved inspection-related conditions at a third party manufacturing facility. While Leqvio was granted marketing authorization by the EC in Europe in December 2020, and Novartis resubmitted its NDA for inclisiran to the FDA in July 2021, any negative impact to future royalty payments and commercial milestone payments that results from a delayed approval in the U.S. could affect our ability to meet the specified repayment thresholds. Additional factors that may have an adverse effect on the Leqvio royalty stream and commercial milestones include:

- companies working to develop new therapies or alternative formulations of products for ASCVD;
- foreign currency movement, which could have a negative impact on Novartis' sales of Leqvio, thereby reducing the royalties;
- any negative developments relating to Leqvio, such as safety, efficacy, or reimbursement issues, could reduce demand for Leqvio;
- any disputes concerning patents, proprietary rights, or license and collaboration agreements could negatively impact our receipt of commercial milestone payments or royalties; and
- adverse regulatory or legislative developments could limit or prohibit the sale of Leqvio, such as restrictions on the use of Leqvio or safety-related label changes, including enhanced risk management programs, which may significantly reduce expected royalty revenue and commercial milestone payments and could require significant expense to address the associated legal and regulatory issues.

If the revenues generated by sales of Leqvio are lower than expected, our business could be materially adversely affected.

***We expect our operating results to fluctuate in future periods, which may adversely affect our stock price.***

Our quarterly operating results have fluctuated in the past, and we believe they will continue to do so in the future. Our operating results may fluctuate due to the impact of the COVID-19 or a future pandemic, the level of success of our commercial efforts and resulting revenues, as well as the variable nature of our operating expenses as a result of the timing and magnitude of expenditures. For example, due to the impact of the COVID-19 pandemic, product revenues in the second quarter of 2020 for ONPATTRO were less than originally forecast. In addition, in one or more future periods, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could substantially decline.

***If the estimates we make, or the assumptions on which we rely, in preparing our condensed consolidated financial statements and/or our projected guidance prove inaccurate, our actual results may vary from those reflected in our projections and accruals.***

Our condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP. The preparation of these condensed consolidated financial statements

requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

Further, from time to time we issue financial guidance relating to our expectations regarding our non-GAAP research and development and selling, general and administrative expenses, and expectations for our cash, cash equivalents and marketable securities available for operations, which guidance is based on estimates and the judgment of management. If, for any reason, our expenses differ materially from our guidance or we utilize our cash more quickly than anticipated, we may have to adjust our publicly announced financial guidance. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline.

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

As of September 30, 2021, we had \$2.33 billion in cash, cash equivalents and marketable securities. We historically have invested these amounts in high-grade corporate notes, commercial paper, securities issued or sponsored 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. Corporate notes may also include foreign bonds denominated in U.S. dollars. These investments are subject to general credit, liquidity, market and interest rate risks. 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 tax law could adversely affect our business and financial condition.***

Our business is subject to numerous international, federal, state, and other governmental laws, rules, and regulations that may adversely affect our operating results, including, taxation and tax policy changes, tax rate changes, new tax laws, or revised tax law interpretations, which individually or in combination may cause our effective tax rate to increase. In the U.S., the rules dealing with federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, enacted in March 2020, which included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 pandemic, including temporary changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

Additionally, the Organization for Economic Co-operation and Development, or OECD, the EC, and individual taxing jurisdictions where we and our affiliates do business have recently focused on issues related to the taxation of multinational corporations. The OECD has released its comprehensive plan to create an agreed set of international rules for fighting base erosion and profit shifting. In addition, the OECD, the EC and individual countries are examining changes to how taxing rights should be allocated among countries considering the digital economy. As a result, the tax laws in the U.S. and other countries in which we and our affiliates do business could change on a prospective or retroactive basis and any such changes could materially adversely affect our business.

#### **Risks Related to Our Dependence on Third Parties**

***We may not be able to execute our business strategy if we are unable to maintain existing or enter into new alliances with other companies that can provide business and scientific capabilities and funds for the development and commercialization of our product candidates. If we are unsuccessful in forming or maintaining these alliances on terms favorable to us, our business may not succeed.***

We are continuing to advance our commercial capabilities, including in marketing, sales, market access and distribution, to support our wholly-owned products. We also continue to advance our growing pipeline of RNAi therapeutic opportunities. However, we may not have adequate capacity or capabilities to advance all of our therapeutic opportunities. Accordingly, we have entered into alliances with other companies and collaborators that we believe can provide such capabilities in certain territories and/or for certain product candidates, and we intend to enter into additional such alliances in the future. Our collaboration strategy is to form alliances that create significant value for us and our collaborators in the advancement of RNAi therapeutics as a new class of innovative medicines. Specifically, with respect to our Genetic Medicine pipeline, as a result of our broad strategic alliance with Sanofi Genzyme formed in 2014, Sanofi Genzyme has the right to develop and commercialize fitusiran globally. In addition, we formed a collaboration with MDCO (which was acquired by Novartis in January 2020) to advance inclisiran. In March 2018, we entered into a discovery collaboration with Regeneron to identify RNAi therapeutics for NASH and potentially other related diseases, and in November 2018, we and Regeneron entered into a separate, fifty-fifty



collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts. In October 2017, we announced an exclusive licensing agreement with Vir for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic HBV infection, and in early 2020, we expanded our exclusive licensing agreement to include the development and commercialization of RNAi therapeutics targeting SARS-CoV-2, the virus that causes the disease COVID-19, as well as up to three human host factor targets relating to susceptibility to coronaviruses, for use in connection with the treatment, palliation, diagnosis or prevention of SARS-CoV-2 and other diseases caused by coronaviruses. In July 2021, we notified Vir that we elected to discontinue ALN-COV, in development for the treatment of COVID-19, and all other COVID-19 research and development activities, based on a portfolio prioritization in view of the availability of highly effective vaccines and alternative treatment options. Following such discontinuation of COVID-19 related activities, we have no further obligations to work on the three COVID-related host factor targets and Vir will have no further rights to such targets under our exclusive licensing agreement. In April 2020, we entered into a development and commercialization collaboration with Dicerna to advance investigational RNAi therapeutics for the treatment of alpha-1 liver disease. With respect to our CNS/Ocular Disease pipeline, in April 2019, we announced a global, strategic collaboration with Regeneron to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic targets expressed in the eye and CNS, in addition to a select number of targets expressed in the liver.

In such alliances, we expect our current, and may expect our future, collaborators to provide substantial capabilities in clinical development, regulatory affairs, and/or marketing, sales and distribution. Under certain of our alliances, we also may expect our collaborators to develop, market and/or sell certain of our product candidates. We may have limited or no control over the development, sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. For example, we will rely entirely on (i) Regeneron for the development and commercialization of all programs targeting eye diseases (subject to limited exceptions), and potentially other CNS and liver programs, (ii) Novartis for all future development and commercialization of Leqvio worldwide, and (iii) Sanofi Genzyme for the development and commercialization of fitusiran worldwide. In the case of each such collaboration referenced in clauses (i)-(iii) above, we are entitled to royalties on the sales of each of these products. If our collaborators are not successful in their development and/or commercialization efforts, our future revenues from RNAi therapeutics for these indications may be adversely affected. For example, while Leqvio was granted marketing authorization by the EC in Europe, in December 2020, Novartis received a complete response letter from the FDA stating that the agency could not approve the NDA by the PDUFA action date due to unresolved inspection-related conditions at a third party manufacturing facility. In July 2021, Novartis announced that the resubmission to the FDA for the inclisiran NDA to address the complete response letter was filed with an action date of January 1, 2022. Novartis listed its own site in Schaftanau, Austria, as the manufacturing location for the final finished product within its NDA resubmission. If the revenues generated by the royalties received by Blackstone from us with respect to Leqvio sales do not reach a certain level by the end of 2029, Blackstone will be entitled to a higher royalty percentage beginning in 2030, which would have an adverse impact on our revenues beginning in 2030.

We may not be successful in entering into future alliances on terms favorable to us due to various factors, including our ability to successfully demonstrate proof-of-concept for our technology in humans in certain tissues or disease areas, including our alternative conjugate approach for delivering CNS or ocular product candidates, our ability to demonstrate the safety and efficacy of our specific drug candidates, our ability to manufacture or have third parties manufacture RNAi therapeutics, the strength of our intellectual property and/or concerns around challenges to our intellectual property. For example, our decision in October 2016 to discontinue development of revusiran could give rise to concerns around the safety and/or efficacy of our technology platform or product candidates. In addition, the occurrence of a fatal thrombotic serious adverse event, or SAE, in our fitusiran study in 2017 and a subsequent pause in dosing and enrollment in fitusiran clinical studies in 2020 could contribute to further concerns about the safety of specific therapeutic candidates or therapeutic candidates for specific diseases. Even when we succeed in securing such alliances, we may not be able to maintain them if, for example, development or approval of a product candidate is delayed, challenges are raised as to the validity or scope of our intellectual property, we are unable to secure adequate reimbursement from payors or sales of an approved drug are lower than we expected.

Furthermore, any delay in entering into collaboration agreements would likely either delay the development and commercialization of certain of our product candidates and reduce their competitiveness even if they reach the market, or prevent the development of certain product candidates. Any such delay related to our collaborations could adversely affect our business.

For certain product candidates, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaborations with Regeneron, Novartis, Vir, Dicerna and Sanofi Genzyme. We may not, however, be able to enter into additional collaborations for certain other programs, and the terms of any collaboration agreement we do secure may not be favorable to us. If we are not successful in our efforts to enter into future collaboration arrangements with respect to one or more of our product candidates, we may not have sufficient funds to develop these product candidates or other product candidates internally, or to bring our product candidates to market. If we do not have sufficient funds to develop and bring our product candidates to market, we will not be able to generate revenues from these product candidates, and this will substantially harm our business.

***If any collaborator materially amends, terminates or fails to perform its obligations under agreements with us, the development and commercialization of our product candidates could be delayed or terminated.***

Our dependence on collaborators for capabilities and funding means that our business could be adversely affected if any collaborator materially amends or terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future collaborations, if any, may not be scientifically or commercially successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate. Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. In addition, our collaborators may have additional termination rights for convenience with respect to the collaboration or a particular program under the collaboration, under certain circumstances. For example, our agreement with MDCO, which was acquired by Novartis in January 2020, relating to the development and commercialization of inclisiran worldwide may be terminated by Novartis at any time upon four months' prior written notice, provided if the agreement is terminated by Novartis for convenience, Novartis must grant a license to us under certain of our technology developed in the course of MDCO's activities under the agreement, subject to a royalty to be negotiated between the parties. Moreover, any adverse actions by Novartis with respect to the MDCO agreement or disputes with Novartis regarding each party's rights and obligations under the MDCO agreement could adversely impact our ability to comply with our obligations under our agreements with Blackstone. If we were to lose a commercialization collaborator, we would have to attract a new collaborator or develop expanded sales, distribution and marketing capabilities internally, which would require us to invest significant amounts of financial and management resources.

In addition, if we have a dispute with a collaborator over the ownership of technology or other matters, or if a collaborator terminates its collaboration with us, for breach or otherwise, or determines not to pursue the research, development and/or commercialization of RNAi therapeutics, it could delay our development of product candidates, result in the need for additional company resources to develop product candidates, require us to expend time and resources to develop expanded sales and marketing capabilities on a more expedited timeline, make it more difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities.

Moreover, a collaborator, or in the event of a change in control of a collaborator or the assignment of a collaboration agreement to a third party, the successor entity or assignee, as in the case of MDCO and Novartis, could determine that it is in its interests to:

- pursue alternative technologies or develop alternative products, either on its own or jointly with others, that may be competitive with the products on which it is collaborating with us or which could affect its commitment to the collaboration with us;
- pursue higher-priority programs or change the focus of its development programs, which could affect the collaborator's commitment to us; or
- if it has marketing rights, choose to devote fewer resources to the marketing of our product candidates, if any are approved for marketing, than it does for product candidates developed without us.

If any of these occur, the development and commercialization of one or more products or product candidates could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue such development and commercialization on our own.

***We have limited manufacturing experience and resources and we must incur significant costs to develop this expertise and/or rely on third parties to manufacture our products.***

We have limited manufacturing experience. In order to continue to commercialize our approved products, continue to develop our current product candidates, including vutrisiran, apply for regulatory approvals and, if approved, commercialize future products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. Historically, our internal manufacturing capabilities were limited to small-scale production of material for use in in vitro and in vivo experiments that is not required to be produced under cGMP standards. During 2012, we developed cGMP capabilities and processes for the manufacture of patisiran formulated bulk drug product for late stage clinical trial use and commercial supply. In addition, during 2020, we completed construction and qualification of our cGMP manufacturing facility in Norton, Massachusetts where we will manufacture drug substance for clinical and, eventually, commercial use. In December 2020, we began cGMP operations, and we believe this facility will enable us to initiate manufacturing for multiple new early-stage programs over the next few years, as well as provide us the manufacturing capabilities to support our late-stage and commercial programs in the future.

At the present time, we may manufacture limited quantities of clinical trial materials ourselves, but otherwise we continue to rely on third parties to manufacture the drug substance and finished product we will require for any clinical trials that we initiate and to support the commercial supply of our approved products and any of our other product candidates. There are a limited number of manufacturers that supply synthetic siRNAs. We currently rely on a limited number of CMOs for our supply of synthetic siRNAs. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our CMOs to



meet our delivery time requirements or provide adequate amounts of material to meet our needs, and ultimately delay our clinical trials and potentially put at risk commercial supply, as well as result in additional expense to us. To fulfill our siRNA requirements, we will likely need to secure alternative suppliers of synthetic siRNAs and such alternative suppliers are limited and may not be readily available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. As noted above, in order to ensure long-term supply capabilities for our RNAi therapeutics, we are developing our own capabilities to manufacture drug substance for clinical and commercial use.

In addition to the manufacture of the synthetic siRNAs, we may have additional manufacturing requirements related to the technology required to deliver the siRNA to the relevant cell or tissue type, such as LNPs or conjugates. In some cases, the delivery technology we utilize is highly specialized or proprietary, and for technical and/or legal reasons, we may have access to only one or a limited number of potential manufacturers for such delivery technology. In addition, the scale-up of our delivery technologies could be very difficult and/or take significant time. We also have very limited experience in such scale-up and manufacturing, requiring us to depend on a limited number of third parties, who might not be able to deliver in a timely manner, or at all. Failure by manufacturers to properly manufacture our delivery technology and/or formulate our siRNAs for delivery could result in unusable product, supply delays and shortages. Furthermore, competition for supply from our manufacturers from other companies, a breach by such manufacturers of their contractual obligations or a dispute with such manufacturers would cause delays in our discovery and development efforts, as well as additional expense to us. The CARES Act was enacted in March 2020 in response to the COVID-19 pandemic. Under the CARES Act, manufacturers must have in place a risk management plan that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or active pharmaceutical ingredient is manufactured. The risk management plan will be subject to FDA review during an inspection. If we experience shortages in the supply of our marketed products, our results could be materially impacted. Since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and one of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials or commercial products, which could lead to delays in these trials or issues with our commercial supply.

In developing manufacturing capabilities by building our own manufacturing facilities, we have incurred substantial expenditures, and expect to incur significant additional expenditures in the future. Also, we have had to, and will likely need to continue to, hire and train qualified employees to staff our facilities. If we are unable to manufacture sufficient quantities of material or if we encounter problems with our facilities in the future, we may also need to secure alternative suppliers, and such alternative suppliers may not be available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. Given our dependence on a limited number of CMOs to supply our commercial products and clinical candidates, and our dependence on our own facility, any delay in supply caused by the COVID-19 pandemic could impact our ability to procure sufficient supplies for our approved products, and the development of our product candidates could also be delayed. Any delay or setback in the manufacture of our approved products could impede ongoing commercial supply, which could significantly impact our revenues and operating results. In addition, to the extent we or our partners rely on CMOs outside of the U.S. to supply drug substance for our product candidates, any delays or disruptions in supply caused by the COVID-19 pandemic could have a material adverse impact on the research and development activities and potential commercialization of our or our partners' product candidates.

The manufacturing process for our approved products and any other products that we may develop, is subject to the FDA and foreign regulatory authority approval process and we will need to meet, and will need to contract with CMOs who can meet, all applicable FDA and foreign regulatory authority requirements on an ongoing basis. In addition, if we receive the necessary regulatory approval for any product candidate, we also expect to rely on third parties, including potentially our commercial collaborators, to produce materials required for commercial supply. We may experience difficulty in obtaining adequate manufacturing capacity for our needs and the needs of our collaborators, who we have, in some instances, the obligation to supply. If we are unable to obtain or maintain CMOs for our product candidates and/or our marketed products, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our products.

To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we depend, and will depend in the future, on these third parties, to perform their obligations in a timely manner and consistent with contractual and regulatory requirements, including those related to quality control and quality assurance. The failure of any CMO to perform its obligations as expected, or, to the extent we manufacture all or a portion of our product candidates ourselves, our failure to execute on our manufacturing requirements, could adversely affect our business in a number of ways, including:

- we or our current or future collaborators may not be able to initiate or continue clinical trials of product candidates that are under development;
- we or our current or future collaborators may be delayed in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;
- we may lose the cooperation of our collaborators;
- our facilities and those of our CMOs, and our products could be the subject of inspections by regulatory authorities that could have a negative outcome and result in delays in supply;

- we may be required to cease distribution or recall some or all batches of our products or take action to recover clinical trial material from clinical trial sites; and
- ultimately, we may not be able to meet commercial demands for our products.

***We rely on third parties to conduct our clinical trials, and if they fail to fulfill their obligations, our development plans may be adversely affected.***

We rely on independent clinical investigators, contract research organizations, or CROs, and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our clinical trials. We have contracted, and we plan to continue to contract with, certain third parties to provide certain services, including site selection, enrollment, monitoring, auditing and data management services. These investigators and CROs are not our employees and we have limited control over the amount of time and resources 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 their time and resources away from our programs. Although we depend heavily on these parties, we control only certain aspects of their activity and therefore, we cannot be assured that these third parties will adequately perform all of their contractual obligations to us in compliance with regulatory and other legal requirements and our internal policies and procedures. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with applicable good clinical practice, or GCP, requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development, and to implement timely corrective action to any non-compliance. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites, including in connection with the review of marketing applications. If we or any of our CROs fail to comply with applicable GCP requirements, or fail to take any such corrective action, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, the Pharmaceuticals and Medical Devices Agency in Japan or comparable foreign regulatory authorities may require us to take additional action or perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority in the future, such regulatory authority will determine that any of our clinical trials comply with GCP regulations.

If our third-party service providers cannot adequately and timely fulfill their obligations to us for any reason, including due to disruptions caused by the COVID-19 pandemic on their operations or at the sites they are overseeing, or if the quality and accuracy of our clinical trial data is compromised due to failure by such third party to adhere to our protocols or regulatory requirements or if such third parties otherwise fail to meet deadlines, our development plans and/or regulatory reviews for marketing approvals may be delayed or terminated. As a result, our stock price would likely be negatively impacted, and our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate additional revenues could be delayed.

#### **Risks Related to Managing Our Operations**

***If we are unable to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors, in particular following our recently announced leadership transition, our ability to implement our business plan may be adversely affected.***

We are highly dependent upon our senior management and our scientific, clinical, sales and medical staff. We recently announced our first leadership transition as a publicly traded company with commercial operations. We believe we have put in place a capable management team well-positioned to execute our strategy. Nonetheless, this leadership transition may be viewed negatively by employees, investors and/or our strategic partners. Moreover, attrition associated with this transition could significantly delay or prevent the achievement of product development and commercialization, and other business objectives, and adversely impact our stock price. Our employment arrangements with our key personnel are terminable without notice. We do not carry key person life insurance on any of our employees.

We have grown our workforce significantly over the past several years and anticipate continuing to add additional employees as we focus on achieving our *Alnylam P<sup>5</sup>x25* strategy. We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to attract and reward qualified individuals than we do. In addition, due to the risks associated with developing a new class of medicine, we may face additional challenges in attracting and retaining employees. If we are not successful commercializing our approved products, we may be unable to attract and retain highly qualified sales and marketing professionals to support our approved products and our future products, if approved, including vutrisiran. Accordingly, we may be unable to attract and retain suitably qualified individuals in order to support our growing research, development and global commercialization efforts and initiatives, and our failure to do so could have an adverse effect on our ability to implement our future business plans.

***We may have difficulty expanding our operations successfully as we continue our evolution from a U.S.- and EU-based company primarily involved in discovery, pre-clinical testing and clinical development into a global company that develops and commercializes multiple drugs.***

As we continue the commercial launches of our approved products, and increase the number of product candidates we are developing, we will need to continue to expand our operations in the U.S. and further develop operations in the EU and other geographies, including Asia and Latin America. To date, we have received regulatory approval for ONPATTRO in the U.S., EU, Japan and other countries globally, and as a result of the January 2018 amendment to our Sanofi Genzyme collaboration, we have global development and commercialization rights for ONPATTRO. In addition, we have received regulatory approval for our second RNAi therapeutic, GIVLAARI in the U.S., EU, Brazil, Canada, Japan and have also filed for marketing approval in Switzerland. In November 2020, we received regulatory approval for our third RNAi therapeutic, OXLUMO in the U.S. and EU and in June 2021, we received regulatory approval for OXLUMO in Brazil. We plan to file for additional regulatory approvals for each of our commercially approved products in additional countries during the remainder of 2021 and beyond.

From 2016 through 2020, we grew our workforce significantly and anticipate continuing to hire additional employees globally in the future as we focus on the commercialization of ONPATTRO, GIVLAARI and OXLUMO, preparing for the potential launch of vutrisiran and achieving our *Alnylam* P5x25 strategy. This growth has placed a strain on our administrative and operational infrastructure and, as a result, we will need to continue to develop additional and/or new infrastructure and capabilities to support our growth and obtain additional space to conduct our global operations in the U.S., the EU, Japan, Latin America and other geographies. If we are unable to develop such additional infrastructure or obtain sufficient space to accommodate our growth in a timely manner and on commercially reasonable terms, our business could be negatively impacted. As we continue the commercialization of our approved products, and as the product candidates we develop enter and advance through clinical trials, we will need to continue to expand our global development, regulatory, manufacturing, quality, compliance, and marketing and sales capabilities, or contract with other organizations to provide these capabilities for us. In addition, as our operations continue to expand, we will need to successfully manage additional relationships with various collaborators, suppliers, distributors and other organizations. Our ability to manage our operations and future growth will require us to continue to enhance our operational, financial and management controls and systems, reporting systems and infrastructure, and policies and procedures. We may not be able to implement enhancements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

***The increasing use of social media could give rise to liability.***

Social media is increasingly being used to communicate about our clinical development programs and the diseases our investigational RNAi therapeutics are being developed to treat, and we are utilizing what we believe is appropriate social media in connection with our commercialization efforts for our approved products, and we intend to do the same for our future products, if approved, including vutrisiran. Social media practices in the biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities. For example, for our clinical-stage candidates, patients may use social media channels to comment on their experience in an ongoing blinded clinical study or to report an alleged AE. When such disclosures occur, there is a risk that study enrollment may be adversely impacted, we fail to monitor and comply with applicable adverse event, or AE, reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our investigational products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any online platform, including a blog on the internet, or a post on a website, that can be distributed rapidly and could negatively harm our reputation. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

***Our business and operations could suffer in the event of system failures or unauthorized or inappropriate use of or access to our systems.***

We are increasingly dependent on our information technology systems and infrastructure for our business. We collect, store and transmit sensitive information including intellectual property, proprietary business information and personal information in connection with business operations. The secure maintenance of this information is critical to our operations and business strategy. Some of this information could be an attractive target of criminal attack or unauthorized access and use by third parties with a wide range of motives and expertise, including organized criminal groups, "hacktivists," patient groups, disgruntled current or former employees and others. Cyber-attacks are of ever-increasing levels of sophistication, and despite our security measures, our information technology and infrastructure may be vulnerable to such attacks or may be breached, including due to employee error or malfeasance.

The pervasiveness of cybersecurity incidents in general and the risks of cyber-crime are complex and continue to evolve. Although we are making significant efforts to maintain the security and integrity of our information systems and are exploring various measures to manage the risk of a security breach or disruption, there can be no assurance that our security efforts and

measures will be effective or that attempted security breaches or disruptions would not be successful or damaging. Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage or interruption from computer viruses, unauthorized or inappropriate access or use, natural disasters, pandemics (including COVID-19), terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss of pre-clinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts, as well as delays in the commercialization of our products, and significantly increase our costs. To the extent that any disruption, security breach or unauthorized or inappropriate use or access to our systems were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, including but not limited to patient, employee or vendor information, we could incur notification obligations to affected individuals and government agencies, liability, including potential lawsuits from patients, collaborators, employees, stockholders or other third parties and liability under foreign, federal and state laws that protect the privacy and security of personal information, and the development and potential commercialization of our product candidates could be delayed.

***The results of the United Kingdom's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.***

Following the results of a referendum in 2016, the United Kingdom, or UK, left the EU on January 31, 2020, commonly referred to as "Brexit." Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK was subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules continued to apply, while the future relationship between the UK and EU was formally negotiated. The UK and the EU have signed an EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and has been formally applicable since May 1, 2021. This agreement provides details on how some aspects of the UK and EU's relationship will operate going forwards, however there are still many uncertainties. The long-term effects of Brexit will depend in part on how the EU-UK Trade and Cooperation Agreement, and any future agreements signed by the UK and the EU, take effect in practice. 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 and the wider commercial, legal and regulatory environment, could impact our current and future operations and clinical activities in the UK in the long term.

For example, Brexit could result in the UK significantly altering its regulations affecting the clearance or approval of our product candidates that are developed in the UK, now that UK legislation has the potential to diverge from EU legislation. Any new regulations could add time and expense to the conduct of our business, as well as the process by which our products receive regulatory approval in the UK, the EU and elsewhere. The uncertainty concerning the UK's legal, political and economic relationship with the EU following Brexit may also 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). Any of these effects of Brexit, among others, could adversely affect our business, our results of operations, liquidity and financial condition.

#### **Risks Related to Our Industry**

##### **Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates and the Commercialization of Our Approved Products**

***Any product candidates we or our partners develop may fail in development or be delayed to a point where they do not become commercially viable.***

Before obtaining regulatory approval for the commercial distribution of our product candidates, we must conduct, at our own expense, extensive nonclinical tests and clinical trials to demonstrate the safety and/or efficacy in humans of our product candidates. Nonclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome, and the historical failure rate for product candidates is high. We currently have multiple programs in clinical development, including internal and partnered programs in Phase 3 development, as well as several earlier-stage clinical programs. In January 2021, we announced positive topline results from the HELIOS-A Phase 3 study of vutrisiran, an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis. Based on these positive results, we submitted an NDA for vutrisiran with the FDA in April 2021, which was accepted by the FDA. The FDA has set an action date of April 14, 2022 under PDUFA, and indicated that they were not currently planning an advisory committee meeting as part of the NDA review. In September 2021, we presented additional 9-month data from the HELIOS-A Phase 3 study of vutrisiran, and submitted an MAA in the EU with the EMA. Further, in October 2021, we reported positive topline results for 18-month endpoints and safety from the HELIOS-A Phase 3 study of vutrisiran. However, we may not be able to further advance this or any other product candidate through clinical trials and regulatory approval.

Additionally, several of our planned and ongoing clinical trials, such as our HELIOS-A study, utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when

they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

If we enter into clinical trials, the results from nonclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in subsequent human clinical trials of that product candidate or any other product candidate. There is a high failure rate for drugs proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results. Moreover, our approved products and our current product candidates, employ novel delivery technologies that, with the exception of inclisiran, have yet to be extensively evaluated in human clinical trials and proven safe and effective.

In addition, we, the FDA or other applicable regulatory authorities, or an institutional review board, or IRB, or similar foreign review board or committee, may delay initiation of or suspend clinical trials of a product candidate at any time for various reasons, including if we or they believe the healthy volunteer subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, adverse side effects of a product candidate or related product on healthy volunteer subjects or patients in a clinical trial could result in our decision, or a decision by the FDA or foreign regulatory authorities, to suspend or terminate the trial, or, in the case of regulatory agencies, a refusal to approve a particular product candidate for any or all indications of use. For example, in October 2016, we announced our decision to discontinue development of revusiran, an investigational RNAi therapeutic that was being developed for the treatment of patients with cardiomyopathy due to hATTR amyloidosis. Our decision followed the recommendation of the revusiran ENDEAVOUR Phase 3 study Data Monitoring Committee to suspend dosing and the observation of an imbalance in mortality in revusiran-treated patients as compared to those on placebo.

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 age and condition of the patients, the stage and severity of disease, the availability of clinical trials for other investigational drugs for the same disease or condition, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. For example, we or our partners may experience difficulty enrolling our clinical trials, including, but not limited to, the ongoing clinical trials for fitusiran, due to the availability of existing approved treatments, as well as other investigational treatments in development. In addition, in November 2018 we announced that due to recruitment challenges, we had discontinued a Phase 2 study of cemdisiran in atypical hemolytic uremic syndrome and are focusing our cemdisiran clinical development efforts in a different indication. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments or safety concerns, including the impact of public health emergencies such as the COVID-19 pandemic, can result in increased costs, longer development times or termination of a clinical trial.

Although our investigational RNAi therapeutics have been generally well-tolerated in our clinical trials to date, new safety findings may emerge. For example, in September 2017, we announced that we had temporarily suspended dosing in all ongoing fitusiran studies pending further review of a fatal thrombotic SAE that occurred in a patient with hemophilia A without inhibitors who was receiving fitusiran in our Phase 2 OLE study. More recently, in October 2020, Sanofi Genzyme voluntarily paused dosing in all ongoing fitusiran clinical studies to assess reports of non-fatal thrombotic events in patients participating in the ATLAS Phase 3 program. Following an assessment of available data and alignment with regulators, patients restarted on fitusiran under amended protocols in ongoing adolescent and adult clinical studies. In October 2021, Sanofi Genzyme announced that a potential filing date for fitusiran has been moved to 2024 due to the introduction of a lower dose cohort in the ongoing phase 3 studies.

As demonstrated by the discontinuation of our revusiran program in October 2016, the temporary suspension of dosing in September 2017 in our fitusiran studies, as well as Sanofi Genzyme's voluntary pause of fitusiran studies in October 2020, the occurrence of SAEs and/or AEs can result in the suspension or termination of clinical trials of a product candidate by us, our partners, or the FDA or a foreign regulatory authority. The occurrence of SAEs and/or AEs could also result in refusal by the FDA or a foreign regulatory authority to approve a particular product candidate for any or all indications of use.

Clinical trials also require the review, oversight and approval of IRBs, or, outside of the U.S., an independent ethics committee, which continually review clinical investigations and protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB or ethics committee approval can prevent or delay the initiation and completion of clinical trials, and the FDA or foreign regulatory authorities may decide not to consider any data or information derived from a clinical

investigation not subject to initial and continuing IRB or ethics committee review and approval, as the case may be, in support of a marketing application.

Our product candidates that we develop may encounter problems during clinical trials that will cause us, an IRB, ethics committee or regulatory authorities to delay, suspend or terminate these trials, or that will delay or confound the analysis of data from these trials. If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected, or development of any of our other product candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected product candidate and for other product candidates we are developing.

A failure of one or more of our clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, nonclinical testing and the clinical trial process that could delay or prevent regulatory approval or our ability to commercialize our product candidates, including:

- our nonclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional nonclinical testing or clinical trials, or we may abandon projects that we expect to be promising;
- delays in filing IND applications or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs/ethics committees in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- conditions imposed on us by an IRB or ethics committee, or the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- problems in engaging IRBs or ethics committees to oversee clinical trials or problems in obtaining or maintaining IRB or ethics committee approval of trials;
- delays in enrolling patients and volunteers into clinical trials, and variability in the number and types of patients and volunteers available for clinical trials, including as a result of the COVID-19 pandemic;
- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including the current COVID-19 pandemic;
- high drop-out rates for patients and volunteers in clinical trials;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours;
- inadequate supply or quality of product candidate materials or other materials necessary for the conduct of our clinical trials or disruption or delays in the clinical supply due to the COVID-19 or a future pandemic;
- greater than anticipated clinical trial costs;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- poor or disappointing effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site or records of any clinical or nonclinical investigation;
- failure of our third-party contractors or investigators to comply with regulatory requirements, including GCP and cGMP, or otherwise meet their contractual obligations in a timely manner, or at all;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- interpretations of data by the FDA and similar foreign regulatory agencies that differ from ours.

Even if we successfully complete clinical trials of our product candidates, any given product candidate may not prove to be a safe and effective treatment for the disease for which it was being tested.

***We or our partners may be unable to obtain U.S. or foreign regulatory approval for our or our partnered product candidates and, as a result, we or our partners may be unable to commercialize such product candidates.***

Our and our partnered product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, pricing, marketing and distribution of drugs. Rigorous nonclinical 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 the product candidates we and our partners are developing will not obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

The time required to obtain FDA and other 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 nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We or our partners may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the drugs we or our partners are developing represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these drugs. The lack of policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we or our partners may submit. Moreover, the FDA may respond to these submissions by defining requirements we or our partners may not have anticipated. Such responses could lead to significant delays in the development of our or our partnered product candidates. In addition, because there may be approved treatments for some of the diseases for which we or our partners may seek approval, or treatments in development which are approved by the time we or they apply for approval, in order to receive regulatory approval, we or they may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Interruption or delays in the operations of the FDA, EMA and comparable foreign regulatory agencies due to the COVID-19 pandemic, may impact the review, inspection and approval timelines for our or our partnered product candidates. For example, as of May 26, 2021, the 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 and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. 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 ongoing COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In December 2020, the FDA issued a complete response letter regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the PDUFA action date due to unresolved facility inspection-related conditions. In July 2021, Novartis announced that the resubmission to the FDA of the inclisiran NDA to address the complete response letter was filed with an action date of January 1, 2022; however any such interruption or delay by the FDA, EMA or comparable foreign regulatory agency in light of the COVID-19 pandemic could have a material adverse effect on our efforts to obtain regulatory approval for our product candidates, including vutrisiran, or our collaborator Novartis' efforts to obtain FDA approval for inclisiran, which could have a material adverse effect on our financial results.

Any delay or failure in obtaining required approvals for our product candidates or our partnered product candidates could have a material adverse effect on our ability to generate revenues from any product candidate for which we or our partners may seek approval in the future. Furthermore, any regulatory approval to market any product may be subject to limitations on the approved uses for which we or our partners may market the product or the labeling or other restrictions, which could limit each such product's market opportunity and have a negative impact on our results of operations and our stock price. In addition, the FDA has the authority to require a Risk Evaluation and Mitigations Strategy, or REMS, plan as part of an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, 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. In the EU, we or our partners could be required to adopt a similar plan, known as a risk management plan, and our products could be subject to specific risk minimization measures, such as restrictions on prescription and supply, the conduct of post-marketing safety or efficacy studies, or the distribution of patient and/or prescriber educational materials. In either instance, these limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

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

***Even if we or our partners obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we or our partners fail to comply with continuing U.S. and foreign requirements, our approvals could be limited or withdrawn, we could be subject to other penalties, and our business would be seriously harmed.***

Following any initial regulatory approval of drugs we or our partners may develop, including our three approved drugs, we will also be subject to continuing regulatory oversight, including the review of adverse drug experiences and clinical results that

are reported after our drug products are made commercially available. This would include results from any post-marketing tests or surveillance to monitor the safety and efficacy of our approved drugs or other drug products required as a condition of approval or agreed to by us. The regulatory approvals that we receive for ONPATTRO, GIVLAARI and OXLUMO, as well as any regulatory approvals we receive for any other product candidates, including vutrisiran, may also be subject to limitations on the approved uses for which the product may be marketed. Other ongoing regulatory requirements include, among other things, submissions of safety and other post-marketing information and reports, registration and listing, as well as continued compliance with good practice quality guidelines and regulations, including current good manufacturing practice, or cGMP, requirements and GCP requirements for any clinical trials that we conduct post-approval. In addition, we are conducting, and intend to continue to conduct, clinical trials for our product candidates, and we intend to seek approval to market our product candidates, in jurisdictions outside of the U.S., and therefore will be subject to, and must comply with, regulatory requirements in those jurisdictions.

The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug and to require withdrawal of the product from the market. The FDA also has the authority to require a REMS plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. As our approved products are used commercially, we or others could identify previously unknown side effects or known side effects could be observed as being more frequent or severe than in clinical studies or earlier post-marketing periods, in which case:

- sales of our approved products may be more modest than originally anticipated;
- regulatory approvals for our approved products may be restricted or withdrawn;
- we may decide, or be required, to send product warning letters or field alerts to physicians, pharmacists and hospitals;
- additional nonclinical or clinical studies, changes in labeling, adoption of a REMS plan, or changes to manufacturing processes, specifications and/or facilities may be required; and
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above occurrences could reduce or prevent sales of our approved products, increase our expenses and impair our ability to successfully commercialize one or more of these products.

The CMO and manufacturing facilities we use to make our approved products and certain of our current product candidates, including our Cambridge facility, our Norton facility, and Agilent and other CMOs, will also be subject to periodic review and inspection by the FDA and other regulatory agencies. For example, Agilent and our Cambridge-based facility were subject to regulatory inspection by the FDA and the EMA in connection with the review of our applications for regulatory approval for ONPATTRO and GIVLAARI, and may be subject to similar inspection in connection with any subsequent applications for regulatory approval of one or more of our products filed in other territories. The discovery of any new or previously unknown problems with our facilities or our CMOs, or our or their manufacturing processes or facilities, may result in restrictions on the drug or CMO or facility, including delay in approval or, in the future, withdrawal of the drug from the market. We have developed cGMP capabilities and processes for the manufacture of patisiran formulated bulk drug product for commercial use. In addition, in 2020, we completed construction of a cGMP manufacturing facility for drug substance for clinical and, eventually, commercial use. We may not have the ability or capacity to manufacture material at a broader commercial scale in the future. We may manufacture clinical trial materials or we may contract a third party to manufacture these materials for us. Reliance on CMOs entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the CMO for regulatory compliance.

If we or our collaborators, CMOs or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we may seek to market our products, we or they may be subject to, among other things, fines, warning letters, holds on clinical trials, refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

***Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which could prevent us from becoming profitable.***

The product candidates that we are developing are based upon new technologies or therapeutic approaches. Key participants in pharmaceutical marketplaces, such as physicians, third-party payors and consumers, may not accept a product intended to improve therapeutic results based on RNAi technology. As a result, it may be more difficult for us to convince the medical community and third-party payors to accept and use our product, or to provide favorable reimbursement.

Other factors that we believe will materially affect market acceptance of our product candidates include:

- the timing of our receipt of any marketing approvals, the terms of any approvals and the countries in which approvals are obtained;



- the safety and efficacy of our product candidates, as demonstrated in clinical trials and as compared with alternative treatments, if any;
- relative convenience and ease of administration of our product candidates;
- the willingness of patients to accept potentially new routes of administration or new or different therapeutic approaches and mechanisms of action;
- the success of our physician education programs;
- the availability of adequate government and third-party payor reimbursement;
- the pricing of our products, particularly as compared to alternative treatments, and the market perception of such prices and any price increase that we may implement in the future; and
- availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat and the relative risks, benefits and costs of those treatments.

For example, ONPATTRO utilizes an intravenous mode of administration with pre-medication that physicians and/or patients may not readily adopt, or which may not compete favorably with other available options, including inotersen, marketed by Akcea in several countries, which is administered subcutaneously, or tafamidis, marketed by Pfizer in several countries, which is in pill form. In addition, fitusiran represents a new approach to treating hemophilia which may not be readily accepted by patients and their caregivers.

***We are a multi-product commercial company, and expect to continue to invest significant financial and management resources to continue to build our marketing, sales, market access and distribution capabilities and further establish our global commercial infrastructure. Even if we successfully scale our commercial capabilities, the market may not be receptive to our commercial products.***

We are a young commercial company, having received our first product approval only three years ago, and have established our capabilities for marketing, sales, market access and distribution over the last several years. We currently expect to rely on third parties to launch and market certain of our product candidates in certain geographies, if approved. However, we intend to commercialize ONPATTRO, GIVLAARI and OXLUMO, as well as several of our late-stage product candidates if approved, including vutrisiran, on our own globally in major markets. Accordingly, we have developed internal marketing, sales, market access and distribution capabilities as part of our core product strategy initially in the U.S., Europe and Japan, with expansion ongoing globally, which has, and will continue to, require significant financial and management resources. For those products for which we will perform marketing, sales, market access and distribution functions ourselves, including ONPATTRO, GIVLAARI, OXLUMO and, if approved, vutrisiran, and for future products we successfully develop where we may retain certain product development and commercialization rights, we could face a number of additional risks, including:

- developing and retaining our global sales, marketing and administrative infrastructure and capabilities;
- hiring, training, managing and supervising our personnel worldwide;
- the cost of establishing, or leveraging an established, marketing or sales force, which may not be justifiable in light of the revenues generated by any particular product and/or in any specific geographic region; and
- our direct sales and marketing efforts may not be successful.

If we are unable to continue to develop and scale our own global marketing, sales, market access and distribution capabilities for ONPATTRO, GIVLAARI, OXLUMO and any future products, including vutrisiran, we will not be able to successfully commercialize our products without reliance on third parties.

***The patient populations suffering from hATTR amyloidosis, AHP and PH1 are small and have not been established with precision. If the actual number of patients is smaller than we estimate, or if we cannot raise awareness of these diseases and diagnosis is not improved, our revenue and ability to achieve profitability from these products may be adversely affected.***

Our estimates regarding the potential market size for ONPATTRO, GIVLAARI, OXLUMO or any future products, including vutrisiran, at the time we commence commercialization, may be materially different from the actual market size, including as a result of the indication approved by regulatory authorities, which could result in significant changes in our business plan and may have a material adverse effect on our results of operations and financial condition. For example, the indication approved by the FDA for ONPATTRO is for the treatment of the polyneuropathy of hATTR amyloidosis and not for the treatment of cardiomyopathy or other manifestations of the disease. In addition, the U.S. label does not include data from the exploratory cardiac endpoints included in our APOLLO Phase 3 study. This could have an adverse impact on the market opportunity for ONPATTRO in the U.S. In addition, our efforts to raise disease awareness and improve diagnosis of hATTR amyloidosis have been and may in the future be impacted by the COVID-19 pandemic. For example, Alnylam Act<sup>®</sup>, our third-party genetic screening initiative in the U.S., Canada and Brazil, experienced a decrease in submitted samples in the second quarter of 2020 as a result of the COVID-19 pandemic. As is the case with most orphan diseases, if we cannot successfully raise awareness of these diseases and improve diagnosis, it will be more difficult or impossible to achieve profitability.

***We may incur significant liability if enforcement authorities allege or determine that we are engaging in commercial activities or promoting our commercially approved products in a way that violates applicable regulations.***

Physicians have the discretion to prescribe approved drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Off-label uses are common across medical specialties. Although the FDA and other regulatory agencies that approve drug products do not regulate a physician's practice of medicine or choice of treatments, the FDA and other regulatory agencies regulate a manufacturer's communications regarding off-label use and prohibit off-label promotion, as well as the dissemination of false or misleading labeling or promotional materials, including by their agents. Manufacturers and their agents may not promote drugs for off-label uses or provide off-label information in the promotion of drug products that is not consistent with the approved labeling for those products. For example, we may not promote ONPATTRO in the U.S. for use in any indications other than the treatment of the polyneuropathy of hATTR amyloidosis in adults. The FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained. In April 2021, we received a subpoena from the U.S. Department of Justice, U.S. Attorney's Office for the District of Massachusetts, requiring production of documents pertaining to our marketing and promotion of ONPATTRO (patisiran) in the U.S. We are cooperating with the U.S. Attorney's Office and producing documents in response to the subpoena. Current and former officers and employees also have received subpoenas in connection with the preservation and production of related materials. Given the ongoing nature of the investigation, it is possible that the U.S. Attorney's Office for the District of Massachusetts or other government entities may request other information from, or issue other subpoenas, findings or similar documents to, us, our related entities and their respective directors, officers and employees. If we are found to have improperly marketed or promoted ONPATTRO in connection with such subpoenas, we may be subject to a broad range of civil, administrative and criminal penalties, including injunctive relief related to ONPATTRO promotional activities, substantial fines or penalties, and other legal or equitable sanctions. Any adverse decision, finding, allegation, or exercise of enforcement or regulatory discretion could harm our business, prospects, operating results, and financial condition. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Notwithstanding regulations related to product promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading and non-promotional scientific exchange concerning their products, and we intend to engage in medical education activities and communicate with healthcare providers in compliance with all applicable laws and regulatory guidance. Nonetheless, the FDA, other applicable regulatory authorities, competitors, and other third parties may take the position that we are not in compliance with such regulations, and if such non-compliance is proven, it could harm our reputation, financial condition or divert financial and management resources from our core business, and would have a material adverse effect on our business, financial condition and results of operations. Moreover, any threatened or actual government enforcement actions or lawsuits by third parties could also generate adverse publicity, which could decrease demand for our products and require that we devote substantial resources that could be used productively on other aspects of our business.

In addition to our medical education efforts, we also offer patient support services to assist patients receiving treatment with our commercially approved products. Manufacturers have increasingly become the focus of government investigation of patient support programs based on allegations that through such services illegal inducements are provided to physicians and/or patients, leading to improper utilization of government resources through Medicare, Medicaid and other government programs. Companies that are found to have violated laws such as the federal Anti-Kickback Statute and/or False Claims Act, or FCA, face significant liability, including civil and administrative penalties, criminal sanctions, and potential exclusion from participation in government programs. We have designed our programs in a manner that we believe complies with all applicable laws and regulations and have implemented a robust compliance program to support a compliant corporate culture and compliance with such laws.

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

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. We are actively monitoring these regulations as we market and sell ONPATTRO, GIVLAARI and OXLUMO, and as several of our other programs move through late stages of development. However, a number of our programs are currently in the earlier stages of development and we will not be able to assess the impact of price regulations for such programs for a number of years. We might obtain regulatory approval for a product, including one or more of our approved products, 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 and potentially in other countries due to reference pricing.

Our ability to commercialize our approved products or any future products, including vutrisiran, successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. One or more of our approved

products and other products for which we are able to obtain marketing approval, including vutrisiran, may not be considered cost-effective, and the amount reimbursed may be insufficient to allow us to sell such product(s) or any future products, including vutrisiran on a competitive basis. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for drug products. In the U.S., we have entered into at least 30 value-based agreements, or VBAs, and are negotiating additional VBAs with commercial health insurers. The goal of these agreements is to ensure that we are paid based on the ability of our commercially approved products to deliver results in the real world setting comparable to those demonstrated in clinical trials, and the agreements are structured to link our approved products' performance in real-world use to financial terms. Partnering with payers on these agreements is intended to provide more certainty to them for their investment and help accelerate coverage decisions for patients. If the prices we are able to charge for our products, or the reimbursement provided for such products, is inadequate in light of our development and other costs, or if reimbursement is denied, our return on investment could be adversely affected. In addition, we have stated publicly that we intend to grow through continued scientific innovation rather than arbitrary price increases. Specifically, we have stated that we will not raise the price of any product for which we receive marketing approval over the rate of inflation, as determined by the consumer price index for urban consumers (approximately 5.3% currently) absent a significant value driver. Our patient access philosophy could also negatively impact the revenues we are able to generate from the sale of one or more of our products in the future.

Some of the drugs we market need to be administered under the supervision of a physician or other healthcare professional on an outpatient basis, including ONPATTRO, GIVLAARI and OXLUMO. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under the Medicare Part B program if:

- they are incident to a physician's services;
- they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice; and
- they have been approved by the FDA and meet other requirements of the statute.

There may be significant delays in obtaining coverage for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or foreign regulatory authorities. Moreover, eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution or that covers a particular provider's cost of acquiring the drug. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S.

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 drugs, 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 U.S. Department of Health and Human Services, or HHS, to provide a report on actions to combat excessive pricing of prescription drugs, continue to clarify and improve the approval framework for generic drugs and identify and address any efforts to impede generic drug competition, 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. In response, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the Most Favored Nation, or MFN, Model may materially and adversely affect the price we receive for any of our commercially approved products. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the MFN Model under which Medicare Part B reimbursement rates will be calculated for certain drugs 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. However, on August 6, 2021, CMS announced a proposed rule to rescind the MFN rule. 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. Pursuant to court order, the removal and additional of the aforementioned safe harbors have been delayed until

January 1, 2023. 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 it will continue to seek new legislative measures to control drug costs.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

A number of other legislative and regulatory changes in the healthcare system in the U.S. and other major healthcare markets have been proposed or enacted in recent months and years, and such efforts have expanded substantially in recent years. These developments could, directly or indirectly, affect our ability to sell ONPATTRO, GIVLAARI, OXLUMO or future products, if approved, including vutrisiran, at a favorable price.

In particular, in March 2010, the Patient Protection and Affordable Care Act, also referred to as the Affordable Care Act, or the ACA, was signed into law. This legislation changed the system of healthcare insurance and benefits intended to broaden coverage and control costs. The law also contains provisions that affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Among the provisions affecting pharmaceutical companies are the following:

- Mandatory rebates for drugs sold into the Medicaid program were increased, and the rebate requirement was extended to drugs used in risk-based Medicaid managed care plans.
- The 340B Drug Pricing Program under the Public Health Service Act was extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.
- Pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the “donut hole.”
- Pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company’s market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.
- The law provides that approval of an application for a follow-on biologic product may not become effective until 12 years after the date on which the reference innovator biologic product was first licensed by the FDA, with a possible six-month extension for pediatric products. After this exclusivity ends, it will be easier for generic manufacturers to enter the market, which is likely to reduce the pricing for such products and could affect our profitability.
- The law creates a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected.
- The law expands eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer’s Medicaid rebate liability.
- The law expands the entities eligible for discounts under the Public Health Service Act pharmaceutical pricing program.
- The law expands healthcare fraud and abuse laws, including the civil FCA and the federal Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance.
- The law establishes new requirements to report financial arrangements with physicians and teaching hospitals and to annually report drug samples that manufacturers and distributors provide to physicians.
- The law establishes a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.
- The law established the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery methods.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year,

which went into effect in April 2013 and will remain in effect through 2030; however, pursuant to the CARES Act, and subsequent legislation, these Medicare sequester reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for our approved products or any of our product candidates for which we may obtain regulatory approval, including vutrisiran, or the frequency with which our products or any future product, including vutrisiran, is prescribed or used.

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

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. 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.

At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing. Some of these measures include price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the U.S. to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from one or more of our approved products or other product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

***We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Failure to comply with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.***

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. From time to time, we may engage third parties to conduct clinical trials outside of the U.S., to sell our products abroad, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

***Governments outside the U.S. may impose strict price controls, which may adversely affect our revenues.***



The pricing of prescription pharmaceuticals is also subject to governmental control outside the U.S. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

In some countries, including Member States of the EU, or Japan, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Moreover, political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of a product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval, which is time-consuming and costly. We cannot be sure that such prices and reimbursement will be acceptable to us or our strategic partners. 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 pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of our approved products or any future products, including vutrisiran, in those countries would be negatively affected. Another impact from the tightening pricing control could be felt from greater competition from less expensive generic or biosimilar products once the exclusivity expires; the governments have adopted policies to switch prescribed products to generic versions in order to cut the medical cost.

***If we or our collaborators, CMOs or service providers fail to comply with healthcare laws and regulations, or legal obligations related to privacy, data protection and information security, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our products and may harm our reputation.***

As a manufacturer of pharmaceuticals, we are subject to federal, state, and comparable foreign healthcare laws and regulations pertaining to fraud and abuse and patients' rights, in addition to legal obligations related to privacy, data protection and information security. These laws and regulations include:

- The U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid.
- The U.S. federal false claims laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government-funded programs such as Medicare or Medicaid that are false or fraudulent, making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which imposes requirements relating to the privacy, security, and transmission of individually identifiable health information; and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information.
- The U.S. federal Open Payments requirements, which were implemented by the CMS pursuant to the Physician Payments Sunshine Act as part of the ACA. Under the Open Payments Program, manufacturers of medical devices, medical supplies, biological products and drugs covered by Medicare, Medicaid and the Children's Health Insurance Programs must report transfers of value, including consulting fees, travel reimbursements, research grants, and other

payments made to physicians (currently 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. Legislation passed in 2018 expands the scope of covered recipients to non-physician providers such as physician assistants and advanced practice nurses, effective in 2022.

- Federal statutory and regulatory requirements applicable to pricing and sales of product to Federal Government Agencies.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- State and foreign laws comparable to each of the above federal laws, including in the EU laws prohibiting giving healthcare professionals any gift or benefit in kind as an inducement to prescribe our products, national transparency laws requiring the public disclosure of payments made to healthcare professionals and institutions, and data privacy laws, in addition to anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to government reimbursement programs, patient data privacy and security.
- European Privacy Laws including Regulation 2016/679, known as the General Data Protection Regulation, or the GDPR, and the e-Privacy Directive (2002/58/EC), and the national laws implementing each of them, as well as the privacy laws of Japan and other territories. Failure to comply with our obligations under the privacy regime could expose us to significant fines and/or adverse publicity, which could have material adverse effects on our reputation and business.
- The California Consumer Privacy Act of 2018, or CCPA, effective as of January 1, 2020, that gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation.

Some state laws also require pharmaceutical manufacturers to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In the EU, the GDPR replaced the EU Data Protection Directive on May 25, 2018. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, such as including requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such information outside the European Economic Area, or EEA, including to the U.S., providing details to those individuals regarding the processing of their personal data, implementing safeguards to keep personal data secure, having data processing agreements with third parties who process personal data, providing information to individuals regarding data processing activities, responding to individuals' requests to exercise their rights in respect of their personal data, obtaining consent of the individuals to whom the personal data relates, reporting security and privacy breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR substantially increases the penalties to which we could be subject in the event of any non-compliance, including fines of up to €20,000,000 or 4% of total annual global revenue, whichever is greater. The GDPR increases the responsibility and liability of pharmaceutical companies in relation to processing personal data, and companies may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules. In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. 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. Although the UK is regarded as a third country under the EU's GDPR, the EC has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the UK remain unrestricted. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing.

If our operations are found to be in violation of any of the aforementioned requirements, we may be subject to penalties, including civil or criminal penalties (including individual imprisonment), criminal prosecution, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, or the imposition of a corporate integrity agreement with the Office of Inspector General of the Department of Health

and Human Services, any of which could adversely affect our financial results. We are continuing to establish our global compliance infrastructure following the commercial launch of our three products over the last three years in the U.S., EU and multiple other geographies, and as we prepare for the launch of our products in additional countries, assuming regulatory approvals. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

If we or our collaborators, CMOs 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 approved products, or any other future 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;
- untitled letters or warning 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;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- product seizures;
- injunctions; and
- civil and criminal penalties, up to and including criminal prosecution resulting in fines, exclusion from healthcare reimbursement programs and imprisonment.

Moreover, federal, state or foreign laws or regulations are subject to change, and while we, our collaborators, CMOs and/or service providers currently may be compliant, that could change due to changes in interpretation, prevailing industry standards or the legal structure.

***We are subject to governmental regulation and other legal obligations, particularly related to privacy, data protection and information security, and we are subject to consumer protection laws that regulate our marketing practices and prohibit unfair or deceptive acts or practices. Our actual or perceived failure to comply with such obligations could harm our business.***

The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for “special category data,” which includes health, biometric and genetic information of data subjects located in the EU and UK. Further, GDPR provides a broad right for EU Member States to create supplemental national laws, such as laws relating to the processing of health, genetic and biometric data, which could further limit our ability to use and share such data or could cause our costs to increase, and harm our business and financial condition. GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedy in the event the individual believes his or her rights have been violated.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States, which may deviate slightly from the GDPR, may result in fines of up to 4% of total global annual revenue, or €20,000,000, whichever is greater, and in addition to such fines, we may be the subject of litigation and/or adverse publicity, which could have material adverse effect on our reputation and business. As a result of the implementation of the GDPR, we are required to put in place additional mechanisms to ensure compliance with the new data protection rules. For example, the GDPR requires us to make more detailed disclosures to data subjects, requires disclosure of the legal basis on which we can process personal data, may make it harder for us to obtain valid consent for processing, will require the appointment of a data protection officer where sensitive personal data (i.e., health data) is processed on a large scale, introduces mandatory data breach notification requirements throughout the EU and UK, imposes additional obligations on us when we are contracting with service providers and requires us to adopt appropriate privacy governance including policies, procedures, training and data audit.



Significantly, the GDPR imposes strict rules on the transfer of personal data out of the EU to the U.S. or other regions that have not been deemed to offer “adequate” privacy protections. In the past, companies in the U.S. were able to rely upon the EU-U.S. and the Swiss-U.S. Privacy Shield frameworks to legitimize data transfers from the EU and the UK to the U.S. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C-311/18 (Data Protection Commissioner v Facebook Ireland and Maximillian Schrems, or Schrems II) invalidated the EU-U.S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U.S. The CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the EC are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case-by-case basis to ensure the law in the recipient country provides “essentially equivalent” protections to safeguard the transferred personal data as the EU, and required businesses to adopt supplementary measures if such standard is not met. Subsequent guidance published by the European Data Protection Board in June 2021 described what such supplementary measures must be, and stated that businesses should avoid or cease transfers of personal data if, in the absence of supplementary measures, equivalent protections cannot be afforded. On June 4, 2021, the EC published new versions of the SCCs, which seek to address the issues identified by the CJEU’s Schrems II decision and provide further details regarding the transfer assessments that the parties are required to conduct when implementing the New SCCs. However, there continue to be concerns about whether the SCCs and other mechanisms will face additional challenges. Similarly, the Swiss data protection authority determined the Swiss-U.S. Privacy Shield framework was no longer a valid mechanism for Swiss-U.S. data transfers and also raised questions about the validity of the SCCs as a mechanism for transferring personal data from Switzerland. While Standard Contractual Clauses provide an alternative to our Privacy Shield certification for EU-U.S. data flows, the decision (and certain regulatory guidance issued in its wake) casts doubt on the legality of EU-U.S. data flows in general. Any inability to transfer personal data from the EU to the U.S. in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. The UK is not subject to the EC’s new SCCs but has published a draft version of its International Transfer Agreement, which, once finalized, will enable transfer from the UK.

We are subject to the supervision of local data protection authorities in those jurisdictions where we are monitoring the behavior of individuals in the EU or UK (i.e., undertaking clinical trials). We depend on a number of third parties in relation to the provision of our services, a number of which process personal data of EU and/or UK individuals on our behalf. With each such provider we enter or intend to enter into contractual arrangements under which they are contractually obligated to only process personal data according to our instructions, and conduct or intend to conduct diligence to ensure that they have sufficient technical and organizational security measures in place.

We are also subject to evolving European privacy laws on electronic marketing and cookies. The EU is in the process of replacing the e-Privacy Directive (2002/58/EC) with a new set of rules taking the form of a regulation, which will be directly implemented in the laws of each European member state, without the need for further enactment. While the e-Privacy Regulation was originally intended to be adopted on May 25, 2018 (alongside the GDPR), it is still going through the European legislative process. Draft regulations were rejected by the Permanent Representatives Committee of the Council of EU on November 22, 2019; it is not clear when new regulations will be adopted.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals’ privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

***Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending and services, and any inability on our part to effectively adapt to such changes could substantially affect our financial position, results of operations and cash flows.***

Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least \$1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. Certain of these automatic cuts have been implemented resulting in reductions in Medicare payments to physicians, hospitals, and other healthcare providers, among other things. Due to legislation amending the statute, including the Bipartisan Budget Act of 2018, these reductions will stay in effect through 2030 unless additional Congressional action is taken. Pursuant to the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic. The full impact on our business of these automatic cuts is uncertain.

If other federal spending is reduced, any budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function. 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 our approved products and any other products we may develop, including vutrisiran.

***There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.***

Our business exposes us to significant potential product liability risks that are inherent in the development, testing, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. Following the decision to discontinue clinical development of revusiran, we conducted a comprehensive evaluation of available revusiran data. We reported the results of this evaluation in August 2017, however, our investigation did not result in a conclusive explanation regarding the cause of the mortality imbalance observed in the ENDEAVOUR Phase 3 study. In addition, in September 2017, we announced that we had temporarily suspended dosing in all ongoing fitusiran studies pending further review of a fatal thrombotic SAE and agreement with regulatory authorities on a risk mitigation strategy. Notwithstanding the risks undertaken by all persons who participate in clinical trials, and the information on risks provided to study investigators and patients participating in our clinical trials, including the revusiran and fitusiran studies, it is possible that product liability claims will be asserted against us relating to the worsening of a patient's condition, injury or death alleged to have been caused by one of our product candidates, including revusiran or fitusiran. Such claims might not be fully covered by product liability insurance. In addition, product liability claims could result in an FDA investigation of the safety and effectiveness of our approved products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used, or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. We currently have product liability insurance that we believe is appropriate for our stage of development, including the marketing and sale of our approved products. 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 or insider trading violations, which could significantly harm our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with governmental regulations, comply with healthcare fraud and abuse and anti-kickback laws and regulations in the U.S. and abroad, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including improper trading based upon, information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics and a robust compliance program, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

***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, chemicals and various radioactive compounds. We maintain quantities of various flammable and toxic chemicals in our facilities in Cambridge and Norton that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Cambridge and Norton facilities comply with the relevant guidelines of the City of Cambridge, the town of Norton, 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 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, hazardous or radioactive 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.

### **Risks Related to Patents, Licenses and Trade Secrets**

***If we are not able to obtain and enforce patent protection for our discoveries, our ability to develop and commercialize our product candidates will be harmed.***

Our success depends, in part, on our ability to protect proprietary compositions, methods and technologies that we develop under the patent and other intellectual property laws of the U.S. and other countries, so that we can prevent others from unlawfully using our inventions and proprietary information. However, we may not hold proprietary rights to some patents required for us to manufacture and commercialize our proposed products. Because certain U.S. patent applications are confidential until the patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date which will not be filed in foreign countries, third parties may have filed patent applications for subject matter covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over those applications. For this and other reasons, we may be unable to secure desired patent rights, thereby losing desired exclusivity. Further, we or our licensees may be required to obtain licenses under third-party patents to market one or more of our or our partner's approved products, or further develop and commercialize future products, or continue to develop candidates in our pipeline being developed by us or our licensees. If licenses are not available to us or not available on reasonable terms, we or our licensees may not be able to market the affected products or conduct the desired activities.

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we may rely on third-party collaborators to file patent applications relating to proprietary technology that we develop jointly during certain collaborations. The process of obtaining patent protection is expensive and time-consuming. If our present or future collaborators fail to file and prosecute all necessary and desirable patent applications at a reasonable cost and in a timely manner, our business may be adversely affected. Despite our efforts and the efforts of our collaborators to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary. While issued patents are presumed valid, this does not guarantee that the patent will survive a validity challenge or be held enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, adjudged unenforceable or circumvented by parties attempting to design around our intellectual property. Moreover, third parties or the United States Patent and Trademark Office, or USPTO, may commence interference proceedings involving our patents or patent applications. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications, would be costly, would require significant time and attention of our management, could reduce or eliminate royalty payments to us from third party licensors and could have a material adverse effect on our business.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. Similarly, the ultimate degree of protection that will be afforded to biotechnology inventions, including ours, in the U.S. and foreign countries, remains uncertain and is dependent upon the scope of the protection decided upon by patent offices, courts and lawmakers. Moreover, there are periodic discussions in the Congress of the United States and in international jurisdictions about modifying various aspects of patent law. For example, the America Invents Act, or AIA, included a number of changes to the patent laws of the U.S. If any of the enacted changes do not provide adequate protection for discoveries, including our ability to pursue infringers of our patents for substantial damages, our business could be adversely affected. One major provision of the AIA, which took effect in March 2013, changed U.S. patent practice from a first-to-invent to a first-to-file system. If we fail to file an invention before a competitor files on the same invention, we no longer have the ability to provide proof that we were in possession of the invention prior to the competitor's filing date, and thus would not be able to obtain patent protection for our invention. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents.

Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims that will be allowed in any patents issued to us or to others. We also rely to a certain extent on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.

Failure to obtain and maintain all available regulatory exclusivities, broad patent scope and to maximize patent term restoration or extension on patents covering our products may lead to loss of exclusivity and early generic entry resulting in a loss of market share and/or revenue.

***We license patent rights from third-party owners. If such owners do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, our competitive position and business prospects may be harmed.***

We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business. In particular, we have obtained licenses from, among others, Stanford University, Ionis, the Massachusetts Institute of Technology, or MIT, Whitehead Institute for Biomedical Research, or Whitehead, Max Planck Innovation GmbH (formerly known as Garching Innovation GmbH), or Max Planck, Arbutus Biopharma Corp., or Arbutus, and Dicerna. We also intend to enter into additional licenses to third-party intellectual property in the future.

Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents issue in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we sublicense our rights under various third-party licenses to our collaborators. Any impairment of these sublicensed rights could result in reduced revenues under our collaboration agreements or result in termination of an agreement by one or more of our collaborators.

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

RNAi is a relatively new scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of RNAi patents and have licensed many of these patents from third parties on an exclusive basis. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics.

Specifically, we have a portfolio of patents, patent applications and other intellectual property covering: fundamental aspects of the structure and uses of siRNAs, including their use as therapeutics, and RNAi-related mechanisms; chemical modifications to siRNAs that improve their suitability for therapeutic and other uses; siRNAs directed to specific targets as treatments for particular diseases; delivery technologies, such as in the fields of carbohydrate conjugates and cationic liposomes; and all aspects of our specific development candidates.

As the field of RNAi therapeutics is maturing, patent applications are being fully processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference, re-examination and opposition proceedings, as well as *inter partes* and post-grant review proceedings introduced by provisions of the AIA, which became available to third party challengers on September 16, 2012, in various patent offices relating to patent rights in the RNAi field. In addition, third parties may challenge the validity of our patents. For example, a third party has filed an opposition in the European Patent Office, or EPO, against our owned patent EP 2723758, with claims directed to compositions and methods of ANGPTL3, arguing that the granted claims are invalid. An oral hearing was held at the EPO on February 17, 2021 where the patent was revoked. A notice of appeal of the EPO's decision was filed on June 23, 2021. We expect that additional oppositions will be filed in the EPO and elsewhere, and other challenges will be raised relating to other patents and patent applications in our portfolio. In many cases, the possibility of appeal 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. 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.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need for our siRNA marketed products, our late-stage therapeutic candidates being developed by us or our licensees, including vutrisiran, inclisiran and fitusiran, as well as our other pipeline products. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for siRNA drugs we wish to develop. In addition, there may be issued and pending patent applications that may be asserted against us in a court proceeding or otherwise based upon the asserting party's belief that we may need such patents for our siRNA therapeutic candidates or marketed products, or further develop and commercialize future products such as inclisiran, currently under review with the FDA, or continuing to develop candidates in our pipeline being developed by us or our licensees. Thus, it is possible that one or more organizations will hold patent rights to which we may need a license, or hold patent rights which could be asserted against us. If those organizations refuse to grant us a license to such patent rights on reasonable terms and/or a court rules that we need such patent rights that have been asserted against us and we are not able to obtain a license on reasonable terms, we may be unable to market products, including

ONPATTRO, GIVLAARI or OXLUMO, or perform research and development or other activities covered by such patents. For example, during 2017 and 2018, Silence filed claims in several jurisdictions, including the High Court of England and Wales, and named us and our wholly owned subsidiary Alnylam UK Ltd. as co-defendants. Silence alleged various claims, including that ONPATTRO infringed one or more Silence patents. There were also a number of related actions brought by us or Silence in connection with this intellectual property dispute. In December 2018, we entered into a Settlement and License Agreement with Silence, resolving all ongoing claims, administrative proceedings, and regulatory proceedings worldwide between us regarding, among other issues, patent infringement, patent invalidity and breach of contract.

***If we become involved in patent litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, substantial liability for damages or be required to stop our product development and commercialization efforts.***

Third parties may sue us for infringing their patent rights. For example, in October 2017 Silence sued us in the UK alleging that ONPATTRO and other investigational RNAi therapeutics we or MDCO are developing infringed one or more Silence patents. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others or protect our proprietary information and trade secrets. For example, during the second quarter of 2015, we filed a trade secret misappropriation lawsuit against Dicerna to protect our rights in the RNAi assets we purchased from Merck Sharp & Dohme Corp., or Merck. We and Dicerna settled the ongoing litigation between us in April 2018 and in December 2018 we and Silence settled all ongoing litigation between us. A third party may also claim that we have improperly obtained or used its confidential or proprietary information.

In protecting our intellectual patent rights through litigation or other means, a third party may claim that we have improperly asserted our rights against them. For example, in August 2017, Dicerna successfully added counterclaims against us in the above-referenced trade secret lawsuit alleging that our lawsuit represented abuse of process and claiming tortious interference with its business. In addition, in August 2017, Dicerna filed a lawsuit against us in the United States District Court of Massachusetts alleging attempted monopolization by us under the Sherman Antitrust Act. As noted above, in April 2018, we and Dicerna settled the ongoing litigation between us.

Furthermore, third parties may challenge the inventorship of our patents or licensed patents. For example, in March 2011, The University of Utah, or Utah, filed a complaint against us, Max Planck Gesellschaft Zur Foerderung Der Wissenschaften e.V. and Max Planck Innovation, together, Max Planck, Whitehead, MIT and the University of Massachusetts, claiming that a professor of Utah was the sole inventor, or in the alternative, a joint inventor of certain of our in-licensed patents. Utah was seeking correction of inventorship of the Tuschl patents, unspecified damages and other relief. After several years of court proceedings and discovery, the court granted our motions for summary judgment, and dismissed Utah's state law damages claims as well. During the pendency of this litigation, as well as the Arbutus and Dicerna litigation described above, we incurred significant costs, and in each case, the litigation diverted the attention of our management and other resources that would otherwise have been engaged in other activities.

In addition, in connection with certain license and collaboration agreements, we have agreed to indemnify certain third parties for certain costs incurred in connection with litigation relating to intellectual property rights or the subject matter of the agreements. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and litigation would divert our management's efforts. 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 any litigation or legal proceeding could delay our research, development and commercialization efforts and limit our ability to continue our operations.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon or otherwise violates their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties' patent rights. In addition to any damages we might have to pay, a court could issue an injunction requiring us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially reasonable terms, if at all. In addition, such licenses are likely to be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Moreover, we expect that a number of our collaborations will provide that royalties payable to us for licenses to our intellectual property may be offset by amounts paid by our collaborators to third parties who have competing or superior intellectual property positions in the relevant fields, which could result in significant reductions in our revenues from products developed through collaborations.

***If we fail to comply with our obligations under any licenses or related agreements, we may be required to pay damages and could lose license or other rights that are necessary for developing, commercializing and protecting our RNAi technology, as***



***well as our approved products and any other product candidates that we develop, or we could lose certain rights to grant sublicenses.***

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license or render the license non-exclusive, which could result in us being unable to develop, manufacture, market and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, we could incur significant costs and/or disruption to our business and distraction of our management defending against any breach of such licenses alleged by the licensor. For example, in June 2018, Ionis sent us a notice claiming that it was owed payments under our second amended and restated strategic collaboration and license agreement as a result of the January 2018 amendment of our collaboration agreement with Sanofi Genzyme and the related Exclusive TTR License and AT3 License Terms. Ionis claimed it was owed technology access fees, or TAF's, based on rights granted and amounts paid to us in connection with the Sanofi Genzyme restructuring. In November 2018, we received notice that Ionis had filed a Demand for Arbitration with the Boston office of the American Arbitration Association against us, asserting, among other things, breach of contract. The hearing portion of the arbitration process was completed in June 2020, and post-hearing briefing was completed in the third quarter of 2020. In October 2020, a partial award was issued by the arbitration panel seeking additional information from us. The arbitration panel issued its final award in December 2020, which ruled in favor of Ionis's request for a TAF on certain rights the panel determined we received in the Sanofi restructuring (but rejecting the TAF amount sought by Ionis), and in favor of us in denying Ionis's request for a TAF on a milestone payment received by us in the same restructuring. The panel's final award also denied Ionis's request for pre-judgment interest and attorney's fees. Pursuant to the panel's final award, we paid \$41.2 million to Ionis in January 2021.

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 will be required to pay on sales of each of our approved products or 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 such products. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.***

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers, and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

## **Risks Related to Competition**

***The pharmaceutical market is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to commercialize successfully any drugs that we develop.***

The pharmaceutical market is intensely competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs for the same diseases that we are targeting or expect to target. Many of our competitors have:

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;
- product candidates that are based on previously tested or accepted technologies;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. There are a number of drugs currently under development, which may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. These drugs may be more effective, safer, less

expensive, or marketed and sold more effectively, than any products we develop and commercialize. For example, we developed ONPATTRO for the treatment of hATTR amyloidosis. In August 2018, the FDA approved ONPATTRO lipid complex injection for the treatment of the polyneuropathy of hATTR amyloidosis in adults, and the EC granted marketing authorization for ONPATTRO for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. We are aware of other approved products used to treat this disease, including tafamidis, marketed by Pfizer, which is approved in a number of jurisdictions, and inotersen, developed and marketed by Ionis, as well as product candidates in various stages of clinical development, including an additional investigational drug. Finally, we are aware that BridgeBio Pharma, Inc. (formerly Eidos Therapeutics, Inc.), or BridgeBio, initiated a Phase 3 clinical trial of acoramidis, a TTR stabilizer, in ATTR-CM in February 2019, and completed enrollment of the Phase 3 clinical trial in ATTR-CM in late 2020. BridgeBio anticipates topline results from the ATTR-CM trial in late 2021 and, assuming positive results, expects to submit an application for regulatory approval of acoramidis in 2022 to the FDA. BridgeBio also initiated enrollment in a Phase 3 clinical trial of acoramidis in ATTR-PN patients in the fourth quarter of 2020, and anticipates topline results in 2023. While we believe that ONPATTRO has and will continue to have a competitive product profile, and if approved, that vutrisiran will have a competitive product profile, it is possible that ONPATTRO and/or vutrisiran may not compete favorably with these products and product candidates, or others, and, as a result, may not achieve commercial success. Moreover, positive data and/or the commercial success of competitive products could negatively impact our stock price.

If we continue to successfully develop product candidates, and obtain approval for them, we will face competition based on many different factors, including:

- the safety and effectiveness of our products relative to alternative therapies, if any;
- the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration;
- the timing and scope of regulatory approvals for these products;
- the availability and cost of manufacturing, marketing and sales capabilities;
- the price of our products relative to alternative approved therapies;
- reimbursement coverage; and
- patent position.

We are aware of product candidates in various stages of clinical development for the treatment of PH1 which would compete with OXLUMO, our RNAi therapeutic approved in the U.S. and EU for the treatment of this disease, including Oxabact®, a bacteria-based investigational therapy in development by OxThera AB, reloxaliase an investigational enzyme therapy in Phase 3 development for primary or severe secondary hyperoxaluria by Allena Pharmaceuticals, Inc., and nedosiran, an investigational RNAi therapeutic in development by Dicerna for the treatment of primary hyperoxaluria. In July 2019, the FDA granted a Breakthrough Therapy Designation to nedosiran for the treatment of patients with primary hyperoxaluria, and in August 2021, Dicerna announced positive topline results in its PHYOX2 pivotal clinical trial of nedosiran and expects to submit an NDA to the FDA in the fourth quarter of 2021. In April 2020, we and Dicerna granted each other a non-exclusive cross-license to our respective intellectual property related to lumasiran, and Dicerna's nedosiran product candidate. Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above or on other factors. In addition, our competitors may develop strategic alliances with or receive funding from larger pharmaceutical or biotechnology companies, providing them with an advantage over us. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and the ability to execute on our business plan. Furthermore, we also face competition from existing and new treatment methods that reduce or eliminate the need for drugs, such as the use of advanced medical devices. The development of new medical devices or other treatment methods for the diseases we are targeting could make our product candidates noncompetitive, obsolete or uneconomical.

***We face competition from other companies that are working to develop novel drugs and technology platforms using technology similar to ours. If these companies develop drugs more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs may be adversely affected.***

In addition to the competition we face from competing drugs in general, we also face competition from other companies working to develop novel drugs using technology that competes more directly with our own. We are aware of several other companies that are working to develop RNAi therapeutic products. Some of these companies are seeking, as we are, to develop chemically synthesized siRNAs as drugs. Others are following a gene therapy approach, with the goal of treating patients not with synthetic siRNAs but with synthetic, exogenously-introduced genes designed to produce siRNA-like molecules within cells. Companies working on chemically synthesized siRNAs include, but are not limited to, Takeda Pharmaceutical Company Ltd., or Takeda, Marina Biotech, Inc., Arrowhead Pharmaceuticals, Inc., or Arrowhead, and its subsidiary, Calando

Pharmaceuticals, Inc., or Calando, Quark Pharmaceuticals, Inc., or Quark, Silence, Arbutus, Sylentis, S.A.U., or Sylentis, Dicerna and its collaborators, WAVE Life Sciences Ltd., Arcturus Therapeutics, Inc., and Genevant Sciences, launched by Arbutus and Roivant Sciences. In addition, we granted licenses or options for licenses to Ionis, Benitec Biopharma Ltd., Arrowhead, and its subsidiary, Calando, Arbutus, Quark, Sylentis and others under which these companies may independently develop RNAi therapeutics against a limited number of targets. Any one of these companies may develop its RNAi technology more rapidly and more effectively than us.

In addition, as a result of agreements that we have entered into, Takeda has obtained a non-exclusive license, and Arrowhead, as the assignee of Novartis, has obtained specific exclusive licenses for 30 gene targets, that include access to certain aspects of our technology. We also compete with companies working to develop antisense-based drugs. Like RNAi therapeutics, antisense drugs target mRNAs in order to suppress the activity of specific genes. Akcea Therapeutics, Inc. (acquired by Ionis in October 2020) or Akcea, has received marketing approval for an antisense drug, inotersen that was developed by Ionis, for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis. Several antisense drugs developed by Ionis have been approved and are currently marketed, and Ionis has multiple antisense product candidates in clinical trials. Ionis is also developing antisense drugs using ligand-conjugated GalNAc technology licensed from us, and these drugs have been shown to have increased potency at lower doses in clinical and pre-clinical studies, compared with antisense drugs that do not use such licensed GalNAc technology. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for drugs that target mRNAs to silence specific genes.

In addition to competition with respect to RNAi and with respect to specific products, we face substantial competition to discover and develop safe and effective means to deliver siRNAs to the relevant cell and tissue types. Safe and effective means to deliver siRNAs to the relevant cell and tissue types may be developed by our competitors, and our ability to successfully commercialize a competitive product would be adversely affected. In addition, substantial resources are being expended by third parties in the effort to discover and develop a safe and effective means of delivering siRNAs into the relevant cell and tissue types, both in academic laboratories and in the corporate sector. Some of our competitors have substantially greater resources than we do, and if our competitors are able to negotiate exclusive access to those delivery solutions developed by third parties, we may be unable to successfully commercialize our product candidates.

### **Risks Related to Our Common Stock**

#### ***If our stock price fluctuates, purchasers of our common stock could incur substantial losses.***

The market price of our common stock has fluctuated significantly and may continue to fluctuate significantly in response to factors that are beyond our control. The stock market in general has from time to time experienced extreme price and volume fluctuations, and the biotechnology sector in particular has experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the clinical development progress or operating performance of these companies, including as a result of adverse development events. For example, the trading price for our common stock and the common stock of other biopharmaceutical companies was highly volatile during the initial stages of the COVID-19 pandemic. The COVID-19 pandemic has continued to evolve, and the extent to which the pandemic may impact our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence. These broad market and sector fluctuations have resulted and could in the future result in extreme fluctuations in the price of our common stock, which could cause purchasers of our common stock to incur substantial losses.

#### ***We may incur significant costs from class action litigation.***

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development and commercialization efforts or the development and commercialization efforts of our collaborators and/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. For example, in October 2016, we announced that we were discontinuing the development of revusiran and our stock price declined significantly as a result. When the market price of a stock has been volatile as our stock price has been, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock.

For example, a class action complaint was filed on September 26, 2018 in the United States District Court for the Southern District of New York (and transferred to the United States District Court for the District of Massachusetts by stipulation of the parties and Order of the Court dated November 20, 2018). The complaint, as amended, or the Complaint, alleged that we and our Chief Executive Officer, former Chief Financial Officer and certain of our other executive officers violated certain federal securities laws, specifically under Sections 10(b) and 20(a) of the Exchange Act, and Rule 10b-5 promulgated thereunder. The plaintiff sought unspecified damages on behalf of a purported class of purchasers of our common stock between September 20, 2017 and September 12, 2018. On March 23, 2020, the Court granted our motion to dismiss and dismissed the Complaint without prejudice, and subsequently in March 2021 denied plaintiffs' motion seeking leave to file a further amended complaint. Plaintiffs did not file a notice of appeal from such denial. This type of litigation is often expensive and diverts management's attention and resources, which could adversely affect the operation of our business. If we are ultimately required to pay



significant defense costs, damages or settlement amounts, in excess of our insurance coverage, such payments could adversely affect our operations.

We may be the target of similar litigation in the future. For example, on September 12, 2019, the Chester County Employees Retirement Fund, individually and on behalf of all others similarly situated, filed a purported securities class action complaint alleging violation of federal securities laws against us, certain of our current and former directors and officers, and the underwriters of our November 14, 2017 public stock offering, in the Supreme Court of the State of New York, New York County. While we believe the allegations in the New York State Securities Litigation are without merit, in August 2021 the parties reached an agreement in principle to resolve the matter. Any settlement is subject to court approval. 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 this or any other litigation exceed our insurance coverage, we may be forced to bear some or all of these costs and expenses directly, which could be substantial.

***Future sales of shares of our common stock, including by our significant stockholders, us or our directors and officers, could cause the price of our common stock to decline.***

A small number of our stockholders beneficially own a substantial amount of our common stock. As of September 30, 2021, our seven largest stockholders beneficially owned in excess of 50% of our outstanding shares of common stock. If our significant stockholders, or we or our officers and directors, sell substantial amounts of our common stock in the public market, or there is a perception that such sales may occur, the market price of our common stock could be adversely affected. Sales of common stock by our significant stockholders might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

***Regeneron's ownership of our common stock could delay or prevent a change in corporate control.***

As of May 21, 2019, the closing date of the stock purchase in connection with the 2019 Regeneron collaboration, Regeneron held approximately 4% of our outstanding common stock and has the right to increase its ownership up to 30%. This concentration of ownership could harm the market price of our common stock in the future by:

- delaying, deferring or preventing a change in control of our company;
- impeding a merger, consolidation, takeover or other business combination involving our company; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company.

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

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

- a classified board of directors;
- a prohibition on actions by our stockholders by written consent;
- limitations on the removal of directors; and
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% 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% 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.

**ITEM 6. EXHIBITS**

10.1***#	<a href="#">Letter Agreement between the Registrant and Laurie B. Keating dated September 6, 2021</a>
31.1	<a href="#">Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended</a>
31.2	<a href="#">Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended</a>
32.1	<a href="#">Certification of principal executive officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code</a>
32.2	<a href="#">Certification of principal financial officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code</a>
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)
*	Schedules, exhibits and similar supporting attachments or agreements to this exhibit are omitted pursuant to Item 601(b)(2) of Regulation S-K. The Registrant agrees to furnish a supplemental copy of any omitted schedule or similar attachment to the Securities and Exchange Commission upon request.
**	Management contracts or compensatory plans or arrangements.
#	Filed herewith.
†	Certain portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K because such information is both (i) not material to investors and (ii) information that the Registrant treats as private or confidential.

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.

ALNYLAM PHARMACEUTICALS, INC.

Date: October 28, 2021

/s/ John M. Maraganore  
\_\_\_\_\_  
John M. Maraganore, Ph.D.  
Chief Executive Officer  
(Principal Executive Officer)

Date: October 28, 2021

/s/ Jeffrey V. Poulton  
\_\_\_\_\_  
Jeffrey V. Poulton  
Executive Vice President, Chief Financial Officer  
(Principal Financial and Accounting Officer)

September 6, 2021

Laurie B. Keating,  
at the address on file with  
Alnylam Pharmaceuticals, Inc.

Dear Laurie:

In connection with your retirement as Executive Vice President, Chief Legal Officer and Secretary of Alnylam Pharmaceuticals, Inc. (the "Company"), this letter agreement (the "Letter Agreement") sets forth the terms of your retirement and your transition to providing consulting services for the Company. If you agree with the terms described in this Letter Agreement, which include a general release, please sign in the space provided below and return it to me. You must also reaffirm the release and restrictive covenants in this Letter Agreement following your Transition Date as described in Paragraph No. 12(b) (your "Reaffirmation").

#### **Retirement and Transition**

1. Your retirement will become effective and your employment with the Company will terminate as of the close of business on September 10, 2021 (your "Transition Date"). You will be paid, at your current annual salary, for time worked through your Transition Date (and receive your full benefits through such date) and for unused and accrued vacation time (if any) as of your Transition Date, in each case less lawful deductions, and will be reimbursed for any pre-Transition Date expenses submitted and documented to the extent such expenses are reimbursable under the Company's Travel & Entertainment Expense policy and/or other applicable policy.

2. As of your Transition Date, you will resign automatically from your position as Executive Vice President, Chief Legal Officer and Secretary of the Company and from any other positions as an employee, officer or director of the Company or any direct or indirect subsidiary without any further action by you or the Company, although you further agree to sign any specific resignation letters as may be requested by the Company.

3. After your Transition Date, except as provided in Paragraph No. 5, you will no longer be entitled to receive any benefits paid by or participate in any benefit programs offered by the Company to its employees. You will receive, under separate cover, information concerning your right to continue your health insurance benefits after that date in accordance with COBRA.

## Consulting Services

4. From your Transition Date through the 18-month anniversary of your Transition Date (your “Consulting Period”), under the oversight of the Company, you agree to assist the Company as a consultant with respect to the types of matters that were subject to your purview as a Company employee, as reasonably requested by the Executive Chair of the Company, or his designee, with reasonable advance notice (your “Consulting Services”). You agree to devote so much of your time and effort as is reasonable and adequate to perform your Consulting Services, although your Consulting Services will be limited to ten (10) hours per month during the Consulting Period, unless otherwise mutually agreed. The Company will pay you \$500 per hour or portion thereof in the event that it requests your Consulting Services beyond the ten (10) hours per month agreed to here. You agree to comply with all lawful directions and policies of the Company, and applicable professional conduct rules governing attorneys, while performing your Consulting Services. The Company will reimburse you for all pre-approved reasonable and documented out-of-pocket expenses incurred by you in the provision of the Consulting Services.

5. As compensation for your Consulting Services and for your other obligations and promises in this Letter Agreement, including for the general release set forth in Paragraph No. 10, and provided you do not revoke your acceptance of this Letter Agreement or your Reaffirmation, in each case pursuant to Paragraph No. 13, the Company agrees as follows:

- a. During the first twelve months of your Consulting Period, the Company will pay you a monthly fee equal to one-twelfth of your current base rate of pay of \$545,900 per year, payable on or before the fifteenth day of each month, commencing in October 2021.
- b. Notwithstanding your retirement prior to the conclusion of fiscal year 2021, the Company will pay you a pro rata annual bonus at the time 2021 bonuses under the Company’s Annual Incentive Program are paid to then-existing executive officers of the Company, which will be prior to March 15, 2022. Your annual bonus for 2021 will be determined by the People, Culture and Compensation Committee of the Company’s Board of Directors (“Compensation Committee”) based on actual performance for 2021 and then multiplied by the number of days in the year up to and including your Transition Date and divided by 365.
- c. The Company will pay you the amount it would have contributed toward the cost of your health coverage premium for twelve months as if you were actively employed. Payment will be made in a lump sum within ten (10) business days following the effectiveness of your Reaffirmation. You acknowledge that if you properly elect COBRA, you will be required to pay the full amount of any COBRA premium directly to the Company’s COBRA administrator.

## d. Treatment of Equity Awards

- i. You will not be entitled to receive any additional equity awards after your Transition Date.
  - ii. Notwithstanding your resignation as an employee (which shall be considered a termination without “Cause” for purposes of your equity awards), your previously issued equity awards (including but not limited to stock options and PSUs) will continue to vest during your Consulting Period, and your outstanding vested stock options will remain exercisable during, and for three months following, your Consulting Period, in each case as provided herein and in the terms of the respective Company stock incentive plan and award agreement pursuant to which such equity awards were granted.
  - iii. In addition, any outstanding, vested and unexercised stock options you hold on its expiration date shall be exercised by the Company on its expiration by a “net exercise” arrangement and with withholding satisfied by shares retained from the stock option, each as provided under the applicable provisions of any applicable equity plan(s), including, without limitation, the Company’s 2009 and 2018 Stock Incentive Plans, as amended (collectively the “Equity Plans”) and as previously approved by the Compensation Committee, as a result of which you shall receive the number of shares of common stock underlying the option reduced by the number of shares equal to the aggregate exercise price of the option divided by the fair market value on the date of exercise and further reduced by the number of shares equal to the aggregate withholding due divided by the fair market value on such date; provided, that where stock is being used to satisfy such tax obligations, the total tax withholding cannot exceed the Company’s minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income), unless withholding at a higher rate would not result in adverse accounting treatment (in which case such withholding shall not exceed maximum statutory withholding rates).
- e. The Company will reimburse up to \$15,000 of legal fees and expenses that you reasonably incur in connection with the negotiation and preparation of this Letter Agreement as soon as reasonably practicable following the date hereof.

The Company will cease providing the preceding payments and benefits as of the last day of your Consulting Period, or upon the date of any earlier material breach by you of your consulting obligations or any other obligations hereunder or under your Employee Nondisclosure, Noncompetition and Assignment of Intellectual Property Agreement, attached to this Letter Agreement as **Exhibit A** (the “NDA”). For the avoidance of doubt, as part of the cessation of payments and benefits, all of your outstanding equity awards will stop vesting and all of your outstanding stock options will cease to be exercisable upon any such material breach. Notwithstanding the foregoing, no breach will be treated as a material breach under this Letter Agreement, or as a violation resulting in your then vested equity awards ceasing to be exercisable, unless the Company has: (y) provided you written notice stating with reasonable specificity the applicable facts and circumstances underlying such finding of breach or violation; and (z) provided you with an opportunity to cure (to the extent the Company reasonably determines it is curable) any such breach or violation within thirty (30) days after the receipt of the written notice.

6. You acknowledge and agree that (1) effective upon the Transition Date, you will no longer be designated as an employee, nor will you be designated as a contractor or consultant that is subject to the Company’s Amended and Restated Insider Trading Policy (the “ITP”), (2) from and after the Transition Date and pursuant to the provisions of the ITP, you will remain subject to the restrictions set forth in the ITP until any material nonpublic information possessed by you has become public or is no longer material, and (3) you understand and will comply with the restrictions under applicable securities laws regarding (a) transacting in Company securities on the basis of material nonpublic information concerning the Company and (b) disclosing material nonpublic information to others who might transact in Company securities on the basis of that information.

7. The Company agrees to instruct the current members of its Management Board and its Board of Directors to not, directly or indirectly, through counsel or otherwise, make or publish any written or oral disparaging or defamatory statements about you to any outside third party. Notwithstanding the foregoing, nothing in this Letter Agreement prohibits or prevents the Company, its Board of Directors and its employees from providing information to, or testifying or assisting in any investigation, hearing or proceeding before, any federal, state, or local government agency or official, including (without limitation) with respect to the investigatory response to the subpoena from the U.S. Attorney’s Office for the District of Massachusetts, as well as courts of law.

8. You understand and agree that you would not receive the monies and/or benefits specified in Paragraph No. 5 above, except for your execution of this Letter Agreement and the fulfillment of the promises contained in this Letter Agreement and your Reaffirmation. You also agree that, if the Compensation Committee determines that you have engaged in significant misconduct resulting in a violation of a significant Company policy, law, or regulation relating to manufacturing, promotion, marketing or sale of products or product candidates that causes



material harm to the Company, you shall promptly return to the Company, upon the Compensation Committee's request, any and all payments made pursuant to Paragraph No. 5(a) through 5(c) and amounts realized as a result of Paragraph No. 5(d) (without impacting the validity or enforceability of the general release contained herein). Further, for the avoidance of doubt, all awards made to you prior to August 2018 are subject only to the Company's Clawback Policy, effective December 17, 2014, attached hereto as Exhibit B.

9. The Indemnification Agreement between you and the Company dated September 16, 2016 and the letter agreement between the Company and McDermott Will & Emery dated as of May 19, 2021 shall remain in full force and effect. Furthermore, the terms and benefits of the Indemnification Agreement shall apply to all activities undertaken by you in the performance of consulting services for the Company during the Consulting Period and, thereafter, to any cooperation or assistance you provide to the Company at its request.

### **Release and Restrictive Covenants**

10. In consideration of the payments to be made and the benefits to be provided by the Company to you as set forth in Paragraph No. 5 above and the promises contained in this Letter Agreement, you voluntarily and of your own free will hereby release, forever discharge and hold harmless Alnylam Pharmaceuticals, Inc., its subsidiaries, divisions and affiliates, its present or former officers, directors, trustees, employees, agents, insurers, or successors or assigns from any and all claims, demands, rules or regulations, or any other causes of action of whatever nature, whether known or unknown, through the date you execute this Letter Agreement, including, but not limited to, the National Labor Relations Act, as amended; Title VII of the Civil Rights Act of 1964, as amended; Sections 1981 through 1988 of Title 42 of the United States Code, as amended; the Age Discrimination in Employment Act of 1967, as amended; the Older Workers Benefit Protection Act; the Immigration Reform Control Act, as amended; the Employee Retirement Income Security Act of 1974, 29 U.S.C. § 1001, et seq.; the Occupational Safety and Health Act, as amended; the Civil Rights Act of 1866, 29 U.S.C. § 1981, et seq.; the Rehabilitation Act of 1973, 29 U.S.C. § 701, et seq.; the Americans With Disabilities Act of 1990, as amended; the Civil Rights Act of 1991; the Family and Medical Leave Act; the Equal Pay Act; the Massachusetts Law Against Discrimination, G.L. c. 151B; the Massachusetts Wage Payment Statute, G.L. c. 149, §§ 148, 148A, 148B, 149, 150, 150A-150C, 151, 152, 152A, et seq.; the Massachusetts Wage and Hour Laws, G.L. c. 151 § 1A et seq.; the Massachusetts Privacy Statute, G.L. c. 214, § 1B; the Massachusetts Wage Payment Statute, G.L. c. 149, § 148 et seq.; the Massachusetts Sexual Harassment Statute, G.L. c. 214 § 1C; the Massachusetts Civil Rights Act, G.L. c. 12, § 11H, the Massachusetts Equal Rights Act, G.L. c. 93, § 102; the Massachusetts Equal Pay Act, G.L. c. 149, § 105A; the Massachusetts Parental Leave Law, G.L. c. 149, § 105D; the Massachusetts Family and Medical Leave Law, G.L. c. 175M; or any other federal or state law, regulation, or ordinance; any public policy, contract, tort, or common law; or any allegation for costs, fees, or other expenses including attorneys' fees incurred in these matters. In addition, if any claim is not subject to release, to the extent permitted by law, you

waive any right or ability to be a class or collective action representative or to otherwise participate in any putative or certified class, collective or multi-party action or proceeding based on such a claim in which the Company or any other releasee identified in this Letter Agreement is a party.

Notwithstanding the foregoing, you are not waiving any rights you may have to (a) your own vested accrued employee benefits, including under the Company's retirement benefit plan(s); outstanding equity awards (e.g. stock options and PSUs) granted to you that are vested as of the date hereof or that vest as of the end of your Consulting Period and related agreements entered into with you under the Company's Equity Plans; and your right to reimbursement for any out-of-pocket business expenses authorized to be incurred and reimbursed pursuant to Company policies, as of your Transition Date, (b) rights pursuant to the Indemnification Agreement (and the related May 19, 2021 letter agreement referenced above), for the term specified therein and any other rights, to the extent applicable, for defense and indemnification for actions taken by you in the course and scope of your employment with the Company and/or its subsidiaries and affiliates; (c) benefits and/or the right to seek benefits under applicable workers' compensation and/or unemployment compensation statutes; (d) pursue claims which by law cannot be waived by signing this Letter Agreement; (e) enforce this Letter Agreement; and/or (f) challenge the validity of this Letter Agreement.

11. You agree not to disparage or otherwise publish or communicate defamatory statements about the Company and any director, officer, employee, agent or contractor and/or the products and services of the Company to any outside third party. Except as required by law or otherwise permitted herein, you further agree not to make or publish any written or oral statements concerning any legal or regulatory positions taken by the Company. Violation of this paragraph shall be deemed a material breach of this Letter Agreement. Notwithstanding the foregoing, nothing in this Letter Agreement prohibits or prevents you from providing information to, or testifying or assisting in any investigation, hearing or proceeding before, any federal, state, or local government agency or official, including (without limitation) with respect to the investigatory response to the subpoena from the U.S. Attorney's Office for the District of Massachusetts, as well as courts of law; provided that such information is not protected by the attorney-client privilege owned by the Company, which privilege can only be waived by the Company. You hereby acknowledge that you lawfully entered into your NDA and that it currently remains in effect, except as expressly provided herein. In further consideration for the monies and benefits provided to you in this Letter Agreement, by signing this Letter Agreement, you are reaffirming the post-employment restrictive covenants and the other terms and conditions of your NDA, as set forth herein. You understand that the Company would not provide you with the monies and benefits under this Letter Agreement but for your acknowledgment and reaffirmation of these obligations under your NDA. You also affirm that, except as otherwise agreed in writing by the Company's Chief Human Resources Officer (or a duly authorized representative of the Company), you will return to the Company all Company keys, files, records (and copies thereof), equipment (including, but not limited to, computer hardware, software,

printers, wireless handheld devices, cellular phones, etc.), Company identification, and any other Company-owned property otherwise in your possession or control, on or before October 10, 2021, and have left intact, and will for so long as you have access continue to keep intact, all electronic Company documents in your possession or control, including but not limited to, those that you developed or helped develop during your employment.

12. (a) You acknowledge that you have been afforded until September 26, 2021, a period of at least twenty-one (21) days, to consider the meaning and effect of this Letter Agreement. You are advised to consult with an attorney, and you acknowledge that you have had the opportunity to do so. You agree that any modifications, material or otherwise, do not restart or affect in any manner the original consideration period for the proposal made to you by the Company.

(b) In addition, you must reaffirm Paragraphs No. 10 and 11 as of your Transition Date (as defined above, your "Reaffirmation"). If your Reaffirmation does not become effective by your revocation pursuant to Paragraph No. 13, you will not be eligible to receive the monies and benefits set forth in Paragraph No. 5 above.

13. You may revoke your acceptance of Paragraphs No. 4 through 12 of this Letter Agreement for a period of seven (7) calendar days following the day you sign it, and you may revoke your Reaffirmation for a period of seven (7) calendar following the day you sign your Reaffirmation. Any revocation must be submitted, in writing, to Kelley Boucher, Chief Human Resources Officer and state, "I hereby revoke [my acceptance] [my reaffirmation] of Paragraphs No. 4 through 12 of the Letter Agreement, including the general release." The revocation must be personally delivered by email to kboucher@alnylam.com within such seven (7) calendar day period. Paragraphs No. 4 through 12 of this Letter Agreement, or Reaffirmation thereof (as the case may be), shall not become effective or enforceable until the revocation period has expired with no revocation by you received by the Company. If the last day of the revocation period is a Saturday, Sunday, or legal holiday in Massachusetts then the revocation period shall not expire until the next following day which is not a Saturday, Sunday, or legal holiday.

#### **Additional Provisions**

14. This Letter Agreement, which will be construed under Massachusetts law, may not be modified, altered, or changed except upon express written consent of both parties wherein specific reference is made to this Letter Agreement. You agree that any claims or causes of action which arise out of or relate in any way to this Letter Agreement shall, to the fullest extent permitted by law, be settled by confidential arbitration by a single arbitrator under the auspices of the American Arbitration Association ("AAA") in Boston, Massachusetts in accordance with the Employment Dispute Resolution Rules of the AAA, including, but not limited to, the rules and procedures applicable to the selection of an arbitrator. The parties agree that the parties shall bear their own costs and attorneys fees except when Massachusetts law provides that the prevailing

party is to be awarded their costs and attorney fees. Notwithstanding the above, the Company shall pay the entire filing fee for any arbitration involving clawback, forfeiture or recoupment of vested options. In the event that any person or entity other than you or the Company may be a party with regard to any such controversy or claim, such controversy or claim shall be submitted to confidential arbitration subject to such other person or entity's agreement. Judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. This Paragraph No. 14 shall be specifically enforceable. Notwithstanding the foregoing, this Paragraph No. 14 shall not preclude either party from pursuing a court action for the sole purpose of obtaining a temporary restraining order or a preliminary injunction in circumstances in which such relief is appropriate; provided that any other relief shall be pursued through a confidential arbitration proceeding pursuant to this Paragraph No. 14.

15. Except as previously disclosed to the Company, you hereby warrant that as of the date you sign this Letter Agreement, you have not commenced, filed, participated in, offered testimony, or assisted any other investigation, hearing, or any proceeding before any federal, state, or local government agency relating to or against the Company. You further warrant that you have disclosed, or will disclose prior to the execution of this Letter Agreement, any and all known violations of law during your tenure at the Company. Nothing in this Letter Agreement prohibits or prevents you from filing a charge with or participating, testifying, or assisting in any investigation, hearing, or other proceeding before the U.S. Equal Employment Opportunity Commission, the National Labor Relations Board or a similar agency enforcing federal, state or local anti-discrimination laws. However, to the maximum extent permitted by law, you agree that if such an administrative claim is made to such an anti-discrimination agency, you will not be entitled to recover any individual monetary relief or other individual remedies. In addition, nothing in this Letter Agreement, including but not limited to the release of claims and the confidentiality and non-disparagement clauses, or the NDA prohibits you from: (1) reporting possible violations of federal law or regulations, including any possible securities laws violations, to any governmental agency or entity, including but not limited to the U.S. Department of Justice, the Securities and Exchange Commission, the U.S. Congress, or any agency Inspector General; (2) making any other disclosures that are protected under the whistleblower provisions of federal law or regulations; or (3) otherwise fully participating in any federal whistleblower programs, including but not limited to any such programs managed by the Securities and Exchange Commission and/or the Occupational Safety and Health Administration. Moreover, nothing in this Letter Agreement prohibits or prevents you from receiving individual monetary awards or other individual relief by virtue of participating in such federal whistleblower programs.

16. You affirm that you have been paid and have received all leave (paid or unpaid), compensation, wages, bonuses, commissions, severance pay, and/or benefits to which you may be entitled and that no other leave (paid or unpaid), compensation, wages, bonuses, commissions, severance pay, and/or benefits are due to you, except as provided in this Letter Agreement. You further affirm that you have no known workplace injuries or occupational diseases and have been provided and/or have not been denied any leave requested under the Family and Medical Leave

Act. You also affirm that you have not been retaliated against for reporting any allegations of wrongdoing by the Company or its officers. In addition, you affirm that all decisions regarding your pay and benefits through the date of your signature of this Letter Agreement were not discriminatory based on age, disability, race, color, sex, religion, national origin or any other classification protected by law.

17. You agree to reasonably cooperate in any investigation, defense or prosecution of any claims, investigations, actions or other matters now in existence or which may be brought in the future against or on behalf of the Company, including (without limitation) with respect to the investigatory response to the subpoena from the U.S. Attorney's Office for the District of Massachusetts and the ongoing shareholder litigation pending in state court in New York. Your cooperation in connection with such claims, investigations or actions shall include, but not be limited to, being reasonably available to meet with the Company's counsel, with the participation of your legal counsel, to prepare for discovery or any mediation, arbitration, trial, administrative hearing or other proceeding or to act as a witness when reasonably requested by the Company at mutually agreeable times and at locations mutually convenient to you and the Company, provided that prior to such meeting, the Company or its counsel will provide you (and your counsel if you so request) with access to those materials about which the Company and its counsel would intend to seek information from you pursuant to your obligation to provide reasonable cooperation. Nothing herein shall require you to provide anything other than truthful information. The Company shall reimburse you for all reasonable and documented out of pocket expenses incurred in the provision of such assistance. For avoidance of doubt, such expenses do not include attorneys' fees unless expressly provided in your Indemnification Agreement. You acknowledge that any material violation of this Paragraph No. 17 will result in irreparable harm to the Company and, in addition to other available remedies, it shall be entitled to immediate injunctive relief and an award in an amount equal to the fees paid to you for your Consulting Services as the date of such breach, and the Company shall be excused from making any further payments for your Consulting Services.

18. The parties agree that neither this Letter Agreement, nor the furnishing or acceptance of consideration for this Letter Agreement, shall be deemed or construed at any time for any purpose as an admission by you or the Company of any liability or unlawful conduct of any kind. Should any provision of this Letter Agreement be declared illegal or unenforceable by any court of competent jurisdiction and cannot be modified to be enforceable, excluding the general release language, such provision shall immediately become null and void, leaving the remainder of this Letter Agreement in full force and effect. However, if the general release is found to be invalid, you agree to execute a valid release of the claims which are the subject of this Letter Agreement and/or are referred to in the general release paragraph above.

19. After you execute this Agreement, neither you nor your attorneys, or any person acting by, through, under or in concert with you or them, shall disclose any of the terms of or amount paid under this Letter Agreement or the negotiation thereof to any individual or entity

(other than to state that the Company has filed this Letter Agreement as a public document); provided, however, that the foregoing shall not prevent such disclosures by you to your attorney, financial and tax advisors and/or your immediate family, or as may be required by law. Notwithstanding the confidentiality obligations set forth in this Paragraph No. 19 or elsewhere in this Letter Agreement, you understand that, pursuant to the Defend Trade Secrets Act of 2016 ("DTSA"), you will not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret (as opposed to information protected from disclosure by the attorney-client privilege) that: (A) is made (i) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. You further understand that if a court of law or arbitrator determines that you misappropriated Company trade secrets willfully or maliciously, including by making permitted disclosures without following the requirements of the DTSA as detailed in this Paragraph No. 19, then the Company may be entitled to an award of exemplary damages and attorneys' fees against you.

20. This Letter Agreement, which includes a general release, represents the complete agreement between you and the Company, and fully supersedes any prior agreements or understandings between the parties, other than (a) your NDA, (b) your Indemnification Agreement and the letter agreement between the Company and McDermott Will & Emery referred to herein, (c) any equity incentive plans and any award agreement evidencing an equity award under any equity incentive plan and (d) the provisions of the Company's Clawback Policy, consistent with the provisions of Paragraph No. 8 above. You acknowledge that you have not relied on any representations, promises, or agreements of any kind made to you in connection with your decision to sign this Letter Agreement, except those set forth in this Letter Agreement.

21. The Company may withhold from any amounts or benefits payable under this Letter Agreement income taxes and payroll taxes that are required to be withheld pursuant to any applicable law or regulation.

22. This Letter Agreement may be signed in counterparts, each of which when so signed shall be deemed an original, and the counterparts together shall constitute one and the same agreement. A copied, scanned or faxed signature shall be treated the same as an original.

23. Although the Company does not guarantee the tax treatment of any payments under this Letter Agreement, the intent of the parties is that the payments and benefits hereunder be exempt from, or comply with, Section 409A of the Internal Revenue Code of 1986, as amended, and all Treasury Regulations and guidance promulgated thereunder ("Code Section 409A") and to the maximum extent permitted this Letter Agreement shall be limited, construed and interpreted in accordance with such intent. In no event whatsoever shall the Company or its affiliates or their respective officers, directors, employees or agents be liable for any additional tax, interest or penalties that may be imposed on you by Code Section 409A or damages based upon payments and/or benefits payable hereunder not being exempt from or not complying with

Code Section 409A, unless such failure is due to breach of this Letter Agreement by the Company. If a payment made under this Letter Agreement that is nonqualified deferred compensation subject to Code Section 409A may be made in more than one taxable year depending on when you sign this Letter Agreement, payment shall be made in the second taxable year. Notwithstanding any other provision of this Letter Agreement to the contrary, to the extent that any reimbursement of expenses constitutes “deferred compensation” under Code Section 409A, such reimbursement shall be provided no later than December 31 of the year following the year in which the expense was incurred. The amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year. The amount of any in-kind benefits provided in one year shall not affect the amount of in-kind benefits provided in any other year. For purposes of Code Section 409A (including, without limitation, for purposes of Treasury Regulation Section 1.409A-2(b)(2)(iii)), the right to receive payments in the form of installment payments shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment shall at all times be considered a separate and distinct payment. Whenever a payment under this Letter Agreement may be paid within a specified period, the actual date of payment within the specified period shall be within the sole discretion of the Company. Notwithstanding any other provision of this Agreement to the contrary, if at the time of your separation from service (as defined in Code Section 409A), you are a “Specified Employee”, then the Company will defer the payment or commencement of any nonqualified deferred compensation subject to Code Section 409A payable upon separation from service (without any reduction in such payments or benefits ultimately paid or provided to you) until the date that is six (6) months following separation from service or, if earlier, the earliest other date as is permitted under Code Section 409A (and any amounts that otherwise would have been paid during this deferral period will be paid in a lump sum on the day after the expiration of the six (6) month period or such shorter period, if applicable). You will be a “Specified Employee” for purposes of this Letter Agreement if, on the date of your separation from service, you are an individual who is, under the method of determination adopted by the Company designated as, or within the category of employees deemed to be, a “Specified Employee” within the meaning and in accordance with Treasury Regulation Section 1.409A-1(i).



The Company would like to extend its profound gratitude and appreciation to you for your leadership and countless contributions to the success of the Company over many years of service, and would also like to express its sincere hope for success in your next chapter.

Very truly yours,

/s/ John M. Maraganore, Ph.D.

John M. Maraganore, Ph.D.

Chief Executive Officer  
Alnylam Pharmaceuticals, Inc.

You have been advised in writing that you have a period of more than twenty-one (21) days to consider the release in this Letter Agreement, and that it must be signed and returned to be effective. You have also been advised to consult with an attorney prior to the execution of this Letter Agreement.

Having elected to execute this Letter Agreement, to fulfill the promises set forth in this Letter Agreement, and to receive thereby the payments and benefits set forth in Paragraph No. 5 above, you freely and knowingly, and after due consideration, enter into this Letter Agreement intending to waive, settle, and release all claims you have or might have against the Company, its subsidiaries, divisions and affiliates, its present or former officers, directors, trustees, employees, agents, insurers, or successors or assigns, as set forth herein.

Date: September 6, 2021

/s/ Laurie B. Keating  
Laurie B. Keating

## CERTIFICATION

I, John M. Maraganore, Ph.D., certify that:

- 1) I have reviewed this Quarterly Report on Form 10-Q of Alnylam 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 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.

Dated: October 28, 2021

/s/ John M. Maraganore

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John M. Maraganore, Ph.D.  
Chief Executive Officer

## CERTIFICATION

I, Jeffrey V. Poulton, certify that:

- 1) I have reviewed this Quarterly Report on Form 10-Q of Alnylam 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 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.

Dated: October 28, 2021

/s/ Jeffrey V. Poulton

Jeffrey V. Poulton  
Executive Vice President, Chief Financial Officer

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT  
TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Alnylam Pharmaceuticals, Inc. (the “Company”) for the quarter ended September 30, 2021 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, John M. Maraganore, Ph.D., Chief Executive Officer of the Company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: October 28, 2021

/s/ John M. Maraganore

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John M. Maraganore, Ph.D.  
Chief Executive Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT  
TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report on Form 10-Q of Alnylam Pharmaceuticals, Inc. (the “Company”) for the quarter ended September 30, 2021 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, Jeffrey V. Poulton, Executive Vice President, Chief Financial Officer, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: October 28, 2021

/s/ Jeffrey V. Poulton

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Jeffrey V. Poulton  
Executive Vice President, Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.