

ALNYLAM PHARMACEUTICALS, INC.  
Form 10-Q  
May 04, 2018

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 March 31, 2018

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 77-0602661  
(State or Other Jurisdiction of (I.R.S. Employer  
Incorporation or Organization) Identification No.)

300 Third Street,

Cambridge, MA 02142  
(Address of Principal Executive Offices) (Zip Code)

(617) 551-8200

(Registrant's Telephone Number, Including Area Code)

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer

(Do not check if a smaller reporting company)

Smaller reporting company

Emerging growth company

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

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

At April 30, 2018, the registrant had 100,522,411 shares of Common Stock, \$0.01 par value per share, outstanding.

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## ALNYLAM PHARMACEUTICALS, INC.

## CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

(Unaudited)

|  | March 31, 2018 | December 31, 2017 |
|--|----------------|-------------------|
| <b>ASSETS</b>  |                |                   |
| Current assets:  |                |                   |
| Cash and cash equivalents  | \$ 396,149     | \$ 645,361        |
| Marketable securities  | 1,171,715      | 1,045,257         |
| Billed and unbilled collaboration receivables  | 50,768         | 34,002            |
| Prepaid expenses and other current assets  | 66,665         | 40,120            |
| Total current assets   | 1,685,297      | 1,764,740         |
| Marketable securities  | 648            | 13,919            |
| Property, plant and equipment, net   | 201,979        | 181,900           |
| Restricted investments   | 30,000         | 30,000            |
| Other assets   | 5,215          | 4,171             |
| Total assets   | \$ 1,923,139   | \$ 1,994,730      |
| <b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>  |                |                   |
| Current liabilities:   |                |                   |
| Accounts payable   | \$ 13,206      | \$ 28,355         |
| Accrued expenses   | 63,824         | 72,203            |
| Deferred rent  | 2,498          | 1,988             |
| Deferred revenue   | 35,855         | 41,705            |
| Total current liabilities  | 115,383        | 144,251           |
| Deferred rent, net of current portion  | 10,817         | 6,626             |
| Deferred revenue, net of current portion   | 7,676          | 43,075            |
| Long-term debt   | 30,000         | 30,000            |
| Other liabilities  | 4,458          | 4,347             |
| Total liabilities  | 168,334        | 228,299           |
| Commitments and contingencies (Note 5)   |                |                   |
| Stockholders' equity:  |                |                   |
| Preferred stock, \$0.01 par value per share, 5,000,000 shares authorized and no shares |                |                   |
| issued and outstanding at March 31, 2018 and December 31, 2017                         | —              | —                 |
| Common stock, \$0.01 par value per share, 125,000,000 shares authorized;               |                |                   |
| 100,468,061 shares issued and outstanding at March 31, 2018; 99,666,549                |                |                   |
| shares issued and outstanding at December 31, 2017                                     | 1,005          | 997               |
| Additional paid-in capital   | 4,009,342      | 3,947,552         |
| Accumulated other comprehensive loss   | (34,853 )      | (34,433 )         |
| Accumulated deficit  | (2,220,689 )   | (2,147,685 )      |
| Total stockholders' equity   | 1,754,805      | 1,766,431         |
| Total liabilities and stockholders' equity   | \$ 1,923,139   | \$ 1,994,730      |

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

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## ALNYLAM PHARMACEUTICALS, INC.

## CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands, except per share amounts)

(Unaudited)

|  | Three Months Ended<br>March 31, |             |
|--|---------------------------------|-------------|
|  | 2018                            | 2017        |
| Net revenues from collaborators  | \$21,899                        | \$18,960    |
| Operating expenses:  |                                 |             |
| Research and development (1)   | 96,857                          | 86,984      |
| General and administrative (1)   | 72,447                          | 38,487      |
| Total operating expenses   | 169,304                         | 125,471     |
| Loss from operations   | (147,405)                       | (106,511)   |
| Other income (expense):  |                                 |             |
| Interest income  | 5,794                           | 2,128       |
| Other income (expense)   | 335                             | (2,907)     |
| Total other income (expense)   | 6,129                           | (779)       |
| Loss before income taxes   | (141,276)                       | (107,290)   |
| Benefit from income taxes  | 62                              | —           |
| Net loss   | \$(141,214)                     | \$(107,290) |
| Net loss per common share - basic and diluted                                      | \$(1.41)                        | \$(1.25)    |
| Weighted-average common shares used to compute basic and diluted net loss per      |                                 |             |
| common share   | 99,979                          | 86,027      |
| Comprehensive loss:  |                                 |             |
| Net loss   | \$(141,214)                     | \$(107,290) |
| Unrealized loss on marketable securities, net of tax                               | (420)                           | (1,936)     |
| Reclassification adjustment for realized loss on marketable securities included in |                                 |             |
| net loss   | —                               | 1,549       |
| Comprehensive loss   | \$(141,634)                     | \$(107,677) |

(1) Stock-based compensation expenses included in operating expenses are as follows:

|                            |          |         |
|----------------------------|----------|---------|
| Research and development   | \$10,137 | \$8,691 |
| General and administrative | 9,447    | 7,026   |

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)

|   | Three Months Ended<br>March 31, |             |
|---|---------------------------------|-------------|
|   | 2018                            | 2017        |
| Cash flows from operating activities:                                       |                                 |             |
| Net loss  | \$(141,214)                     | \$(107,290) |
| Adjustments to reconcile net loss to net cash used in operating activities: |                                 |             |
| Depreciation and amortization   | 3,178                           | 3,000       |
| Stock-based compensation  | 19,584                          | 15,717      |
| Charge for 401(k) company stock match                                       | 942                             | 551         |
| Realized loss on sale of marketable equity securities                       | —                               | 1,549       |
| Other   | —                               | 608         |
| Changes in operating assets and liabilities:                                |                                 |             |
| Billed and unbilled collaboration receivables                               | (16,766 )                       | 3,877       |
| Prepaid expenses and other assets   | (27,540 )                       | 3,708       |
| Accounts payable  | (9,042 )                        | (11,067 )   |
| Accrued expenses and other  | (11,767 )                       | (10,855 )   |
| Deferred revenue  | 26,961                          | (128 )      |
| Net cash used in operating activities                                       | (155,664)                       | (100,330)   |
| Cash flows from investing activities:                                       |                                 |             |
| Purchases of property, plant and equipment                                  | (21,257 )                       | (36,152 )   |
| Purchases of marketable securities  | (358,433)                       | (86,803 )   |
| Sales and maturities of marketable securities                               | 244,876                         | 198,031     |
| Net cash (used in) provided by investing activities                         | (134,814)                       | 75,076      |
| Cash flows from financing activities:                                       |                                 |             |
| Proceeds from exercise of stock options and other types of equity           | 42,094                          | 2,769       |
| Payments for repurchase of common stock for employee tax withholding        | (572 )                          | (53 )       |
| Net cash provided by financing activities                                   | 41,522                          | 2,716       |
| Net decrease in cash, cash equivalents and restricted cash                  | (248,956)                       | (22,538 )   |
| Cash, cash equivalents and restricted cash, beginning of period             | 646,832                         | 195,088     |
| Cash, cash equivalents and restricted cash, end of period                   | \$397,876                       | \$172,550   |

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 the same such amounts shown in the condensed consolidated statements of cash flows:

|                           | At Ended March 31, |           |
|---------------------------|--------------------|-----------|
|                           | 2018               | 2017      |
| Cash and cash equivalents | \$396,149          | \$171,079 |

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|  |           |           |
|--|-----------|-----------|
| Restricted cash included in long-term other assets             | 1,727     | 1,471     |
| Total cash, cash equivalents, and restricted cash shown in the |           |           |
| condensed consolidated statements of cash flows                | \$397,876 | \$172,550 |

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



ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

(Unaudited)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The accompanying condensed consolidated financial statements of Alnylam Pharmaceuticals, Inc. 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, 2017, which were included in our Annual Report on Form 10-K that was filed with the Securities and Exchange Commission, or SEC, on February 15, 2018. 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.

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. Actual results could differ from those estimates.

Liquidity

Based on our current operating plan, we believe that our cash, cash equivalents and fixed income marketable securities at March 31, 2018, together with the cash we expect to generate under our current alliances, will be sufficient to enable us to advance our Alnylam 2020 strategy for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q.

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. 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 then outstanding. 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 table sets forth for the periods presented the potential common shares (prior to consideration of the treasury stock method) excluded from the calculation of net loss per common share because their inclusion would be anti-dilutive, in thousands:

|                                  | At March 31, |        |
|----------------------------------|--------------|--------|
|                                  | 2018         | 2017   |
| Options to purchase common stock | 12,515       | 12,048 |
| Unvested restricted common stock | 157          | 163    |
|                                  | 12,672       | 12,211 |

### Equity

Total stockholders' equity at March 31, 2018 decreased by \$11.6 million compared to December 31, 2017. This decrease was related primarily to our net loss, partially offset during the three months ended March 31, 2018 by an adjustment to the opening balance of our accumulated deficit related to the adoption of the new revenue standard on January 1, 2018, described below under the heading "Recent Accounting Pronouncements," as well as increases to additional paid-in capital due to proceeds from the exercise of stock options and stock-based compensation.

## Fair Value Measurements

The fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are observable, such as quoted prices (adjusted), interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. The fair value hierarchy level is determined by the lowest level of significant input.

## Investments in Marketable Securities and Cash Equivalents

We invest our excess cash balances in short-term and long-term marketable debt and equity securities. We classify our investments in marketable debt securities as either held-to-maturity or available-for-sale based on facts and circumstances present at the time we purchased the securities. At each balance sheet date presented, we classified all of our investments in debt securities as available-for-sale. We report available-for-sale debt securities at fair value at each balance sheet date and include any unrealized holding gains and losses (the adjustment to fair value) in accumulated other comprehensive income (loss), a component of stockholders' equity. At March 31, 2018, the balance in our accumulated other comprehensive loss was composed solely of activity related to our fixed income marketable securities and our investment in equity securities of Regulus Therapeutics Inc., or Regulus. Realized gains and losses are determined using the specific identification method and are included in other income (expense). We recognized \$1.5 million of realized losses from sales of our Regulus available-for-sale securities as other expense in our condensed consolidated statement of comprehensive loss during the three months ended March 31, 2017. If any adjustment to fair value reflects a decline in the value of the fixed income marketable securities, we consider all available evidence to evaluate the extent to which the decline is "other than temporary," including our intention to sell and, if so, mark the investment to market through a charge to our condensed consolidated statements of comprehensive loss. We did not record any impairment charges related to our fixed income marketable securities during the three months ended March 31, 2018 or 2017. Our marketable securities are classified as cash equivalents if the original maturity, from the date of purchase, is 90 days or less, and as marketable securities if the original maturity, from the date of purchase, is in excess of 90 days. Our cash equivalents are composed of commercial paper, corporate notes, U.S. government-sponsored enterprise securities, U.S. treasury securities and money market funds.

During the second quarter of 2017, we sold all our remaining holdings in Regulus. We accounted for our investment in Regulus as an available-for-sale marketable security. Intra-period tax allocation rules require us to allocate our provision for income taxes between continuing operations and other categories of earnings, such as other comprehensive income. In periods in which we have a year-to-date pre-tax loss from continuing operations and pre-tax income in other categories of earnings, such as other comprehensive income, we must allocate the tax provision to the other categories of earnings. We then record a related tax benefit in continuing operations. Upon sales of our available-for-sale marketable securities, we apply the aggregate portfolio approach to recognize the related tax provision or benefit into income (loss) from continuing operations. As a result, the disproportionate tax effect remains in accumulated other comprehensive income (loss) as long as we maintain an investment portfolio. At March 31, 2018 and December 31, 2017, there was \$32.8 million of accumulated other comprehensive loss, net of tax, recorded on our condensed consolidated balance sheets related to our investment in Regulus.

## Revenue Recognition

We have entered into collaboration agreements with leading pharmaceutical and life sciences companies, including Sanofi Genzyme, the specialty care global business unit of Sanofi, and The Medicines Company, or MDCO. The terms of our collaboration agreements may include consideration such as non-refundable license fees, funding of

research and development services, payments due upon the achievement of clinical and pre-clinical performance-based development milestones, regulatory milestones, manufacturing services, sales-based milestones and royalties on product sales.

On January 1, 2018, we adopted the new revenue standard, discussed below under the heading “Recent Accounting Pronouncements,” which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. Our adoption of the new revenue standard had a material impact on our condensed consolidated financial statements, as discussed below under the heading “Recent Accounting Pronouncements.” This new revenue standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of the new revenue standard, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when collectability of the consideration to which we are entitled in

exchange for the goods or services we transfer to the customer is determined to be probable. At contract inception, once the contract is determined to be within the scope of the new revenue standard, we assess whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation. Goods and services that are determined not to be distinct are combined with other promised goods and services until a distinct bundle is identified. We then allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled.

We recognize the transaction price allocated to upfront license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from the other performance obligations identified in the contract. If the license is considered to not be distinct from other performance obligations, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied (i) at a point in time, but only for licenses determined to be distinct from other performance obligations in the contract, or (ii) over time; and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from license payments. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Many of our collaboration agreements entitle us to additional payments upon the achievement of performance-based milestones. These milestones are generally categorized into three types: development milestones, generally based on the advancement of our pipeline and initiation of clinical trials; regulatory milestones, generally based on the submission, filing or approval of regulatory applications such as a New Drug Application, or NDA, in the United States; and sales-based milestones, generally based on meeting specific thresholds of sales in certain geographic areas. For each collaboration that includes development milestone payments, we evaluate whether it is probable that the consideration associated with each milestone will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are considered constrained and excluded from the transaction price until they meet this threshold. Milestones tied to regulatory approval, and therefore not within our control, are considered constrained until such approval is received. Upfront and ongoing development milestones per our collaboration agreements are not subject to refund if the development activities are not successful. At the end of each subsequent reporting period, we re-evaluate the probability of a significant reversal of the cumulative revenue recognized for our milestones, and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues from collaborators and loss in the period of adjustment. We exclude sales-based royalties and milestone payments from the transaction price until the sale occurs (or, if later, the underlying performance obligation to which some or all of the royalty has been allocated has been satisfied, or partially satisfied), because the license to our intellectual property is deemed to be the predominant item to which the royalties relate as it is the primary driver of value. Currently, we have not recognized any royalty revenue resulting from any of our agreements.

The new revenue standard requires us to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which we have sold the same performance obligation separately are not available, we are required to estimate the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever we determine that a contract should be accounted for as a combined performance obligation over time, we determine the period over which the performance obligations will be performed and revenue will be recognized.

Revenue is recognized using the proportional performance method. Direct labor hours or full-time equivalents are typically used as the measure of performance. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement.

We evaluate our collaborative agreements for proper classification in our consolidated statements of comprehensive loss based on the nature of the underlying activity. Transactions between collaborators recorded in our consolidated statements of comprehensive loss are recorded on either a gross or net basis, depending on the characteristics of the collaborative relationship. We generally reflect amounts due under our collaborative agreements related to cost-sharing of development activities as revenue if we have a vendor-customer relationship with our collaborator. Costs incurred or shared with our collaboration partners that are deemed to be joint-risk sharing activities are recorded as an adjustment to the related operating expense captions.

For revenue generating arrangements where we, as a vendor, provide consideration to a licensor or collaborator, as a customer, we apply the accounting standard that governs such transactions. This standard addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the transaction price unless we receive an identifiable benefit for the payment and we can reasonably

estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of the transaction price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer, and then as an expense. Payments that are not deemed to be a reduction of the transaction price are recorded as an expense.

Consideration that does not meet the requirements to satisfy the above revenue recognition criteria is recorded as deferred revenue in the accompanying condensed consolidated balance sheets. Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with our existing collaboration agreements, we have recorded on our condensed consolidated balance sheets short-term and long-term deferred revenue based on our best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months. Amounts that we expect will not be recognized within the next 12 months are classified as long-term deferred revenue. However, this estimate is based on our current operating plan and, if our operating plan should change in the future, we may recognize a different amount of deferred revenue over the next 12-month period.

The estimate of deferred revenue also reflects management's estimate of the periods of our involvement in certain of our collaborations. Our performance obligations under these collaborations consist of participation on steering committees and the performance of other research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in revenue recognition amounts. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that we recognize and record in future periods. At March 31, 2018, we had short-term and long-term deferred revenue of \$35.9 million and \$7.7 million, respectively, related to our collaborations.

Amounts are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less or the amount is immaterial. At March 31, 2018, we have not capitalized any costs to obtain any of our contracts.

#### Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued a new revenue recognition standard, which we refer to as the new revenue standard, which amends revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The new revenue standard provides a five-step framework whereby revenue is recognized when control of promised goods or services are transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The new revenue standard also requires enhanced disclosures pertaining to revenue recognition in both interim and annual periods. In August 2015, the FASB deferred the effective date of the new revenue standard from January 1, 2017 to January 1, 2018. In March 2016, the FASB issued amendments to clarify the implementation standard on principal versus agent considerations. In April 2016, the FASB issued amendments to clarify the standard on accounting for licenses of intellectual property and identifying performance obligations. In May 2016, the FASB issued amendments related to collectibility, non-cash consideration, the presentation of sales and other similar taxes collected from customers and transition. The new revenue standard allows for adoption using a full retrospective method or a modified retrospective method. On January 1, 2018, we adopted the new revenue standard by applying the modified retrospective method to all contracts that were not completed as of January 1, 2018. As a result, while reporting periods beginning on our adoption of the new revenue standard are

presented under the new revenue standard, prior period amounts have not been adjusted and continue to be presented under the revenue standard in effect prior to January 1, 2018. For contracts that were modified prior to our adoption of the new revenue standard, we reflected the aggregate effect of all modifications that occurred before the beginning of the earliest period presented when identifying performance obligations and allocating the transaction price in accordance with an available practical expedient. Our implementation approach included performing a detailed review of our collaboration agreements not completed as of the transition date. In addition, we designed internal controls to enable the preparation of financial information and have reached conclusions on key accounting assessments related to the new revenue standard, including our assessment that the impact of accounting for costs incurred to obtain a contract is immaterial. There was no impact to cash from or used in operating, financing or investing activities on our condensed consolidated statement of cash flows as a result of the adoption of the new revenue standard.



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The following table summarizes the cumulative effect to our condensed consolidated balance sheet upon the adoption of the new revenue standard on January 1, 2018, in thousands:

|  | Balance at<br>December<br>31, 2017 | Adjustments  | Balance at<br>January 1,<br>2018 |
|--|------------------------------------|--------------|----------------------------------|
| Condensed Consolidated Balance Sheet     |                                    |              |                                  |
| Deferred revenue, current portion        | \$41,705                           | \$ (34,463 ) | \$7,242                          |
| Deferred revenue, net of current portion | \$43,075                           | \$ (33,747 ) | \$9,328                          |
| Accumulated deficit                      | \$(2,147,685)                      | \$ 68,210    | \$(2,079,475)                    |

The adoption of the new revenue standard resulted in a cumulative reduction of \$68.2 million of deferred revenue with a corresponding adjustment to the opening balance of accumulated deficit recorded in the first quarter of 2018. This adjustment is due primarily to the application of the new revenue standard to our collaboration agreements with Sanofi Genzyme, MDCO and Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko Kirin. In addition, as a result of the cumulative reduction in deferred revenue, our corresponding deferred tax asset was reduced by \$13.6 million, which was offset by a corresponding decrease to our valuation allowance. These offsetting adjustments were recorded to our accumulated deficit in the first quarter of 2018.

A substantial portion of the incremental \$68.2 million adjustment is the result of the application of the new revenue standard regarding how entities should measure progress in satisfying performance obligations and the contract's transaction price. In particular, for Sanofi Genzyme and MDCO, the adoption of the new revenue standard resulted in the recognition of previously deferred revenue of \$45.7 million and \$4.5 million, respectively, due to the change in the way we measure our performance under each agreement, from a straight-line method to a proportional performance model. As a result, at January 1, 2018, the balance of remaining deferred revenues was \$3.5 million and \$1.2 million, respectively, related to Sanofi Genzyme and MDCO. In addition, the adoption of the new revenue standard resulted in the recognition of \$15.5 million of previously deferred revenue related to our Kyowa Hakko Kirin agreement. Under the revenue standard in effect at the time this agreement was executed, we had been unable to reasonably estimate our period of performance under the Kyowa Hakko Kirin agreement as we were unable to estimate the timeline of our deliverables related to the fixed-price option granted to Kyowa Hakko Kirin for any additional compounds, an obligation that was bundled with all other deliverables into a single unit of accounting. Under the new revenue standard, two distinct performance obligations were identified. The first distinct performance obligation included a license to our program targeting respiratory syncytial virus, or RSV, infection, related know-how and updates, manufacturing supply services and joint steering committee services. The second distinct performance obligation included the fixed-price option to a future follow-on compound. We allocated all consideration to the first performance obligation because the second performance obligation was deemed to have a de minimis relative selling price due to its low likelihood of occurring, in part due to our discontinuation of our RSV program. Given this fact pattern, because we do not expect to incur any future costs related to our RSV program, we concluded our performance obligations were complete in the period prior to our adoption of the new revenue standard and therefore, there would not be a future significant reversal of revenue. As a result, we recorded the \$15.5 million of deferred revenue as of December 31, 2017 as an adjustment to the opening balance of our accumulated deficit on January 1, 2018.

In accordance with the new revenue standard requirements, the following tables summarize the impact of adoption on our condensed consolidated balance sheet and condensed consolidated statement of comprehensive loss, in thousands:

|  | At March 31, 2018 |  |                                       |
|--|-------------------|--|---------------------------------------|
|  |                   | Balances<br>Without<br>Adoption of<br>New<br>Revenue<br>Standard | Effect of<br>Change<br>Higher/(Lower) |
| Condensed Consolidated Balance Sheet     | As<br>Reported    |  |                                       |
| Deferred revenue, current portion        | \$35,855          | \$52,860   | \$ (17,005 )                          |
| Deferred revenue, net of current portion | \$7,676           | \$25,669   | \$ (17,993 )                          |
| Accumulated deficit                      | \$(2,220,689)     | \$(2,255,772)  | \$ (35,083 )                          |

|  | Three Months Ended March 31, 2018 |  |                                       |
|--|-----------------------------------|--|---------------------------------------|
|  |                                   | Balances<br>Without<br>Adoption<br>of New<br>Revenue<br>Standard | Effect of<br>Change<br>Higher/(Lower) |
| Condensed Consolidated Statement of Comprehensive Loss | As<br>Reported                    |  |                                       |
| Net revenues from collaborators                        | \$21,899                          | \$55,026   | \$ (33,127 )                          |
| Net loss   | \$(141,214)                       | \$(108,087)  | \$ 33,127                             |
| Net loss per common share - basic and diluted          | \$(1.41 )                         | \$(1.08 )  | \$ 0.33                               |

In addition to the reduction to deferred revenues recorded and corresponding offset to the accumulated deficit described above, on January 6, 2018, we and Sanofi Genzyme entered into an amendment to our 2014 Sanofi Genzyme collaboration. In connection and simultaneously with entering into the amendment to the 2014 Sanofi Genzyme collaboration, we and Sanofi Genzyme also entered into an Exclusive License Agreement with respect to all TTR products, including patisiran, ALN-TTRsc02 and any back-up products, referred to as the Exclusive TTR License, and the ALN-AT3 Global License Terms with respect to fitusiran and any back-up products, referred to as the AT3 License Terms. Please read Note 2 for a discussion of our accounting related to the 2014 Sanofi Genzyme collaboration, as amended in January 2018, together with the Exclusive TTR License and the AT3 License Terms.

In January 2016, the FASB issued a new standard on recognition and measurement of financial assets and financial liabilities. The new standard impacts the accounting for equity investments, financial liabilities under the fair value option, and the presentation and disclosure requirements for financial instruments. All equity investments in unconsolidated entities (other than those accounted for under the equity method of accounting) will generally be measured at fair value with changes in fair value recognized through earnings. There will no longer be an available-for-sale classification (changes in fair value reported in other comprehensive income (loss)) for equity securities with readily determinable fair values. In addition, the FASB clarified the need for a valuation allowance on deferred tax assets resulting from unrealized losses on available-for-sale debt securities. In general, the new standard will require modified retrospective application to all outstanding instruments, with a cumulative effect adjustment recorded to opening retained earnings. This standard became effective for us on January 1, 2018. This standard did not have a significant impact on our condensed consolidated financial statements and related disclosures for the three months ended March 31, 2018. However, we expect this standard to have an impact on our condensed consolidated financial statements and related disclosures beginning in the second quarter of 2018 as a result of the 983,208 shares of Dicerna Pharmaceuticals, Inc., or Dicerna, common stock that we received under a settlement agreement entered into in April 2018, described more fully below at Note 5.

In February 2016, the FASB issued a new leasing standard that requires that all lessees recognize the assets and liabilities that arise from leases on the condensed consolidated balance sheet and disclose qualitative and quantitative information about its leasing arrangements. The new standard will be effective for us on January 1, 2019. Early adoption is permitted. We are currently evaluating the timing of our adoption and the expected impact that this standard could have on our condensed consolidated financial statements and related disclosures.

In November 2016, the FASB issued a new standard that requires restricted cash and restricted cash equivalents be included with cash and cash equivalents when reconciling the total beginning and ending amounts for the periods shown on the condensed consolidated statements of cash flows. The new standard became effective for us on January 1, 2018 using a retrospective transition method for each period presented. For the years ended December 31, 2017 and 2016, our restricted cash and restricted cash equivalents were not significant. This standard did not have a significant impact on our condensed consolidated financial statements and related disclosures.

In March 2017, the FASB issued a new standard that amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period for the premium to the earliest call date. The new standard will be effective for us on January 1, 2019. Early adoption is permitted. We are currently evaluating the timing of our adoption and the expected impact that this standard could have on our condensed consolidated financial statements and related disclosures.

In March 2018, the FASB issued a new standard to incorporate SEC Staff Accounting Bulletin No. 118, or SAB 118, which addresses the accounting implications of the Tax Cuts and Jobs Act, or TCJA, enacted on December 22, 2017. SAB 118 allows a company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date and was effective upon issuance. We continue to assess the TCJA, and in certain areas, have made reasonable estimates of the effects on our condensed consolidated financial statements and tax disclosures,

described more fully below at Note 6.

#### Subsequent Events

We did not have any material recognized subsequent events. However, we did have a nonrecognized subsequent event with respect to a Settlement Agreement and General Release, or the Settlement Agreement, entered into by us and Dicerna, resolving all ongoing litigation between the parties, which is more fully described below at Note 5.

## 2. COLLABORATION AGREEMENTS

The following table summarizes our total consolidated net revenues from collaborators, for the periods indicated, in thousands:

| Description                           | Three Months<br>Ended March 31, |          |
|---------------------------------------|---------------------------------|----------|
|                                       | 2018                            | 2017     |
| Sanofi Genzyme                        | \$18,853                        | \$12,277 |
| MDCO                                  | 1,295                           | 6,364    |
| Other                                 | 1,751                           | 319      |
| Total net revenues from collaborators | \$21,899                        | \$18,960 |

The following table summarizes our total consolidated net revenues from collaborators, using the prior revenue standard, for the periods indicated, in thousands:

| Description                           | Three Months Ended March 31, |          |
|---------------------------------------|------------------------------|----------|
|                                       | 2018                         | 2017     |
| Sanofi Genzyme                        | \$50,430                     | \$12,277 |
| MDCO                                  | 2,845                        | 6,364    |
| Other                                 | 1,751                        | 319      |
| Total net revenues from collaborators | \$55,026                     | \$18,960 |

The following table presents the balance of our contract liabilities at January 1, 2018 and March 31, 2018, in thousands, which at March 31, 2018 includes the achievement of the \$50.0 million milestone under our collaboration with Sanofi Genzyme as discussed below:

|                       | At<br>January<br>1, 2018 | At<br>March<br>31,<br>2018 |
|-----------------------|--------------------------|----------------------------|
| Contract liabilities: |                          |                            |
| Deferred revenues     | \$16,570                 | \$43,531                   |

During the three months ended March 31, 2018, we recognized the following revenues as a result of the change in the contract liability balances, in thousands:

| Revenue recognized in the period from:                                | Three Months Ended March 31, 2018 |
|---|-----------------------------------|
| Amounts included in contract liability at the beginning of the period | \$ 5,883                          |

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 the research and development expenses incurred by type that are directly attributable to each significant agreement for the periods indicated, in thousands:

|  | Three Months Ended March 31, |              |              |              |
|--|------------------------------|--------------|--------------|--------------|
|  | 2018                         |              | 2017         |              |
|  | Sanofi                       |              | Sanofi       |              |
|  | Genzyme MDCO                 | Genzyme MDCO | Genzyme MDCO | Genzyme MDCO |
| Research and development                   |                              |              |              |              |
| Clinical trial and manufacturing           | \$ 10,523                    | \$ 641       | \$ 40,575    | \$ 5,095     |
| External services                          | 2,673                        | —            | 567          | —            |
| Other                                      | 509                          | —            | 1,436        | 24           |
| Total research and<br>development expenses | \$ 13,705                    | \$ 641       | \$ 42,578    | \$ 5,119     |

The research and development expenses incurred for each significant agreement consist of costs incurred for external development and manufacturing services for which we are reimbursed, licensing payments made to the counterparty to such agreement and costs directly attributable to Sanofi Genzyme transition services. In addition, these expenses include a reasonable estimate of compensation and related costs as billed to our counterparties. As part of our revenue recognition policy, the costs in the above table are considered as an input in our determination of transaction price when they relate to consideration received for the delivery of goods or services. For the three months ended March 31, 2018 and 2017, we did not incur material general and administrative expenses related to our significant agreements.

## Product Alliances

### Sanofi Genzyme Collaboration

In January 2014, we entered into a global, strategic collaboration with Sanofi Genzyme to discover, develop and commercialize RNAi therapeutics as Genetic Medicines to treat orphan diseases, referred to as the 2014 Sanofi Genzyme collaboration. The 2014 Sanofi Genzyme collaboration superseded and replaced the previous collaboration between us and Sanofi Genzyme entered into in October 2012 to develop and commercialize RNAi therapeutics targeting transthyretin, or TTR, for the treatment of hereditary ATTR amyloidosis, including patisiran and revusiran, in Japan and the Asia-Pacific region.

On January 6, 2018, we and Sanofi Genzyme entered into an amendment to our 2014 Sanofi Genzyme collaboration. In connection and simultaneously with entering into the amendment to the 2014 Sanofi Genzyme collaboration, we and Sanofi Genzyme also entered into the Exclusive TTR License and the AT3 License Terms. As a result, we have the exclusive right to pursue the further global development and commercialization of all TTR products, including patisiran, ALN-TTRsc02 and any back-up products, and Sanofi Genzyme has the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products. The January 2018 transaction was subject to customary closing conditions and clearances, including clearance under the Hart-Scott-Rodino Antitrust Improvements Act, and closed during the first quarter of 2018.

### 2012 Sanofi Genzyme Agreement

Under the 2012 Sanofi Genzyme agreement, Sanofi Genzyme paid us an upfront cash payment of \$22.5 million. We were also entitled to receive certain milestone payments under the 2012 Sanofi Genzyme agreement. In the fourth quarter of 2013, we earned \$11.0 million in patisiran development milestones under the 2012 Sanofi Genzyme agreement.

We determined that the deliverables under the 2012 Sanofi Genzyme agreement included the license, a joint steering committee and any additional TTR-specific RNAi therapeutic compounds that comprised the ALN-TTR program. We also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and undelivered joint steering committee and any additional TTR-specific RNAi therapeutic compounds did not have standalone value due to the specialized nature of the services to be provided by us. In addition, while Sanofi Genzyme had the ability to grant sublicenses, it could not sublicense all or substantially all of its rights under the 2012 Sanofi Genzyme agreement. The uniqueness of our services and the limited sublicense right were indicators that standalone value was not present in the arrangement. Therefore the deliverables were not separable and, accordingly, the license and undelivered services were treated as a single unit of accounting. We were unable to reasonably estimate the period of performance under the 2012 Sanofi Genzyme agreement, as we were unable to estimate the timeline of our deliverables related to the deliverable for any additional TTR-specific RNAi therapeutic compounds.

Through December 31, 2013, under the prior revenue standard, we had deferred all revenue, or \$33.5 million, under the 2012 Sanofi Genzyme agreement.

### 2014 Sanofi Genzyme Collaboration, as amended in January 2018

In January 2014, we entered into the 2014 Sanofi Genzyme collaboration. As noted above, the 2014 Sanofi Genzyme collaboration superseded and replaced the 2012 Sanofi Genzyme agreement and was amended in January 2018, at which time we also entered into the Exclusive TTR License and the AT3 License Terms.

The 2014 Sanofi Genzyme collaboration is structured as an exclusive relationship for the worldwide development and commercialization of RNAi therapeutics in the field of Genetic Medicines, which includes our current and future

Genetic Medicine programs that reach Human Proof-of-Principle Study Completion (as defined in the Sanofi Genzyme master agreement), or Human POP, by the end of 2019, subject to extension to the end of 2021 in various circumstances. We will retain product rights in the United States, Canada and Western Europe, referred to as the Alnylam Territory, while Sanofi Genzyme will obtain exclusive rights to develop and commercialize collaboration products in the rest of the world, referred to as the Sanofi Genzyme Territory, together with worldwide rights for one product. Sanofi Genzyme's rights under the 2014 Sanofi Genzyme collaboration, described in detail below, are structured as an opt-in that is triggered upon achievement of Human POP. We maintain development control for all programs prior to Sanofi Genzyme's opt-in and maintain development and commercialization control after Sanofi Genzyme's opt-in for all programs in the Alnylam Territory. We will retain global rights to any RNAi therapeutic Genetic Medicine program that does not reach Human POP by the end of 2019, subject to certain limited exceptions. We retain full rights to all current and future RNAi therapeutic programs outside of the field of Genetic Medicines, including the right to form new collaborations.



Under the 2014 Sanofi Genzyme collaboration, Sanofi Genzyme's specific license rights and the programs which Sanofi Genzyme opted into prior to the 2018 amendment include the following:

**Regional license terms and programs** — Upon opt-in, we will retain product rights in the Alnylam Territory, while Sanofi Genzyme will obtain exclusive rights to develop and commercialize the product in the Sanofi Genzyme Territory. Sanofi Genzyme can elect this license for any of our current and future Genetic Medicine programs that complete Human POP by the end of 2019, subject to limited extension. Development costs for products once Sanofi Genzyme exercises an option will be shared between Sanofi Genzyme and us, with Sanofi Genzyme responsible for twenty percent of the global development costs. Sanofi Genzyme will be required to make payments totaling up to \$75.0 million per regional product, consisting of up to \$55.0 million in development milestones and \$20.0 million in commercial milestones. Sanofi Genzyme will also be required to pay tiered double-digit royalties up to twenty percent for each regional product based on annual net sales, if any, of such regional product by Sanofi Genzyme, its affiliates and sublicensees. Upon the effective date of the 2014 Sanofi Genzyme collaboration, Sanofi Genzyme expanded the scope of its regional license and collaboration for patisiran, which was originally established under the 2012 Sanofi Genzyme agreement. In September 2015, Sanofi Genzyme elected to opt into our fitusiran clinical development program for the treatment of hemophilia and other rare bleeding disorders under the regional license terms. Cost-sharing for the fitusiran program began in January 2016 under the regional license terms. Sanofi Genzyme also had the right to elect to co-develop and co-commercialize fitusiran in the Alnylam Territory pursuant to the co-development/co-commercialize license terms described below. In November 2016, Sanofi Genzyme exercised this right and elected to co-develop and co-commercialize fitusiran in the Alnylam Territory. In addition, during 2016, Sanofi Genzyme elected not to opt into the development and commercialization of givosiran or cemdisiran in the Sanofi Genzyme Territory.

Sanofi Genzyme's rights with respect to patisiran and fitusiran were modified in connection with the 2018 amendment, the Exclusive TTR License and the AT3 License Terms, as described below. Sanofi Genzyme continues to have the right to opt into our future rare genetic disease programs for development and commercialization in the Sanofi Genzyme Territory under the regional license terms.

**Co-development/co-commercialize license terms and programs** — Upon opt-in, we retained product rights in the Alnylam Territory, while Sanofi Genzyme obtained exclusive rights to develop and commercialize the product in the Sanofi Genzyme Territory, and to co-commercialize the product in the Alnylam Territory. Upon the effective date of the 2014 Sanofi Genzyme collaboration, Sanofi Genzyme expanded its regional rights for revusiran, which were originally granted under the 2012 Sanofi Genzyme agreement, to include a co-development/co-commercialize license and collaboration. In October 2016, we decided to discontinue development of revusiran. In our TTR program, we are also developing ALN-TTRsc02. Sanofi Genzyme had a right to elect a co-development/co-commercialize license for ALN-TTRsc02. As noted above, in November 2016, Sanofi Genzyme exercised its right to elect a co-development/co-commercialize license for fitusiran. Development costs for co-development/co-commercialize products, once Sanofi Genzyme exercised an option, were shared between Sanofi Genzyme and us, with Sanofi Genzyme responsible for fifty percent of the global development costs. In connection with the exercise of its co-development/co-commercialize rights for fitusiran, Sanofi Genzyme paid us approximately \$6.0 million in January 2017 for its incremental share of co-development costs incurred from January 2016 through September 2016. Sanofi Genzyme was required to make certain milestone payments for fitusiran, and, prior to the discontinuation of the revusiran program, was required to make certain milestone payments for revusiran. In December 2014, we earned a development milestone payment of \$25.0 million based upon the initiation of the first global Phase 3 clinical trial for revusiran. Sanofi Genzyme was also obligated to pay us a milestone of \$25.0 million upon the dosing of the first patient in our ATLAS Phase 3 program for fitusiran. In addition, Sanofi Genzyme was required to pay tiered double-digit royalties up to twenty percent for each co-development/co-commercialize product based on annual net sales, if any, in the Sanofi Genzyme Territory for such co-development/co-commercialize product by Sanofi Genzyme, its affiliates and sublicensees. The parties were to share profits equally and we expected to book product sales in the Alnylam Territory.

In connection with the 2018 amendment, the Exclusive TTR License and the AT3 License Terms, as described below, we and Sanofi Genzyme agreed to terminate the co-development and co-commercialization rights related to revusiran, ALN-TTRsc02 and fitusiran under the 2014 Sanofi Genzyme collaboration. No future rights will be granted to Sanofi Genzyme for co-development and co-commercialization under the 2014 Sanofi Genzyme collaboration, as amended by the 2018 amendment.

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Global license terms and programs — Sanofi Genzyme continues to have one right to a global license through 2019, subject to limited extension, for a future Genetic Medicine program that was not one of our defined Genetic Medicine programs as of the effective date of the 2014 Sanofi Genzyme collaboration. Upon opt-in, Sanofi Genzyme will obtain a worldwide license to develop and commercialize the product. Sanofi Genzyme shall be responsible for one hundred percent of global development costs for a global license product. Sanofi Genzyme will be required to make payments totaling up to \$200.0 million for such global product, including up to \$100.0 million in development milestones and \$100.0 million in commercial milestones. Sanofi Genzyme will also be required to pay tiered double-digit royalties up to twenty percent for such global product based on annual net sales, if any, of each global product by Sanofi Genzyme, its affiliates and sublicensees. During the first quarter of 2018, Sanofi Genzyme elected not to exercise its global option for our lumasiran program.

#### Exclusive TTR License and AT3 License Terms

As noted above, the 2018 amendment, together with the Exclusive TTR License and the AT3 License Terms, revise the terms and conditions of the 2014 Sanofi Genzyme collaboration to (i) provide us the exclusive right to pursue the further global development and commercialization of all TTR products, including patisiran, ALN-TTRsc02 and any back-up products, (ii) provide Sanofi Genzyme the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products and (iii) terminate the previous co-development and co-commercialization rights related to revusiran, ALN-TTRsc02 and fitusiran under the 2014 Sanofi Genzyme collaboration. Going forward, we are funding all development and commercialization costs for patisiran and ALN-TTRsc02. We are also funding development and commercialization costs for fitusiran through the transition period, up to a cap of \$50.0 million, after which Sanofi Genzyme will fund all development and commercialization costs for fitusiran. We expect to substantially complete the transition of the fitusiran program to Sanofi Genzyme by mid-2018. Each party is responsible for its costs associated with the transfer of the respective program to the other party.

Under the 2018 amendment and the Exclusive TTR License, Sanofi Genzyme will be eligible to receive (i) royalties up to twenty-five percent, increasing over time, based on annual net sales of patisiran in territories excluding the United States, Canada and Western Europe, provided royalties on annual net sales of patisiran in Japan will be twenty-five percent beginning as of the effective date of the Exclusive TTR License, (ii) tiered royalties of fifteen to thirty percent based on global annual net sales of ALN-TTRsc02 (consistent with the royalties due to us from Sanofi Genzyme on fitusiran), and (iii) tiered royalties of up to fifteen percent based on global annual net sales of any back-up products, in each case by us, our affiliates and our sublicensees. Except as described below, there will be no additional milestones due to either party with respect to patisiran, ALN-TTRsc02 or fitusiran.

In consideration for the rights granted to Sanofi Genzyme under the 2018 amendment and the AT3 License Terms, Sanofi Genzyme is required to make one milestone payment of \$50.0 million following the dosing of the first patient in the ATLAS Phase 3 program for fitusiran. This milestone was achieved in the first quarter of 2018. In addition, we will be eligible to receive tiered royalties of fifteen to thirty percent based on global annual net sales of fitusiran and up to fifteen percent based on global annual net sales of any back-up products, in each case by Sanofi Genzyme, its affiliates and its sublicensees. We and Sanofi Genzyme intend to enter into a supply agreement to provide for the supply of fitusiran to Sanofi Genzyme for ongoing clinical studies, and, at Sanofi Genzyme's request, commercial sales. Sanofi Genzyme also has the right to manufacture fitusiran.

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 from Sanofi Genzyme under the 2014 Sanofi Genzyme collaboration, as amended, or the AT3 License Terms.

The 2014 Sanofi Genzyme collaboration, as amended, will continue to be governed by an alliance joint steering committee that is comprised of an equal number of representatives from each party. Additional committees manage various aspects of each regional and global program and oversee certain matters, including transition planning, that may arise under the Exclusive TTR License and the AT3 License Terms.

As noted above, the Sanofi Genzyme collaboration originally entered into in 2012 was materially modified during its term when the agreement was amended in 2014, prior to our adoption of the new revenue standard on January 1, 2018. In accordance with the new revenue standard, we evaluated the Sanofi Genzyme collaboration with the aggregate effect of all modifications when identifying performance obligations, determining the transaction price and allocating the transaction price. We determined that certain promises included in these agreements are within the scope of the new revenue standard since Sanofi Genzyme is a customer with respect to the license of the rights to its territories. We also determined, however, that certain aspects of these agreements are within the scope of the collaboration accounting guidance with respect to co-commercialization activities as these activities are joint risk-sharing and are not reflective of a vendor-customer relationship. We apply the new revenue standard to all promises associated with the transfer of goods and services to a customer.

We concluded that Sanofi Genzyme meets the definition of a customer as we are delivering intellectual property and know-how rights as well as research and development activities for the TTR programs and fitusiran programs in support of territories in which we are not jointly sharing the risks and rewards. We concluded that the accounting for the original 2014 Sanofi Genzyme collaboration, and the collaboration, as amended, should be assessed as separate contracts for (i) the patisiran and revusiran (TTR) programs, upon the initiation of the 2014 Sanofi Genzyme collaboration, and (ii) the subsequent opt-in by Sanofi Genzyme for the fitusiran program. In addition, we determined that the Sanofi Genzyme collaboration met the requirements to be accounted for as a contract, including that it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services that will be delivered to Sanofi Genzyme. We identified contract promises or deliverables for licenses to our intellectual property and know-how rights, associated development activities, joint steering committee participation and information exchange. We determined that, pursuant to the new revenue standard (and consistent with our accounting prior to the adoption of the new revenue standard), the performance obligations were not separately identifiable and were not distinct (and did not have standalone value) due to the specialized nature of the services to be provided by us and the dependent relationship between the performance obligations. Given this fact pattern, we have concluded each of the TTR and fitusiran contracts have a single identified or combined performance obligation.

When applying the previous revenue standard, we determined that the co-commercialization activities prior to the 2018 amendment were within the scope of the collaboration accounting standard since both parties would actively participate in the co-commercialization and be subject to significant risks and rewards. As a result of this determination, we recorded any payments or cash receipts for these joint risk-sharing activities as an adjustment to the related operations expense captions. The amounts recorded as a reduction of our selling, general and administrative activities were not material.

The transaction price as of January 1, 2018 of \$127.6 million for the 2014 Sanofi Genzyme collaboration related to the license to the TTR programs included the \$22.5 million upfront payment and \$11.0 million of development milestone payments earned under the now superseded 2012 Sanofi Genzyme agreement, a \$25.0 million development milestone payment for revusiran achieved in 2014, the estimated patisiran and revusiran cost-share reimbursements of \$63.6 million and \$57.0 million, net of payments to Sanofi Genzyme, respectively, and the \$51.5 million equity discount related to the stock purchase agreement, described below. Since the fair value of the stock at the time of closing was more than the consideration received by the Company by \$51.5 million, we reduced the transaction price of the license and collaboration contract, treating the equity discount in a manner consistent with a payment to the customer. The transaction price related to our license to the fitusiran program as of January 1, 2018, accounted for as a separate agreement, included estimated fitusiran development cost-share reimbursements of \$147.3 million, net of payments to Sanofi Genzyme. There are no refund provisions in the agreement and, therefore, none of the consideration received to date has been excluded from the transaction price calculation. None of the unearned milestones as of January 1, 2018 were included in the transaction price, as all unearned milestone amounts were determined to be fully constrained. We considered several factors, including that achievement of the milestones is outside our control and contingent upon success in clinical trials and regulatory decisions and the licensee's efforts. Any consideration related to sales-based royalties (including milestones) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Sanofi Genzyme and as a result have also been excluded from the transaction price. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

We allocated the transaction price to the combined performance obligation. We have determined that this combined performance obligation is satisfied over time based on our performance that is creating or enhancing an asset that Sanofi Genzyme controls. In this instance, Sanofi Genzyme received control over the asset, or the licensed intellectual property, and know-how, at the time the contract was executed since the licensed intellectual property and know-how meet the definition of functional intellectual property per the new revenue standard, which defines functional intellectual property as intellectual property that derives a substantial portion of its utility from its standalone functionality rather than the entity's ongoing activities (thus, once the asset is fully developed, our ongoing involvement is not required for the licensee to derive value). The other promises included in the performance

obligation, however, are enhancing the controlled asset, and thus the combined performance obligation is being satisfied over time.

The new revenue standard requires a single method of measuring performance for each performance obligation satisfied over time. Since we do not have a reliable method of estimating progress based upon its outputs, it was determined that the most reliable method of estimating progress would be using a cost-to-cost input method. We have determined that our completion of certain clinical and regulatory development tasks is relevant and directly related to our progress in completing the combined performance obligation. As such, we measured our progress upon adoption and will continue to measure our progress during each reporting period based upon the amount of development costs incurred divided by the total amount of development costs expected to be incurred over the course of the agreement. We exclude costs that are not related to our completion of this performance obligation, such as the completion of tasks (and incurring of costs) associated with the marketing and commercialization of the drug. We estimated our internal costs during the last three years, excluding non-reimbursable costs that were not deemed to directly relate to the delivery of the development services to Sanofi Genzyme. Historically, we have been unable to reliably measure our performance based upon our lack of historical experience in completing the development of a drug candidate and have, as a result, defaulted to straight-line attribution for many of our licensing agreements. At the time of adoption of the new revenue standard, however, we have completed a substantial portion of our development obligations and determined we have sufficient information to estimate the remaining development costs for the fitusiran program and sufficient experience to reasonably estimate our development costs.

We determined that the 2018 amendment, together with the Exclusive TTR License and the AT3 License Terms, referred to as the 2018 restructured agreement, are included in the scope of the modification provisions of the new revenue standard. We had identified that the agreement for the TTR programs under the 2014 Sanofi Genzyme collaboration should be accounted for separately from any subsequent option exercises, including with respect to fitusiran. Therefore, we concluded it is appropriate to account for the 2018 restructured agreement as two separate modifications to the 2014 Sanofi Genzyme collaboration: one related to the TTR programs and one related to the fitusiran program. Our conclusions related to scoping under the prior revenue standard are consistent with the new revenue standard.

As noted above, the 2018 amendment, together with the Exclusive TTR License, provide us with the exclusive right to pursue the further global development and commercialization of all TTR products, including patisiran. We are responsible for all development and commercialization costs for patisiran and ALN-TTRsc02. As of the 2018 restructured agreement, we are no longer required to complete the delivery of any of the performance obligations under the agreement related to the TTR programs. As a result, the transaction price prior to the 2018 amendment has been reduced as we are no longer entitled to cost-share reimbursements or any of the previously constrained consideration, such as milestones and royalties. Since the 2018 amendment affected the transaction price but did not add any incremental and distinct performance obligations, we concluded this amendment should be accounted for as a change to the existing agreement and recorded the revenue on a cumulative catch-up basis. At the time of the 2018 amendment, we had \$2.9 million in revenue deferred as a contract liability on our condensed consolidated balance sheet related to this contract for TTR programs, all of which we recognized in the first quarter of 2018 under the proportional performance model as we no longer expected to incur costs associated with the delivery of goods or services. If we had not adopted the new revenue standard, at the time of the 2018 restructured agreement, we would have \$25.8 million of deferred revenues on our condensed consolidated balance sheet that would have been recognized in full upon the date of the 2018 restructured agreement as we would have similarly concluded there were no ongoing deliverables under the 2018 restructured agreement related to the TTR programs. We expect to record future royalties payable to Sanofi Genzyme with respect to any sales of patisiran within cost of goods sold as Sanofi Genzyme is no longer considered our customer after the 2018 restructured agreement for sales of all TTR products, including patisiran, and as such, these royalty payments are outside of the scope of the new revenue standard, including with respect to principal versus agent guidance.

The 2018 amendment, together with the AT3 License Terms, as noted above, provide Sanofi Genzyme the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products and terminates the previous co-development and co-commercialization rights related to fitusiran under the 2014 Sanofi Genzyme collaboration. The 2018 restructured agreement provides a broader license that permits global development, manufacturing and commercialization, and we are required to facilitate the transfer of all ongoing activities, contracts, intellectual property, know-how and other materials and information related to fitusiran to Sanofi Genzyme.

In connection with the 2018 restructured agreement for fitusiran, we will fund development and commercialization costs for fitusiran through the transition period, which is expected to end in mid-2018, up to a limit of \$50.0 million. The only milestone under the 2018 restructured agreement, which was achieved in the first quarter of 2018 following the dosing of the first patient in the ATLAS Phase 3 program for fitusiran, is considered variable consideration for the license and transition services related to the fitusiran program. We have agreed to reimburse Sanofi Genzyme for certain transition activities that are reflected as a reduction in the transaction price. As a result, the transaction price has been reduced as we are no longer entitled to cost-share reimbursements or any of the previously constrained consideration, such as milestones and royalties.

We concluded that the modification that resulted from the 2018 restructured agreement related to fitusiran would be treated as a termination and replacement of the 2014 Sanofi Genzyme collaboration and accounted for prospectively as the remaining license and transition services are considered distinct from that under the agreement prior to this modification. However, the incremental consideration under the 2018 restructured agreement does not directly reflect the standalone selling price of the incremental performance obligation. Therefore, we concluded the 2018 restructured

agreement for fitusiran should be accounted for on a prospective basis. At the time of the 2018 amendment, we had \$0.6 million in revenue deferred as a contract liability on our condensed consolidated balance sheet related to the 2014 Sanofi Genzyme collaboration for the fitusiran program. As of March 31, 2018, the transaction price of the 2018 restructured agreement for fitusiran is \$45.0 million, primarily related to the \$50.0 million milestone that was achieved in the first quarter of 2018. Consistent with our accounting prior to this 2018 modification, we are applying the sales-based royalty under the new revenue standard to exclude from the transaction price the royalties earned on Sanofi Genzyme's sales of fitusiran as we have determined in the context of all the performance obligations, including those delivered prior to the 2018 modification, that the value of the broader license will continue to represent a substantial portion of the value provided to Sanofi Genzyme; and therefore the license to the intellectual property is the predominant item to which the royalty relates.

We have determined that Sanofi Genzyme's right to purchase additional clinical and commercial material from us reflects optional purchases that are distinct from other performance obligations. Revenues associated with these purchases will be recognized as Sanofi Genzyme obtains control of any purchased material.



We are recognizing the transaction price of the 2018 restructured agreement related to fitusiran under a separate proportional performance model as we perform transition services over the transition period, expected to end in mid-2018. We are measuring our performance based on a percentage of our costs expected to be incurred, currently estimated to be \$43.6 million. In the first quarter of 2018, under the proportional performance model, we recognized \$16.0 million related to the 2018 restructured agreement for fitusiran. If we had not adopted the new revenue standard, at the time of the 2018 restructured agreement, we would have \$23.4 million of deferred revenues on our condensed consolidated balance, that would have represented an incremental \$22.8 million to the transaction price. Similar to under the new revenue standard, we consider the 2018 restructured agreement related to fitusiran to include a combined performance obligation. Under the prior revenue standard and our historical practice to account for contract modifications, we would apply a separate model to the consideration. Historically, we have measured our performance under our models based on the passage of time due to our inability to estimate performance under another method. However, as a result of the 2018 restructured agreement related to fitusiran, we have the ability to measure our performance under the prior revenue standard based on costs expected to be incurred, and therefore measure performance under the prior standard consistent with that of the new revenue standard. Under the prior revenue standard, we would have recorded \$24.6 million in the first quarter of 2018.

We determined that the opt-in rights that Sanofi Genzyme continues to have for future Genetic Medicine programs represent separate and additional optional purchases that Sanofi Genzyme may receive from us in future periods.

#### Accounting for Equity Purchases In Connection with our 2014 Sanofi Genzyme Collaboration

Upon the closing of the equity transaction in February 2014, we sold to Sanofi Genzyme 8,766,338 shares of our common stock and Sanofi Genzyme paid \$700.0 million in aggregate cash consideration to us. As a condition to the closing of the equity transaction, Sanofi Genzyme entered into an investor agreement with us containing provisions regarding Sanofi Genzyme's holding and "standstill" obligations, additional purchase, voting and registration rights, as well as certain other rights and obligations of the parties.

We recorded the issuance of 8,766,338 shares of our common stock under the stock purchase agreement using the price of our common stock on the date the shares were issued to Sanofi Genzyme. Based on the common stock price of \$85.72, the fair value of the shares issued was \$751.5 million, which was \$51.5 million in excess of the proceeds received from Sanofi Genzyme for the issuance of our common stock. This \$51.5 million has been reflected as a reduction of the transaction price for the ALN-TTR programs. In addition, due to intraperiod tax allocation rules, upon closing of the equity transaction we recorded a benefit from income taxes of \$15.2 million due to the Sanofi Genzyme equity purchase being recorded in additional paid-in capital, net of tax.

In accordance with the investor agreement, as a result of our issuance of shares in connection with our acquisition of Sirna Therapeutics, Inc., or Sirna, in March 2014, Sanofi Genzyme exercised its right to purchase an additional 344,448 shares of our common stock for \$23.0 million. In addition, in connection with our public offerings, Sanofi Genzyme exercised its right to purchase directly from us, in concurrent private placements, 744,566 shares of common stock in January 2015 at the public offering price resulting in \$70.7 million in proceeds to us and 297,501 shares of common stock in May 2017 at the public offering price resulting in \$21.4 million in proceeds to us. The sales of common stock to Sanofi Genzyme were not registered as part of these public offerings, though they were consummated simultaneously with the public offering.

Sanofi Genzyme also has the right at the beginning of each year to purchase a number of shares of our common stock based on the number of shares we issued during the previous year for compensation-related purposes. Sanofi Genzyme exercised this right to purchase directly from us 196,251 shares of our common stock in January 2015 for \$18.3 million and 205,030 shares of our common stock in February 2016 for \$14.3 million. The sales of these shares to Sanofi Genzyme were consummated as private placements.

Sanofi Genzyme currently holds approximately 11 percent of our outstanding common stock.

We applied the guidance in the equity accounting standard for the stock purchase arrangement since the sale of our equity is not part of our ordinary activities and, therefore, does not qualify as a contract with a customer that is within the scope of the new revenue standard.

## 3. FAIR VALUE MEASUREMENTS

The following tables present information about our assets that are measured at fair value on a recurring basis at March 31, 2018 and December 31, 2017, and indicate the fair value hierarchy of the valuation techniques we utilized to determine such fair value, in thousands:

| Description                                     | At<br>March 31,<br>2018 | Quoted                                      |  |  |
|---|-------------------------|---|--|--|
|   |                         | Prices in<br>Active<br>Markets<br>(Level 1) | Significant<br>Observable<br>Inputs<br>(Level 2) | Significant<br>Unobservable<br>Inputs<br>(Level 3) |
| <b>Cash equivalents:</b>                        |                         |   |  |  |
| Commercial paper                                | \$19,981                | \$—   | \$19,981   | \$ —   |
| Corporate notes                                 | 5,168                   | —   | 5,168  | —  |
| U.S. treasury securities                        | 5,491                   | —   | 5,491  | —  |
| Money market funds                              | 231,854                 | 231,854                                     | —  | —  |
| <b>Marketable securities (fixed income):</b>    |                         |   |  |  |
| Certificates of deposit                         | 33,541                  | —   | 33,541   | —  |
| Commercial paper                                | 96,539                  | —   | 96,539   | —  |
| Corporate notes                                 | 401,035                 | —   | 401,035  | —  |
| U.S. government-sponsored enterprise securities | 378,861                 | —   | 378,861  | —  |
| U.S. treasury securities                        | 262,387                 | —   | 262,387  | —  |
| Restricted cash (money market funds)            | 1,474                   | 1,474                                       | —  | —  |
| <b>Total</b>                                    | <b>\$1,436,331</b>      | <b>\$233,328</b>                            | <b>\$1,203,003</b>                               | <b>\$ —</b>  |

| Description                                     | At<br>December 31,<br>2017 | Quoted                                      |  |  |
|---|----------------------------|---|--|--|
|   |                            | Prices in<br>Active<br>Markets<br>(Level 1) | Significant<br>Observable<br>Inputs<br>(Level 2) | Significant<br>Unobservable<br>Inputs<br>(Level 3) |
| <b>Cash equivalents:</b>                        |                            |   |  |  |
| Commercial paper                                | \$ 82,262                  | \$—   | \$82,262   | \$ —   |
| Corporate notes                                 | 18,116                     | —   | 18,116   | —  |
| U.S. government-sponsored enterprise securities | 231,122                    | —   | 231,122  | —  |
| U.S. treasury securities                        | 62,855                     | —   | 62,855   | —  |
| Money market funds                              | 122,986                    | 122,986                                     | —  | —  |
| <b>Marketable securities (fixed income):</b>    |                            |   |  |  |
| Certificates of deposit                         | 30,200                     | —   | 30,200   | —  |
| Commercial paper                                | 56,951                     | —   | 56,951   | —  |
| Corporate notes                                 | 373,252                    | —   | 373,252  | —  |

|   |              |            |              |      |
|---|--------------|------------|--------------|------|
| U.S. government-sponsored enterprise securities | 398,298      | —          | 398,298      | —    |
| U.S. treasury securities                        | 200,475      | —          | 200,475      | —    |
| Restricted cash (money market funds)            | 1,471        | 1,471      | —            | —    |
| Total   | \$ 1,577,988 | \$ 124,457 | \$ 1,453,531 | \$ — |

During the three months ended March 31, 2018 and 2017, there were no transfers between Level 1 and Level 2 financial assets. The carrying amounts reflected in our condensed consolidated balance sheets for cash, billed and unbilled collaboration receivables, other current assets, accounts payable and accrued expenses approximate fair value due to their short-term maturities. The fair value of our long-term debt at March 31, 2018, computed pursuant to a discounted cash flow technique using a market interest rate, was \$30.1 million and is considered a Level 3 fair value measurement. The effective interest rate reflects the current market rate.

#### 4. MARKETABLE SECURITIES

We obtain fair value measurement data for our marketable securities from independent pricing services. We perform validation procedures to ensure the reasonableness of this data. This includes meeting with the independent pricing services to understand the methods and data sources used. Additionally, we perform our own review of prices received from the independent pricing services by comparing these prices to other sources and confirming those securities are trading in active markets.

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The following tables summarize our marketable securities at March 31, 2018 and December 31, 2017, in thousands:

|   | At March 31, 2018 |            |            |             |
|---|-------------------|------------|------------|-------------|
|   | Gross             |            | Gross      |             |
|   | Amortized         | Unrealized | Unrealized |             |
|   | Cost              | Gains      | Losses     | Fair Value  |
| Certificates of deposit                         | \$33,541          | \$ —       | \$ —       | \$33,541    |
| Commercial paper                                | 96,539            | —          | —          | 96,539      |
| Corporate notes                                 | 401,930           | 5          | (900)      | 401,035     |
| U.S. government-sponsored enterprise securities | 379,692           | —          | (831)      | 378,861     |
| U.S. treasury securities                        | 262,722           | —          | (335)      | 262,387     |
| Total   | \$1,174,424       | \$ 5       | \$ (2,066) | \$1,172,363 |

|   | At December 31, 2017 |            |            |             |
|---|----------------------|------------|------------|-------------|
|   | Gross                |            | Gross      |             |
|   | Amortized            | Unrealized | Unrealized |             |
|   | Cost                 | Gains      | Losses     | Fair Value  |
| Certificates of deposit                         | \$30,200             | \$ —       | \$ —       | \$30,200    |
| Commercial paper                                | 56,951               | —          | —          | 56,951      |
| Corporate notes                                 | 373,736              | 11         | (495)      | 373,252     |
| U.S. government-sponsored enterprise securities | 399,281              | —          | (983)      | 398,298     |
| U.S. treasury securities                        | 200,649              | 1          | (175)      | 200,475     |
| Total   | \$1,060,817          | \$ 12      | \$ (1,653) | \$1,059,176 |

We classify our debt security investments based on their contractual maturity dates. The following table summarizes our available-for-sale debt securities by contractual maturity, at March 31, 2018, in thousands:

|   | At March 31, 2018 |             |
|---|-------------------|-------------|
|   | Amortized Cost    | Fair Value  |
| Less than one year                            | \$1,173,776       | \$1,171,715 |
| Greater than one year but less than two years | 648               | 648         |
| Total   | \$1,174,424       | \$1,172,363 |

## 5. COMMITMENTS AND CONTINGENCIES

### Manufacturing Facility

In April 2016, we purchased 12 acres of undeveloped land in Norton, Massachusetts. We are constructing a manufacturing facility at this site for drug substance, including small interfering RNAs, or siRNAs, and siRNA conjugates, for clinical and commercial use. At March 31, 2018 and December 31, 2017, property, plant and

equipment, net, on our condensed consolidated balance sheets reflects \$158.2 million and \$140.5 million, respectively, of land and associated costs related to the construction of our drug substance manufacturing facility.

#### Credit Agreements

On April 29, 2016, we entered into (i) a Credit Agreement, or the BOA Credit Agreement, with Alnylam U.S., Inc., our wholly-owned subsidiary, as the borrower, us, as a guarantor, and Bank of America N.A., or BOA, as the lender and (ii) a Credit Agreement, or the Wells Credit Agreement, together with the BOA Credit Agreement, the Credit Agreements, by and among Alnylam U.S., Inc., as the borrower, us, as a guarantor, and Wells Fargo Bank, National Association, or Wells, as the lender. The Credit Agreements were entered into in connection with the planned build out of our new drug substance manufacturing facility.

The BOA Credit Agreement provided for a \$120.0 million term loan facility and was scheduled to mature on April 29, 2021. In December 2017, we repaid in full the \$120.0 million outstanding principal amount under the BOA Credit Agreement and the BOA Credit Agreement terminated in accordance with its terms upon repayment of the outstanding indebtedness. The Wells Credit Agreement provides for a \$30.0 million term loan facility and matures on April 29, 2021. The proceeds of the borrowing under the BOA Credit Agreement were, and under the Wells Credit Agreement are, to be used for working capital and general corporate purposes. Interest on borrowings under the BOA Credit Agreement was, and under the Wells Credit Agreement is calculated based on LIBOR plus 0.45 percent, except in the event of default. The borrower may prepay loans under the Wells Credit Agreement at any time, without premium or penalty, subject to certain notice requirements and LIBOR breakage costs.

The obligations of the borrower and us under the BOA Credit Agreement were, and under the Wells Credit Agreement are secured by cash collateral in an amount equal to, at any given time, at least 100 percent of the principal amount of all term loans outstanding under such Credit Agreement at such time. At each of March 31, 2018 and December 31, 2017, we have recorded \$30.0 million of cash collateral in connection with the Wells Credit Agreement as restricted investments on our condensed consolidated balance sheets. The Wells Credit Agreement contains limited representations and warranties and limited affirmative and negative covenants, including quarterly reporting obligations, as well as certain customary events of default.

## Litigation

From time to time, we are a party to 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 product candidates, and challenges by us to the scope, validity or enforceability of the patents held by others. These include claims by third parties that we infringe their patents. 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.

## Silence Litigation

On October 17, 2017, Silence Therapeutics plc, or Silence, served its previously announced claim in the High Court of England and Wales, or the High Court, issued in the name of Silence Therapeutics GmbH against Alnylam UK Ltd., Alnylam Pharmaceuticals, Inc., and The Medicines Company UK Ltd, referred to collectively as the Defendants. The claim seeks a declaration that patisiran, fitusiran, givosiran and inclisiran, together, the Products, are protected by Silence's European Patent No. 2 258 847, referred to as the '847 patent, within the meaning of the Supplementary Protection Certificate, or SPC, Regulation of the European Union. The claim alleges that any marketing authorization for any of these Products granted to any of the Defendants is a valid authorization within the meaning of the SPC Regulation, to support an application for an SPC by Silence for each of the Products, allegedly allowing Silence to extend the expiration date of its '847 patent on a Product-by-Product basis, based on the amount of time in regulatory review for each of the Products, again on a Product-by-Product basis, up to a statutory maximum. In addition, Silence is seeking costs, interest and other unspecified relief.

On October 31, 2017, the Defendants acknowledged service of the claim served by Silence contesting jurisdiction of the High Court. On November 30, 2017, the Defendants submitted substantive defenses to the claim.

On October 27, 2017, we, through our affiliate Alnylam UK Ltd., and The Medicines Company UK Ltd filed and served a claim against Silence Therapeutics GmbH and Silence in the High Court seeking revocation of the '847 patent, as well as a declaration of non-infringement by each of the Products of the '847 patent, and costs and interest among other potential remedies. The High Court has set a trial date of December 3, 2018 for all claims between Silence and the Defendants.

On December 13, 2017, we filed an opposition with the European Patent Office seeking revocation of the '847 patent in its entirety. Although we believe the '847 patent is invalid and not infringed by our Products and that, therefore, Silence would not be entitled to obtain an SPC based on any of our Products, litigation and opposition proceedings are subject to inherent uncertainty, as noted above, and a court or patent office could ultimately rule against us or find that Silence's patents are valid.

On March 29, 2018 we filed, and on April 6, 2018 served, an action against Silence in the United States District Court for the District of Massachusetts seeking a declaratory judgement of non-infringement by patisiran of Silence U.S. Patent Nos: 7,893,245; 8,324,370; 8,933,215; 9,222,092; and 9,695,423.

On April 2, 2018, we filed a petition for Post Grant Review of Silence U.S. Patent No. 9,695,423 with the U.S. Patent and Trademark Office seeking a cancellation of all claims as being unpatentable under 35 U.S.C. §§ 112 and 102.

On April 3, 2018, Silence amended its claim in the High Court of England and Wales further alleging that patisiran and fitusiran infringe its recently granted patent EP 1 857 547, referred to as the '547 patent, and seeking an injunction as well as monetary damages based on such alleged infringement. On April 23, 2018, Silence served patent infringement proceedings against us in Portugal alleging that patisiran infringes the '547 patent. Silence is seeking a permanent injunction against the commercialization of patisiran in Portugal. We believe the '547 patent is invalid and not infringed by any of our products and intend to vigorously defend against these claims in both the United Kingdom and Portugal and also intend to file an opposition with the European Patent Office seeking to revoke the '547 patent in its entirety.



## Dicerna Litigation

On June 10, 2015, we filed a trade secret misappropriation lawsuit against Dicerna in the Superior Court of Middlesex County, Massachusetts seeking to stop misappropriation by Dicerna of our confidential, proprietary and trade secret information related to the RNAi assets we purchased from Merck, including certain N-acetylgalactosamine, or GalNAc, conjugate technology. In addition to permanent injunctive relief, we were also seeking monetary damages from Dicerna. In August 2017, Dicerna successfully added counterclaims against us in the trade secret lawsuit alleging that our lawsuit represented abuse of process and claiming tortious interference with its business. In September 2017, we filed a motion to dismiss Dicerna's counterclaims, which motion was denied. 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. In October 2017, we filed a motion to dismiss the antitrust lawsuit.

On April 18, 2018, we and Dicerna entered into a Settlement Agreement resolving all ongoing litigation between the companies. The terms of the Settlement Agreement include mutual releases and dismissal with prejudice of all claims and counterclaims in the following litigation between the parties: (i) Alnylam Pharmaceuticals, Inc. v. Dicerna Pharmaceuticals, Inc., No. 15-4126, pending in the Massachusetts Superior Court for Middlesex County; and (ii) Dicerna Pharmaceuticals, Inc. v. Alnylam Pharmaceuticals, Inc., No. 1:17-cv-11466, pending in the United States District Court for the District of Massachusetts.

Under the terms of the Settlement Agreement, Dicerna will pay us an aggregate of \$25.0 million, including an upfront cash payment of \$2.0 million and 983,208 shares of Dicerna common stock, valued at \$10.0 million, and an additional \$13.0 million over the next four years, the timing of which will be dependent upon revenue Dicerna receives pursuant to future partnerships and collaborations related to GalNAc-conjugated RNAi research and development, provided that such additional amount must be paid by no later than April 18, 2022. In addition, Dicerna will be restricted in its development and other activities relating to oligonucleotide-based therapeutics directed toward a defined set of targets, for periods ranging from 18 months up to four years. The Settlement Agreement does not include any license to our GalNAc conjugate intellectual property or any licenses to any other intellectual property from either party. Nor does the Settlement Agreement include any admission of liability or wrongdoing by either company.

## 6. INCOME TAXES

For the three months ended March 31, 2018, we recorded a benefit from income taxes of \$62,000 with respect to a \$0.8 million benefit for refundable credits related to the TCJA offset by foreign income taxes.

Our preliminary estimate of the TCJA and the remeasurement of our deferred tax assets and liabilities is subject to the finalization of management's analysis related to certain matters, such as developing interpretations of the provisions of the TCJA, changes to certain estimates and the filing of our tax returns. U.S. Treasury regulations, administrative interpretations or court decisions interpreting the TCJA may require further adjustments and changes in our estimates. The final determination of the TCJA and the remeasurement of our deferred assets and liabilities will be completed as additional information becomes available, but no later than one year from the enactment of the TCJA. For the three months ended March 31, 2018, there were no changes to management's analysis originally performed as of December 31, 2017.



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

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. The statements contained in this Quarterly Report on Form 10-Q that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. Without limiting the foregoing, the words “may,” “will,” “should,” “could,” “expects,” “plans,” “intends,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” “target,” “goal” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. All forward-looking statements included in this Quarterly Report on Form 10-Q are based on information available to us up to, and including, the date of this document, and we expressly disclaim any obligation to update any such forward-looking statements to reflect events or circumstances that arise after the date hereof. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain important factors, including those set forth in this Item 2 — “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” as well as under Part II, Item 1A — “Risk Factors” and elsewhere in this Quarterly Report on Form 10-Q. You should carefully review those factors and also carefully review the risks outlined in other documents that we file from time to time with the Securities and Exchange Commission, or SEC.

### Overview

We are a global biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. RNAi is a naturally occurring biological pathway within cells for sequence-specific silencing and regulation of gene expression. We are harnessing the RNAi pathway to develop a potential new class of innovative medicines, known as RNAi therapeutics. RNAi therapeutics are comprised of small interfering RNA, or siRNA, and function upstream of today’s medicines by potently silencing messenger RNA, or mRNA, that encode for disease-causing proteins, thus preventing them from being made. This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

Our research and development strategy is to target genetically validated liver-expressed genes that have been implicated in the cause or pathway of human disease. We utilize a lipid nanoparticle, or LNP, or N-acetylgalactosamine, or GalNAc, conjugate approach to enable hepatic delivery of siRNAs. 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.

Specifically, our broad pipeline of investigational RNAi therapeutics is focused in three Strategic Therapeutic Areas, or “STARS:” Genetic Medicines; Cardio-Metabolic Diseases; and Hepatic Infectious Diseases. We are committed to the advancement of our Alnylam 2020 strategy, which is to achieve a company profile with three marketed products and ten RNAi therapeutic clinical programs, including four in late stages of development, across our three STARS by the end of 2020. In December 2017, we filed our first new drug application, or NDA, and marketing authorisation application, or MAA, for patisiran. In January 2018, we announced that the European Medicines Agency, or EMA, has accepted the MAA and initiated its review. Patisiran was previously granted an accelerated assessment by the EMA. In February 2018, we announced that the United States Food and Drug Administration, or FDA, has accepted our NDA and granted our request for priority review, with an action date of August 11, 2018. If approved, we expect to launch patisiran and may begin generating product revenues in 2018.

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 Sanofi Genzyme, the specialty care global business unit of Sanofi, The Medicines Company, or MDCO, and Vir Biotechnology, Inc. In addition, in late 2017, we joined a research consortium with the UK Biobank, Regeneron Pharmaceuticals, Inc., or Regeneron, and four major pharmaceutical companies aimed at generating 500,000 human exome sequences linked to medical records by the end of 2019. We and each of the other collaborators agreed to

commit \$10.0 million to enable an acceleration of sequencing timelines. We believe that the broad and ongoing access to detailed health and full exome sequencing data for the 500,000 UK Biobank participants will greatly enhance our target identification and validation efforts, contributing to the sustainability of our RNAi therapeutics product engine.

In March 2018, we entered into a discovery collaboration with Regeneron to identify RNAi therapeutics for the chronic liver disease nonalcoholic steatohepatitis, or NASH, and potentially other related diseases, and we and Regeneron plan to enter into a separate, fifty-fifty collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts.

In March 2018, we also entered into a manufacturing services agreement with Agilent Technologies, Inc. providing for the commercial supply of patisiran drug substance by Agilent for an initial five-year term.

In April 2018, we and Dicerna Therapeutics, Inc., or Dicerna, entered into a settlement agreement resolving all ongoing litigation between the companies. For a discussion of the terms of the Dicerna settlement, please read Note 5, Commitments and Contingencies – Litigation, to our condensed consolidated financial statements included in Part I, Item 1, “Financial Statements (Unaudited),” of this quarterly report on Form 10-Q.

We have incurred significant losses since we commenced operations in 2002 and expect such losses to continue for the foreseeable future. At March 31, 2018, we had an accumulated deficit of \$2.22 billion. Historically, we have generated losses principally from costs associated with research and development activities, acquiring, filing and expanding intellectual property rights and general administrative costs. 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 and commercial capabilities, including global operations, continued management and growth of our patent portfolio, collaborations and general corporate activities, we expect to incur additional operating losses for the foreseeable future. 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 noted above, in December 2017, submitted our first NDA and MAA for marketing approval for patisiran. However, our development efforts may not be successful and we may not be able to commence sales of patisiran or any other product. If we gain approval for and successfully launch patisiran in 2018, we may begin to generate net revenues from product sales. A substantial portion of our total revenues in recent years has been derived from collaboration revenues from strategic alliances with Sanofi Genzyme and MDCO. In addition to potential revenues from the commercial sale of patisiran and future product candidates, we expect our sources of potential funding for the next several years to continue to be derived primarily 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 licensors, and proceeds from the sale of equity or debt.

#### 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 several programs in late-stage development and one product in registration in the United States and the EU.

The following is a summary of our product development programs as of April 30, 2018. It identifies those programs in which we have achieved human proof-of-concept, or POC, by demonstrating target gene knockdown and/or additional evidence of activity in clinical studies, those programs for which we have received Breakthrough Therapy Designation from the FDA, the development stage of our programs, and our commercial rights to such programs:

During the first quarter of 2018 and recent period, we reported the following updates from our late-stage clinical programs:

• We continued to advance patisiran, an investigational RNAi therapeutic for the treatment of patients with hereditary ATTR amyloidosis, or hATTR, presenting new data from our APOLLO Phase 3 study, including results on the effects of patisiran on cardiomyopathy manifestations and a post-hoc analysis on the effects of patisiran on the composite rate of all-cause hospitalization and mortality. We received acceptance from the FDA and the EMA of patisiran's NDA and MAA, respectively.

• We continued to advance ALN-TTRsc02, a subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis, presenting updated Phase 1 data in March 2018 and announcing receipt of a positive opinion from the EMA Committee for Orphan Medicinal Products for Orphan Drug Designation in the European Union, or EU, for ALN-TTRsc02 for the treatment of ATTR amyloidosis.

• We continued to advance givosiran, an investigational RNAi therapeutic in development for the treatment of acute hepatic porphyrias, or AHPs, presenting new Phase 1 and Phase 1/2 open-label extension, or OLE, study results in April 2018. In addition, we completed enrollment of the first 30 patients in our ENVISION Phase 3 study, which comprise the interim analysis cohort for a potential accelerated approval by the FDA.

o We expect to report interim analysis results in the September timeframe and, pending FDA review of the program at the time of interim analysis and assuming positive results, we expect to submit an NDA at or around year-end 2018.

o Notwithstanding productive discussions with the EMA on a potential accelerated approval pathway for givosiran, we plan to file an MAA on the full dataset from ENVISION, expected in 2019, to optimize market access in Europe.

• We continued to advance lumasiran, an investigational RNAi therapeutic in development for the treatment of primary hyperoxaluria type 1, or PH1, announcing in May 2018 that we have reached alignment with the FDA on a pivotal study design for lumasiran in approximately 25 patients with PH1, using the reduction at six months of urinary oxalate the primary endpoint.

◦ We expect to initiate the lumasiran Phase 3 study in mid-2018, report results in 2019, and, if positive, file an NDA in early 2020.

◦ We have retained global rights to the lumasiran program following the decision by Sanofi Genzyme to decline its opt-in for lumasiran's development and commercialization under our 2014 collaboration agreement.

◦ Lumasiran was granted Breakthrough Therapy Designation by the FDA as well as access to the EMA's Priority Medicines scheme.

- With partner Sanofi Genzyme, we continued to advance fitusiran, an investigational RNAi therapeutic in development for the treatment of hemophilia A and B with or without inhibitors, with the initiation of dosing in the ATLAS Phase 3 program. We expect to fully transition development and commercialization leadership of the fitusiran program to Sanofi Genzyme in mid-2018.

• Our partner, MDCO, completed enrollment in the ORION-9, -10, and -11 Phase 3 studies of inclisiran in 3,660 patients with atherosclerotic cardiovascular disease or heterozygous familial hypercholesterolemia.

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. For example, in October 2016, we announced the discontinuation of our revusiran clinical development program due to safety concerns and in September 2017, we announced that we had temporarily suspended dosing in all ongoing fitusiran studies. Moreover, there are uncertainties specific to any new field of drug discovery, including RNAi. The success of any product candidate we develop is highly uncertain. Due to the numerous risks associated with developing drugs, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts necessary to complete the development of, or the period, if any, in which material net cash inflows will commence from, any potential product candidate.

Any failure to complete any stage of the development of any potential products in a timely manner 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 projects on schedule, 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 three 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 potential new class of innovative medicines. Specifically, with respect to our Genetic Medicine pipeline, we formed a broad strategic alliance with Sanofi Genzyme in 2014 pursuant to which we retain development and commercial rights for our current and future Genetic Medicine products in the United States, Canada and Western Europe, and Sanofi Genzyme will develop and commercialize our current and future Genetic Medicine products for which it elects to opt-in, in the rest of the world, referred to as the Sanofi Genzyme Territory, subject to certain broader rights. In January 2018, we and Sanofi Genzyme amended our 2014 Sanofi Genzyme collaboration and entered into an Exclusive License Agreement with respect to all TTR products, including patisiran, ALN-TTRsc02 and any back-up products, referred to as the Exclusive TTR License, and the ALN-AT3 Global License Terms with respect to fitusiran and any back-up products, referred to as the AT3 License Terms. The 2018 amendment, together with the Exclusive TTR License and the AT3 License Terms, revise the terms and conditions of the 2014 collaboration to (i) provide us with the exclusive right to pursue the further global development and commercialization of all TTR products, including patisiran, ALN-TTRsc02 and any back-up products, (ii) provide

Sanofi Genzyme the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products and (iii) terminate the previous co-development and co-commercialization rights related to revusiran, ALN-TTRsc02 and fitusiran under the 2014 Sanofi Genzyme collaboration. Sanofi Genzyme continues to have the right to opt into our other rare genetic disease programs for development and commercialization in territories outside of the Alnylam Territory as contemplated in the 2014 Sanofi Genzyme collaboration, as well as one right to a global license.

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With respect to our Cardio-Metabolic pipeline, we intend to seek future strategic alliances for these programs, under which we may retain certain product development and commercialization rights, or we may structure as global alliances, as we did in our collaboration with MDCO 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 we and Regeneron plan to enter into a separate, fifty-fifty collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts.

With respect to our Hepatic Infectious Disease pipeline, in October 2017, we announced an exclusive licensing agreement with Vir Biotechnology for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic hepatitis B virus infection.

### Intellectual Property

The strength of our intellectual property portfolio relating to the development and commercialization of siRNAs as therapeutics is essential to our business strategy. We own or license issued patents and pending patent applications in the United States and in key markets around the world claiming fundamental features of siRNAs and RNAi therapeutics as well as those claiming crucial chemical modifications and promising delivery technologies. 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.

We believe that no other company possesses a portfolio of such broad and exclusive rights to the patents and patent applications required for the commercialization of RNAi therapeutics. Our intellectual property estate for RNAi therapeutics includes over 3,800 active cases and over 1,700 granted or issued patents, of which over 600 are issued or granted in the United States, the EU, including by the European Patent Office, or EPO, and Japan. We continue to seek to grow our portfolio through the creation of new technology in this field. In addition, we are very active in our evaluation of third-party technologies. Given the importance of our intellectual property portfolio to our business operations, we intend to vigorously enforce our rights and defend against challenges that have arisen or may arise in this area.

### Critical Accounting Policies and Estimates

#### Revenue Recognition

On January 1, 2018, we adopted the new revenue standard by applying the modified retrospective method to all contracts that were not completed as of January 1, 2018. As a result, while reporting periods beginning on our adoption of the new revenue standard are presented under the new revenue standard, prior period amounts have not been adjusted and continue to be presented under the revenue standard in effect prior to January 1, 2018. The new revenue standard had a material impact on our consolidated financial statements. Please read Note 1 to our condensed consolidated financial statements included in Part I, Item 1, "Financial Statements (Unaudited)," of this quarterly report on Form 10-Q for a discussion of our revenue recognition policy and the impact of this new revenue standard.

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, 2017, which we filed with the SEC on February 15, 2018. There have been no significant changes to our critical accounting policies since the beginning of this fiscal year other than with respect to revenue recognition described above.

#### Results of Operations

The following data summarizes the results of our operations for the periods indicated, in thousands:

|                                 | Three Months Ended |             |
|---------------------------------|--------------------|-------------|
|                                 | March 31,          |             |
|                                 | 2018               | 2017        |
| Net revenues from collaborators | \$21,899           | \$18,960    |
| Operating expenses              | 169,304            | 125,471     |
| Loss from operations            | (147,405)          | (106,511)   |
| Net loss                        | \$(141,214)        | \$(107,290) |

## Discussion of Results of Operations

## Net revenues from collaborators

We generate revenues through research and development collaborations. The following table summarizes our total consolidated net revenues from collaborators, for the periods indicated, in thousands, together with the changes, in thousands:

| Description                           | Three Months<br>Ended March 31, |          | Dollar  |
|---------------------------------------|---------------------------------|----------|---------|
|                                       | 2018                            | 2017     | Change  |
| Sanofi Genzyme                        | \$18,853                        | \$12,277 | \$6,576 |
| MDCO                                  | 1,295                           | 6,364    | (5,069) |
| Other                                 | 1,751                           | 319      | 1,432   |
| Total net revenues from collaborators | \$21,899                        | \$18,960 | \$2,939 |

The following table summarizes our total consolidated net revenues from collaborators, under the prior revenue standard, for the periods indicated, in thousands, together with the changes, in thousands:

| Description                           | Three Months<br>Ended March 31, |          | Dollar   |
|---------------------------------------|---------------------------------|----------|----------|
|                                       | 2018                            | 2017     | Change   |
| Sanofi Genzyme                        | \$50,430                        | \$12,277 | \$38,153 |
| MDCO                                  | 2,845                           | 6,364    | (3,519)  |
| Other                                 | 1,751                           | 319      | 1,432    |
| Total net revenues from collaborators | \$55,026                        | \$18,960 | \$36,066 |

Net revenues from collaborators increased during the three months ended March 31, 2018 as compared to the three months ended March 31, 2017 due primarily to the \$50.0 million milestone payment that was achieved in the first quarter of 2018 upon dosing of the first patient in the ATLAS Phase 3 program for fitusiran under the AT3 License Terms. Upon our adoption of the new revenue standard on January 1, 2018, we recorded a cumulative reduction of \$45.7 million of deferred revenues related to our collaboration with Sanofi Genzyme, resulting in a remaining balance of \$3.5 million. As a result, we recorded significantly lower revenues related to our collaboration with Sanofi Genzyme in the three months ended March 31, 2018 than we would have recorded under the prior revenue standard. In addition, net revenues from collaborators decreased during the first quarter of 2018 due to lower reimbursable activities under our MDCO agreement.

We expect net revenues from collaborators to increase for the second quarter of 2018 as compared to the same period of 2017 and to decrease for the second half of 2018 as compared to the second half of 2017 primarily due to the expected substantial completion in mid-2018 of the transition of the fitusiran program to Sanofi Genzyme. In addition, we expect net revenues from collaborators to decrease for the second half of 2018 as compared to the second half of 2017 as a result of revenue recognized in the fourth quarter of 2017 upon the achievement of a \$20.0 million milestone payment earned under our agreement with MDCO.

We had \$43.5 million of deferred revenue at March 31, 2018, which consists primarily of payments we have received from Sanofi Genzyme for the fitusiran program and from other collaborators but had not yet recognized pursuant to our revenue recognition policies. At December 31, 2017, prior to the adoption of the new revenue standard, we had \$84.8 million of deferred revenue, which consisted of payments we have received from collaborators, primarily Sanofi Genzyme, MDCO and Kyowa Hakko Kirin Co., Ltd., but had not yet recognized pursuant to our revenue recognition policies. As a result of our adoption of the new revenue standard on January 1, 2018, we recorded a cumulative reduction of \$68.2 million of deferred revenue with a corresponding adjustment to accumulated deficit in the first quarter of 2018. Please read Note 1 to our condensed consolidated financial statements included in Part I, Item 1, “Financial Statements (Unaudited),” of this quarterly report on Form 10-Q for a discussion of our revenue recognition policy and the impact of this new revenue standard.

During 2018, if we are successful in obtaining regulatory approval and commercializing patisiran, we may begin to recognize net product revenues. Until we are successful in obtaining regulatory approval for patisiran and our other product candidates and in commercializing such products, we expect our revenues to continue to be derived primarily from our alliances with Sanofi Genzyme and MDCO, as well as other strategic alliances and potential new collaborations and licensing activities, which may include license and other fees, funded research and development, milestone payments and royalties on product sales by our licensors.

## Operating expenses

The following table summarizes our operating expenses for the periods indicated, in thousands and as a percentage of total operating expenses, together with the changes, in thousands:

| Description                | % of                              |                          | % of                              |                          | Dollar Change |
|----------------------------|-----------------------------------|--------------------------|-----------------------------------|--------------------------|---------------|
|                            | Three Months Ended March 31, 2018 | Total Operating Expenses | Three Months Ended March 31, 2017 | Total Operating Expenses |               |
| Research and development   | \$ 96,857                         | 57 %                     | \$ 86,984                         | 69 %                     | \$ 9,873      |
| General and administrative | 72,447                            | 43 %                     | 38,487                            | 31 %                     | 33,960        |
| Total operating expenses   | \$ 169,304                        | 100 %                    | \$ 125,471                        | 100 %                    | \$ 43,833     |

Research and development. The following table summarizes the components of our research and development expenses for the periods indicated, in thousands and as a percentage of total research and development expenses, together with the changes, in thousands:

| Description                             | % of                              |                  | % of                              |                  | Dollar Change |
|---|-----------------------------------|------------------|-----------------------------------|------------------|---------------|
|   | Three Months Ended March 31, 2018 | Expense Category | Three Months Ended March 31, 2017 | Expense Category |               |
| Research and development                |                                   |                  |                                   |                  |               |
| Compensation and related                | \$ 30,266                         | 31 %             | \$ 22,623                         | 26 %             | \$ 7,643      |
| Clinical trial                          | 20,135                            | 21 %             | 17,563                            | 20 %             | 2,572         |
| External services                       | 13,090                            | 14 %             | 7,844                             | 9 %              | 5,246         |
| Manufacturing                           | 10,758                            | 11 %             | 18,075                            | 21 %             | (7,317)       |
| Stock-based compensation                | 10,137                            | 10 %             | 8,691                             | 10 %             | 1,446         |
| Facilities-related                      | 7,553                             | 8 %              | 7,658                             | 9 %              | (105)         |
| Lab supplies and materials              | 2,128                             | 2 %              | 2,146                             | 2 %              | (18)          |
| Other                                   | 2,790                             | 3 %              | 2,384                             | 3 %              | 406           |
| Total research and development expenses | \$ 96,857                         | 100 %            | \$ 86,984                         | 100 %            | \$ 9,873      |

Research and development expenses increased during the three months ended March 31, 2018 as compared to the three months ended March 31, 2017 due primarily to increased compensation and related expenses as a result of an increase in headcount during the period as we expand and advance our development pipeline. In addition, external services expenses increased during the three months ended March 31, 2018 as a result of increased preclinical services related to early stage programs to support our Alnylam 2020 strategy, as well as increased expenses related to regulatory submissions. These increases were partially offset by decreases in manufacturing expenses related to our late stage programs.

During the three months ended March 31, 2018 and 2017, in connection with advancing the activities under our significant agreements, we incurred significant research and development expenses, primarily related to external

development and manufacturing services. The 2018 amendment to the 2014 Sanofi Genzyme collaboration, together with the Exclusive TTR License and the AT3 License Terms, provide us with the exclusive right to pursue the further global development and commercialization of all TTR products and any back-up products and provide Sanofi Genzyme with the exclusive right to pursue the further global development and commercialization of fitusiran and any back-up products. As a result, we expect costs incurred under our significant agreements to decrease. The following table summarizes the expenses incurred under our significant agreements by collaboration partner for the periods indicated, in thousands:

|                | Three Months<br>Ended March 31, |           |
|----------------|---------------------------------|-----------|
|                | 2018                            | 2017      |
| Sanofi Genzyme | \$ 13,705                       | \$ 42,578 |
| MDCO           | 641                             | 5,119     |
| Total          | \$ 14,346                       | \$ 47,697 |

We expect to continue to devote a substantial portion of our resources to research and development expenses to support our goals for 2020. We expect that research and development expenses will increase significantly for the remainder of 2018 as compared to 2017 as we continue to develop our pipeline and advance our product candidates into later-stage development, hire additional employees and prepare regulatory submissions. 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.

A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform. However, certain of our collaboration agreements contain cost-sharing arrangements pursuant to which certain costs incurred under the project are reimbursed. Costs reimbursed under the agreements typically include certain direct external costs and a negotiated full-time equivalent labor rate for the actual time worked on the project. As a result, although a significant portion of our research and development expenses are not tracked on a project-by-project basis, we do track direct external costs attributable to, and the actual time our employees worked on, our collaborations.

General and administrative. The following table summarizes the components of our general and administrative expenses for the periods indicated, in thousands and as a percentage of total general and administrative expenses, together with the changes, in thousands:

| Description                                      | Three<br>Months<br>Ended<br>March 31,<br>2018 | % of<br>Expense<br>Category |          | Three<br>Months<br>Ended<br>March 31,<br>2017 | % of<br>Expense<br>Category | Dollar<br>Change  |
|--|---|-----------------------------|----------|---|-----------------------------|-------------------|
| <b>General and administrative</b>                |   |                             |          |   |                             |                   |
| Consulting and professional services             | \$ 30,430                                     | 42                          | %        | \$ 13,132                                     | 34                          | % \$ 17,298       |
| Compensation and related                         | 23,611  | 33                          | %        | 13,245  | 34                          | % 10,366          |
| Stock-based compensation                         | 9,447   | 13                          | %        | 7,026   | 18                          | % 2,421           |
| Facilities-related                               | 3,555   | 5                           | %        | 2,213   | 6                           | % 1,342           |
| Other  | 5,404   | 7                           | %        | 2,871   | 8                           | % 2,533           |
| <b>Total general and administrative expenses</b> | <b>\$ 72,447</b>                              | <b>100</b>                  | <b>%</b> | <b>\$ 38,487</b>                              | <b>100</b>                  | <b>% \$33,960</b> |

General and administrative expenses increased significantly during the three months ended March 31, 2018 as compared to the three months ended March 31, 2017 due primarily to an increase in commercial and medical affairs headcount and commercial-related services to support corporate growth and prepare for the potential launch of patisiran in 2018, and potential additional product launches in 2019 and thereafter.

We expect that general and administrative expenses will increase significantly on a quarterly basis during the remainder of 2018 as compared to 2017 as we continue to grow our operations, including the continued build-out of our global commercial infrastructure and field team, in preparation for our anticipated first product launch in 2018, but expect that stock-based compensation expenses will be variable due to our determination regarding the probability of vesting for performance-based awards.

#### Liquidity and Capital Resources

The following table summarizes our cash flow activities for the periods indicated, in thousands:

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|  | Three Months Ended<br>March 31, |             |
|--|---------------------------------|-------------|
|  | 2018                            | 2017        |
| Net loss   | \$(141,214)                     | \$(107,290) |
| Adjustments to reconcile net loss to net cash used in    |                                 |             |
| operating activities                                     | 23,704                          | 21,425      |
| Changes in operating assets and liabilities              | (38,154 )                       | (14,465 )   |
| Net cash used in operating activities                    | (155,664)                       | (100,330)   |
| Net cash (used in) provided by investing activities      | (134,814)                       | 75,076      |
| Net cash provided by financing activities                | 41,522                          | 2,716       |
| Net decrease in cash, cash equivalents and restricted    |                                 |             |
| cash   | (248,956)                       | (22,538 )   |
| Cash, cash equivalents and restricted cash, beginning of |                                 |             |
| period   | 646,832                         | 195,088     |
| Cash, cash equivalents and restricted cash, end of       |                                 |             |
| period   | \$397,876                       | \$172,550   |



Since we commenced operations in 2002, we have generated significant losses. At March 31, 2018, we had an accumulated deficit of \$2.22 billion. At March 31, 2018, we had cash, cash equivalents and fixed income marketable securities of \$1.57 billion, compared to \$1.70 billion at December 31, 2017, in each case excluding the \$30.0 million of restricted investments related to our term loan agreement.

In May 2017, we sold an aggregate of 5,000,000 shares of our common stock through an underwritten public offering at a price to the public of \$71.87 per share. As a result of the offering, we received aggregate net proceeds of \$355.2 million, after deducting underwriting discounts and commissions and other offering expenses of \$4.2 million. In November 2017, we sold an aggregate of 6,440,000 shares of our common stock through an underwritten public offering at a price to the public of \$125.00 per share. As a result of the offering, which included the full exercise of the underwriters' option to purchase additional shares, we received aggregate net proceeds of \$784.5 million, after deducting underwriting discounts and commissions and other offering expenses of \$20.5 million.

We have used and intend to continue to use these proceeds for general corporate purposes, including clinical trial costs and other research and development expenses, continued growth of our manufacturing, quality, commercial and medical affairs capabilities to support our transition toward a commercial-stage biopharmaceutical company, the anticipated global commercial launches of patisiran and givosiran and other potential future products, the potential expansion of patisiran commercialization efforts in mixed phenotype populations, assuming consistent product labelling, potential repayment of outstanding indebtedness, potential acquisitions, investments or licenses in businesses, products or technologies that are complementary to our own, working capital, capital expenditures and general and administrative expenses.

Sanofi Genzyme has certain rights to purchase additional shares from us under our investor agreement. In connection with our May 2017 public offering described above, Sanofi Genzyme exercised its right to purchase directly from us, in a concurrent private placement, 297,501 shares of common stock at the public offering price resulting in \$21.4 million in proceeds to us. Sanofi Genzyme currently holds approximately 11 percent of our outstanding common stock.

We invest primarily in money market funds, U.S. government-sponsored enterprise securities, U.S. treasury securities, high-grade corporate notes, certificates of deposit and commercial paper. Corporate notes may also include foreign bonds denominated in U.S. dollars. Our investment objectives are, primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available-for-sale. Fair value is determined based on quoted market prices and models using observable data inputs. We have not recorded any impairment charges to our fixed income marketable securities during the three months ended March 31, 2018 or 2017.

#### Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception. Cash used in operating activities is adjusted for non-cash items to reconcile net loss to net cash used in operating activities. These non-cash adjustments have historically included stock-based compensation and depreciation and amortization.

We expect that we will require significant amounts of cash to fund our operating activities for the foreseeable future as we continue to execute on our Alnylam 2020 strategy through the advancement of our research, development, pre-commercial and potentially commercial initiatives. The actual amount of overall expenditures will depend on numerous factors, including the timing of expenses, the timing and terms of collaboration agreements or other strategic transactions, if any, and the timing and progress of our research, development and commercialization efforts.

The increase in net cash used in operating activities for the three months ended March 31, 2018 compared to the three months ended March 31, 2017 was primarily due to our net loss.

### Investing activities

For the three months ended March 31, 2018 and 2017, net cash provided by or used in investing activities was due primarily to net purchases of our fixed income marketable securities in accordance with management of our liquidity needs. For the three months ended March 31, 2018 and 2017, there were purchases of property, plant and equipment of \$21.3 million and \$36.2 million, respectively, primarily in connection with construction of our drug substance manufacturing facility.

### Financing activities

For the three months ended March 31, 2018 and 2017, net cash of \$41.5 million and \$2.7 million, respectively, provided by financing activities was due primarily to proceeds from the issuance of common stock in connection with stock option exercises.

## Operating Capital Requirements

We currently have programs focused on a number of therapeutic areas and, in December 2017, submitted our first NDA and MAA for marketing approval for patisiran. Our development efforts may not be successful and we may not be able to commence sales of patisiran or any other product. If we are able to gain approval and successfully launch patisiran in 2018, we may begin to generate net revenues from product sales. However, we anticipate that we will continue to generate significant losses for the foreseeable future 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 and commercial capabilities, including global operations, continued management and growth of our intellectual property including our patent portfolio, collaborations and general corporate activities. In addition, we are expanding our manufacturing capabilities, including through construction of a drug substance manufacturing facility in Norton, Massachusetts. In April 2016, our subsidiary, Alnylam U.S., Inc., entered into an aggregate of \$150.0 million in term loan agreements related to the build out of our new drug substance manufacturing facility. In December 2017, we repaid in full \$120.0 million outstanding under one of these term loan agreements. Interest on the borrowings was and is calculated based on LIBOR plus 0.45 percent and obligations were and are secured by cash collateral in an amount equal to, at any given time, at least 100 percent of the principal amount of all term loans outstanding under the agreements at such time. We are the guarantor under the remaining term loan agreement, which matures in April 2021.

Based on our current operating plan, we believe that our existing cash, cash equivalents and fixed income marketable securities, together with the cash we expect to generate under our current alliances, will be sufficient to enable us to advance our Alnylam 2020 strategy for at least the next few years. For reasons discussed below, we may require significant additional funds earlier than we currently expect in order to develop, conduct clinical trials for, manufacture and commercialize any product candidates.

In the future, we may seek additional funding through additional collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. Moreover, the terms of any additional financing may further adversely affect the holdings or the rights of our stockholders. For example, 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 funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. If we are unable to obtain funding on a timely basis, we may be required to significantly delay or curtail one or more of our research or development programs and our ability to achieve our goals for 2020 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.

Even if we are able to raise additional funds in a timely manner, our future capital requirements may vary from what we expect and will depend on many factors, including:

- our progress in demonstrating that siRNAs can be active as drugs and achieve desired clinical effects;
- 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;
  - 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 trials, 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 resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;
- the costs associated with legal activities, including litigation, arising in the course of our business activities and our ability to prevail in any such legal disputes; and
- the timing, receipt and amount of sales and royalties, if any, from our potential products.

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## 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, 2017. There have been no material changes in our contractual obligations and commitments since December 31, 2017.

## Recent Accounting Pronouncements

Please read Note 1 to our condensed consolidated financial statements included in Item 1, “Financial Statements (Unaudited),” of this Quarterly Report on Form 10-Q for a description of recent accounting pronouncements applicable to our business.

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

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research, development and early commercial activities. Our fixed income marketable securities consist primarily of U.S. government-sponsored enterprise securities, U.S. treasury securities, high-grade corporate notes, and commercial paper. Corporate notes may also include foreign bonds denominated in U.S. dollars. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market interest rate at the date of purchase of the financial instrument. If market interest rates were to increase immediately and uniformly by 50 basis points, or one-half of a percentage point, from levels at March 31, 2018, the net fair value of our interest-sensitive financial instruments would have resulted in a hypothetical decline of \$2.3 million. We currently do not seek to hedge this exposure to fluctuations in interest rates. A downgrade in the credit rating of an issuer of a debt security or further deterioration of the credit markets could result in a decline in the fair value of the debt instruments. Our investment guidelines prohibit investment in auction rate securities and we do not believe we have any direct exposure to losses relating from mortgage-based securities or derivatives related thereto such as credit-default swaps. Historically, foreign currency fluctuations have not been material. We did not record any impairment charges to our fixed income marketable securities during the three months ended March 31, 2018.

## ITEM 4. CONTROLS AND PROCEDURES.

Our management, with the participation of our chief executive officer (principal executive officer) and senior vice president, chief financial officer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2018. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or 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 March 31, 2018, our chief executive officer and senior vice president, chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

During the three months ended March 31, 2018, we implemented certain internal controls as a result of our adoption of the new revenue standard on January 1, 2018. There were no other changes in our internal control over financial reporting (as defined in Rules 13a–15(f) and 15d–15(f) under the Exchange Act) that occurred during the three months ended March 31, 2018 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 5, Commitments and Contingencies – Litigation, 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

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. All statements other than statements relating to historical matters should be considered forward-looking statements. When used in this report, the words “believe,” “expect,” “plan,” “anticipate,” “estimate,” “predict,” “may,” “could,” “should,” “intend,” “will,” “forecast,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Any or all of our forward-looking statements in this quarterly report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from those anticipated in forward-looking statements. We explicitly disclaim any obligation to update any forward-looking statements to reflect events or circumstances that arise after the date hereof. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

#### Risks Related to Our Business

#### Risks Related to Being a Clinical Stage Company

Although we have several product candidates in late stage clinical development, including one in registration, there is limited information about our ability to successfully overcome many of the risks and uncertainties encountered by companies in the biopharmaceutical industry.

Although we have product candidates in late stage clinical development and one product under regulatory review for approval in the United States and the EU, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute product development activities using unproven technologies related to both RNAi and to the delivery of siRNAs to the relevant tissues and cells;
- build and maintain a strong intellectual property portfolio;
- gain regulatory acceptance for the development and commercialization of our product candidates and market success for any products we commercialize;

- 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 these objectives, we may not be able to develop product candidates, commercialize products, raise capital, expand our business or continue our operations.

The approach we are taking to discover and develop novel RNAi therapeutics is unproven and may never lead to marketable products.

We have concentrated our efforts and therapeutic product research and development on RNAi technology and our future success depends on the successful development of this technology and products based on it. Neither we nor any other company has received regulatory approval to market therapeutics utilizing siRNAs, the class of molecule we are trying to develop into drugs. The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is still limited. Skepticism as to the feasibility of developing RNAi therapeutics has been expressed in scientific literature. For example, there are potential challenges to achieving safe RNAi therapeutics based on the so-called off-target effects and activation of the interferon response. In addition, decisions by other companies with respect to their RNAi development efforts or their adoption of different or related technologies and the potential success of any such different or related technologies may increase skepticism in the marketplace regarding the potential for RNAi therapeutics.



Relatively few product candidates based on these discoveries have ever been tested in humans. siRNAs may not naturally possess the inherent properties typically required of drugs, such as the ability to be stable in the body, or the ability to enter cells within relevant tissues in order to exert their effects. We have spent and expect to continue to spend large amounts of money developing siRNAs that possess the properties typically required of drugs, and to date, we have only taken one product candidate through Phase 3 development and filed for regulatory approval in the United States and the EU. In addition, these compounds may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. For example, in October 2016, we discontinued development of revusiran, an investigational RNAi therapeutic that was in development for the treatment of patients with cardiomyopathy due to hATTR amyloidosis, due to safety concerns. We conducted a comprehensive evaluation of the revusiran data and 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. If we do not succeed in developing products that gain regulatory approval and succeed in the marketplace, we may not become profitable and the value of our common stock will decline.

Further, our focus solely on RNAi technology for developing drugs, as opposed to multiple, more proven technologies for drug development, increases the risks associated with the ownership of our common stock. If we are not successful in developing and commercializing one or more products using RNAi technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy.

#### Risks Related to Our Financial Results and Need for Financing

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

We have experienced significant operating losses since our inception. At March 31, 2018, we had an accumulated deficit of \$2.22 billion. To date, we have not received regulatory approval to market or sell any products nor generated any revenues from the sale of products. Further, we do not expect to generate any product revenues until at the earliest mid- to late-2018, assuming we receive marketing approval for patisiran. We expect to continue to incur annual net operating losses over the next several years and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. Until we are successful in obtaining regulatory approval for our product candidates and successful in commercializing such products, we anticipate that a significant portion of any revenues we generate over the next several years will be from alliances with pharmaceutical and biotechnology companies, but cannot be certain that we will be able to maintain our existing alliances or secure and maintain new alliances, or meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments. We anticipate that revenues derived from such sources will not be sufficient to make us consistently profitable.

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 be successful 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 in these activities, 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 additional funds to complete our research, development and commercialization activities and if additional funds are not available, we may need to critically limit, 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 any products that are approved for commercial sale. Because we cannot be certain of the length of time or activities associated with successful development of our product candidates, we are unable to estimate the actual funds we will require to develop and commercialize them.

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:

- our progress in demonstrating that siRNAs can be active as drugs and achieve desired clinical effects;
- progress in our research and development programs, as well as what may be required by regulatory bodies to advance these programs;

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- the timing, receipt and amount of milestone and other payments, if any, from present and future collaborators, if any;
  - 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 resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;
- the costs associated with legal activities, including litigation, arising in the course of our business activities and our ability to prevail in any such legal disputes; and
- the timing, receipt and amount of sales and royalties, if any, from our potential products.

If our estimates and predictions relating to these factors are incorrect, we may need to modify our operating plan.

Even if our estimates are correct, we will be required to seek additional funding in the future and intend to do so through either collaborative arrangements, public or private equity offerings or debt financings, 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 2016, our subsidiary, Alnylam U.S., Inc., entered into an aggregate of \$150.0 million in term loan agreements related to the build out of our drug substance manufacturing facility. In December 2017, we repaid in full \$120.0 million outstanding under one such term loan agreement. We are the guarantor under the remaining term loan agreement, which matures in April 2021. Interest on the borrowings is calculated based on LIBOR plus 0.45 percent. During an event of default under the remaining agreement, the obligations under such agreement will bear interest at a rate per annum equal to the interest rate then in effect plus two percent. The obligations under the term loan agreement are secured by cash collateral in an amount equal to, at any given time, at least 100 percent of the principal amount outstanding under such agreement at such time. The remaining agreement includes restrictive covenants that could limit our flexibility in conducting future business activities and further limit our ability to change the nature of our business and, in the event of insolvency, the lender would be paid before holders of equity securities received any distribution of corporate assets. If an event of default occurs, the interest rate would increase and the lender would be entitled to take various actions, including the acceleration of amounts due under the loan. Our ability to satisfy our obligations under this agreement 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.

In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, 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. Moreover, our investor agreement with Sanofi Genzyme provides Sanofi Genzyme with the right, subject to certain exceptions, generally to maintain its ownership position in us until Sanofi Genzyme owns less than 7.5 percent of our outstanding common stock, subject to certain additional limited rights of Sanofi Genzyme to maintain its ownership percentage. In accordance with the investor agreement, to date, Sanofi Genzyme has exercised its right to purchase an additional 344,448 shares of our common stock in connection with our acquisition of Sirna in March 2014, an aggregate of 401,281 shares of our common stock based on its 2014 and 2015 compensation-related rights and an aggregate of 1,042,067 shares of our common stock in connection with our public offerings in January 2015 and May 2017. These purchases allowed Sanofi Genzyme to maintain its ownership level of our outstanding common stock. Sanofi Genzyme currently holds approximately 11 percent of our outstanding common stock. While the exercise of these rights by Sanofi Genzyme has provided us with

an additional \$147.7 million in cash to date, and while any exercise of these rights by Sanofi Genzyme in the future will provide us with further additional cash, these exercises have caused, and any future exercise of these rights by Sanofi Genzyme will also cause further, dilution to our stockholders. Sanofi Genzyme elected not to exercise its compensation-related rights for 2016 and 2017. Additionally, Sanofi Genzyme elected not to exercise its right to purchase additional shares in connection with our public offering in November 2017.

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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, delay the build-out of our global commercial infrastructure or undergo future reductions in our workforce or other corporate restructuring activities, and our ability to achieve our strategy for 2020 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.

If the estimates we make, or the assumptions on which we rely, in preparing our condensed consolidated financial statements 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. 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.

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

At March 31, 2018, we had \$1.57 billion in cash, cash equivalents and fixed income marketable securities, excluding the \$30.0 million of restricted investments related to our term loan agreement. 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 condensed 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.

The effect of comprehensive U.S. tax reform legislation on us, our subsidiaries and our affiliates, whether adverse or favorable, is uncertain.

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. For example, on December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act of 2017, or the TCJA. Among a number of significant changes to the current U.S. federal income tax rules, the TCJA reduces the marginal U.S. corporate income tax rate from 35 percent to 21 percent, introduces a capital investment deduction, limits the current deduction for net interest expense, limits the use of net operating losses to offset future taxable income, and makes extensive changes in the way in which income earned outside the United States is taxed in the United States. The TCJA is complex and far-reaching and we cannot predict with certainty the impact its enactment will have on us. Moreover, that effect, whether adverse or favorable, may not become evident for some period of time.

#### 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 currently are developing capabilities for sales or distribution and also have early capabilities for marketing, sales and market access, as well as limited capacity for drug development due to our growing pipeline of RNAi therapeutic opportunities. Accordingly, we have entered into alliances with other companies and collaborators that we believe can provide such capabilities in certain territories, 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 potential new class of innovative medicines. Specifically, with respect to our Genetic Medicine pipeline, we formed a broad strategic alliance with Sanofi Genzyme in 2014 pursuant to which we retain development and commercial rights for our current and future Genetic Medicine products in the United States, Canada and Western Europe, and Sanofi Genzyme has the right to develop and commercialize our current and future Genetic Medicine products principally in the rest of the world, subject to certain broader rights. In January 2018, we and Sanofi Genzyme amended our 2014 collaboration to provide that we would develop and commercialize patisiran globally and Sanofi Genzyme would develop and commercialize fitusiran globally. With respect to our Cardio-Metabolic Disease pipeline, we intend to

seek future strategic alliances for these programs, under which we may retain certain product development and commercialization rights, or we may structure as global alliances, as we did in our collaboration with MDCO 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 we and Regeneron plan to enter 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 Biotechnology for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic hepatitis B virus infection.

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) Sanofi Genzyme for the development and commercialization of fitusiran worldwide and potentially other of our Genetic Medicine programs in territories outside of the United States, Canada and Western Europe, and (ii) MDCO for all future development and commercialization of inclisiran worldwide. If Sanofi Genzyme and/or MDCO are not successful in their development and/or commercialization efforts, our future revenues from RNAi therapeutics for these indications may be adversely affected. Sanofi Genzyme also has the right to elect one global license for a future Genetic Medicine program that was not one of our defined Genetic Medicine programs as of the effective date of our 2014 collaboration. If and when Sanofi Genzyme elects to take a global license to one of our programs, we will no longer control the development and potential commercialization of such program and any revenues we receive will depend solely on the success of Sanofi Genzyme's efforts. In addition, Sanofi Genzyme may elect not to opt into one or more of our Genetic Medicine programs. For example, during 2016, Sanofi Genzyme elected not to take a regional license for our givosiran and cemdisiran programs and in early 2018, Sanofi Genzyme elected not to take a global license for our lumasiran program. While we intend to advance these programs independently, retaining global development and commercial rights, our ability to advance these programs and successfully develop and commercialize these product candidates may be adversely affected as a result of Sanofi Genzyme's decision.

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, 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 make it more difficult for us to attract collaborators due to concerns around the safety and/or efficacy of our technology platform or product candidates. In addition, our decision in September 2017 to temporarily suspend dosing in all ongoing fitusiran studies pending further review of a fatal thrombotic serious adverse event, or SAE, and agreement with regulatory authorities on a risk mitigation strategy could, notwithstanding the alignment reached with the FDA on a risk mitigation strategy in November 2017 and reinitiation of such studies, contribute to further concerns about the safety of our therapeutic candidates. Even if we do succeed in securing any 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 that we may develop, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaborations with Sanofi Genzyme, MDCO and Vir Biotechnology. 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 that 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 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 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, Sanofi Genzyme has the right to terminate our 2014 collaboration on a product-by-product basis in the event of certain safety concerns. Sanofi Genzyme also has the right to terminate its global license agreement for fitusiran at any time upon six months' prior written notice. If Sanofi Genzyme were to terminate a particular program, we may have to expend significantly more on the development and commercialization of such product candidate. Moreover, our agreement with MDCO relating to the development and commercialization of inclisiran worldwide may be terminated by MDCO at any time upon four months' prior written notice. 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. For example, in March 2011, Arbutus Biopharma Corporation, or ABC (formerly Tekmira Pharmaceuticals Corporation), and Protiva Biotherapeutics, Inc., or Protiva, a wholly owned subsidiary of ABC, and together with ABC, referred to as Arbutus, filed a civil complaint against us claiming, among other things, misappropriation of its confidential and proprietary information and trade secrets. As a result of the litigation, which was settled in November 2012, we were required to expend resources and management attention that would otherwise have been engaged in other activities. In addition, in August 2013, we initiated binding arbitration proceedings to resolve a disagreement with Arbutus regarding the achievement by Arbutus of a \$5.0 million milestone payment under our cross-license agreement relating to the manufacture of ALN-VSP clinical trial material for use in China. The Arbutus arbitration hearing was held in May 2015. In March 2016, the arbitration panel ruled in our favor and as a result, no milestone payment is due to Arbutus at this time. Arbutus did not appeal this ruling.

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, 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 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 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. 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, 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, 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, including, for example, review of our NDA and MAA filings for patisiran. 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 revenues could be delayed.

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 develop our product candidates, apply for regulatory approvals and commercialize our products, if approved, 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 current good manufacturing, or 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, in April 2016, we completed our purchase of a parcel of land in Norton, Massachusetts, where we have commenced construction of a cGMP manufacturing facility for drug substance, including siRNAs and siRNA conjugates, for clinical and commercial use.

We may manufacture limited quantities of clinical trial materials ourselves, but otherwise we currently rely on third parties to manufacture the drug substance and, with the exception of patisiran, the finished product we will require for any clinical trials that we initiate and to support the commercial launch of our first several products. 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. For example, in July 2015, we amended our manufacturing agreement with Agilent, to provide for Agilent to supply, subject to any conflicting obligations under our third-party agreements, a specified percentage of the active pharmaceutical ingredients required for certain of our products in clinical development, as well as other products the parties may agree upon in the future. We will also rely on Agilent to supply the active pharmaceutical ingredients to support the commercial launch of patisiran and in March 2018, we entered into a manufacturing services agreement with Agilent for such commercial supply. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our CMOs, including Agilent, to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are potential synthesis and purification failures and/or contamination during the manufacturing process, as well as other issues with the CMO's facility and ability to comply with the applicable manufacturing requirements, which could result in unusable product and cause delays in our manufacturing timelines 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, including siRNAs and siRNA conjugates, 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. 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.

Given the limited number of suppliers for our delivery technology and drug substance, we have developed cGMP capabilities and processes for the manufacture of patisiran formulated bulk drug product for late stage clinical use and commercial supply. During 2015, we scaled our cGMP manufacturing capacity for patisiran and believe we should have adequate resources to supply our commercial needs. In addition, as noted above, we are developing our own capabilities to manufacture drug substance, including siRNAs and siRNA conjugates, for clinical and commercial use. In developing these manufacturing capabilities by building our own manufacturing facilities, we have incurred substantial expenditures, and expect to incur significant additional expenditures in the future. In addition, the construction and qualification of our drug substance facility is expected to take several years to complete and there are many risks inherent in the construction of a new facility that could result in delays and additional costs, including the need to obtain access to necessary equipment and third-party technology, if any. Also, we have had to, and will likely need to continue to, hire and train qualified employees to staff our facilities. We do not currently have a second source of supply for patisiran formulated bulk

drug product. 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 of patisiran formulated bulk drug product and drug substance, 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. Any delay or setback in the manufacture of patisiran could, assuming approval, delay the launch or ongoing commercial supply, which could significantly impact our revenues and operating results.

The manufacturing process for any 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 these product candidates, 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, including Agilent, 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 Agilent or any other 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, including patisiran;
- 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.

If any CMO with whom we contract, including Agilent, fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials or commercial distribution could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our products or product candidates.



We have no sales or distribution experience and only early capabilities for marketing, sales and market access, and expect to invest significant financial and management resources to establish these capabilities and to establish a global commercial infrastructure.

We have no sales or distribution experience and only early capabilities for marketing, sales and market access. We currently expect to rely heavily on third parties to launch and market certain of our product candidates in certain geographies, if approved. However, we intend to commercialize several of our late-stage products on our own globally, including patisiran, as a result of the January 2018 amendment to our Sanofi Genzyme collaboration, as well as givosiran and lumasiran. Accordingly, we will need to develop internal sales, distribution and marketing capabilities as part of our core product strategy initially in the United States and the EU, then Canada and Switzerland, Central and Eastern Europe, Japan and in other major markets in the rest of the world, which will require significant financial and management resources. For those products for which we will perform sales, marketing and distribution functions ourselves, including patisiran, givosiran and lumasiran, if approved, 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:

- we may not be able to attract and build a significant marketing or sales force;
  - we may not be able to establish our global capabilities and infrastructure in a timely manner;
- the cost of establishing a marketing or sales force 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 develop our own global sales, marketing and distribution capabilities for patisiran and other products, we will not be able to successfully commercialize our products without reliance on third parties.

Credit and financial market conditions may exacerbate certain risks affecting our business from time to time.

Due to tightening of global credit, there may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators. We rely on third parties for several important aspects of our business, including significant portions of our manufacturing needs, development of product candidates and conduct of clinical trials. If such third parties are unable to satisfy their commitments to us, our business could be adversely affected.

Our ability to secure additional financing in addition to our term loan agreement and to satisfy our financial obligations under indebtedness outstanding from time to time will depend upon our future operating performance, which is subject to then prevailing general economic and credit market conditions, including interest rate levels and the availability of credit generally, and financial, business and other factors, many of which are beyond our control. In light of periodic uncertainty in the capital and credit markets, there can be no assurance that sufficient financing will be available on desirable or even any terms to fund investments, acquisitions, stock repurchases, dividends, debt refinancing or extraordinary actions.

#### 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 highly dependent upon our senior management and our scientific, clinical and medical staff. The loss of the service of any of the members of our senior management, including Dr. John Maraganore, our Chief Executive Officer, may significantly delay or prevent the achievement of product development and commercialization, and other business objectives. 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 a significant number of additional employees as we focus on achieving our Alnylam 2020 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 experience disappointing results in a clinical program and our stock price may decline as a result, as was the case following our decision in October 2016 to discontinue our revusiran program, and, to less of an extent, following our temporary suspension of dosing in our fitusiran program in September 2017. As a result, we may face additional challenges in attracting and retaining employees. 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 plan.



We may have difficulty expanding our operations successfully as we evolve 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 increase the number of product candidates we are developing we will also need to expand our operations in the United States and continue to build operations in the EU and other geographies, including Japan. Based on the positive data reported from our APOLLO Phase 3 study of patisiran, we filed an NDA and an MAA for patisiran in December 2017. Assuming regulatory approvals, we are preparing to commercialize patisiran in 2018 and now have global development and commercialization rights for patisiran as a result of the January 2018 amendment to our Sanofi Genzyme collaboration. We also plan to file for regulatory approval in Japan in mid-2018 and in one or more additional countries by the end of the year.

As noted above, we grew our workforce significantly during 2016 and 2017, and anticipate continuing to hire additional employees, including employees in the EU, Japan and other territories, as we focus on the potential commercial launch of patisiran and achieving our Alnylam 2020 strategy. This expected growth is placing a strain on our administrative and operational infrastructure, and we will need to develop additional and/or new infrastructure and capabilities to support our growth and obtain additional space to conduct our operations in the United States, the EU, Japan 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 product candidates we develop enter and advance through clinical trials, we will need 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 expand due to our development progress, we expect that we will need to manage additional relationships with various collaborators, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls and systems, reporting systems and infrastructure, and policies and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

The increasing use of social media platforms presents new risks and challenges.

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 intend to utilize appropriate social media in connection with our commercialization efforts following approval of our drug candidates. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical study or to report an alleged adverse event, or AE. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable AE reporting obligations or 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 social networking website. 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.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events could cause 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 or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including potential lawsuits from patients, collaborators, employees and/or stockholders, 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.

In June 2016, the United Kingdom, or UK, held a referendum in which voters approved an exit from the EU, commonly referred to as "Brexit." This referendum has created political and economic uncertainty, particularly in the UK and the EU, and this uncertainty may persist for years. A withdrawal could, among other outcomes, disrupt the free movement of goods, services and people between the UK and the EU, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in Europe. The UK's vote to exit the EU could also result in similar referendums or votes in other European countries in which we do business. Given the lack of comparable precedent, it is unclear what financial, trade and legal implications the withdrawal of the UK from the EU would have and how such withdrawal would affect us.

For example, Brexit could result in the UK or the EU significantly altering its regulations affecting the clearance or approval of our product candidates that are developed in the UK. 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. In addition, the announcement of Brexit and the withdrawal of the UK from the EU have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. 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

Any product candidates we 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 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. In October 2016, we discontinued development of one of our product candidates, which included a Phase 3 clinical trial. We currently have multiple other programs in clinical development, including several internal programs and two partnered programs currently in Phase 3 development, as well as several earlier stage clinical programs. In November 2017, we reported positive complete results from our APOLLO Phase 3 clinical trial for our lead product candidate, patisiran, and in December 2017, we filed an NDA and an MAA for patisiran. However, we may not be able to further advance these or any other product candidate through clinical trials and regulatory approval.

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. For example, in April 2018, we announced new results from our Phase 1 and Phase 1/2 OLE studies of givosiran. Although the clinical data from these studies are encouraging, the data are preliminary in nature, and based on a limited number of patients with AIP. These data, or other positive data, may not continue for patients with AIP, and may not be repeated or observed in our ongoing ENVISION Phase 3 study. There can be no assurance that our studies with givosiran will ultimately be successful or support further clinical advancement or regulatory approval of this 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, patisiran, givosiran, fitusiran, inclisiran and our other product candidates each employ novel delivery technologies that 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, or DMC, to suspend dosing and the observation of an imbalance in mortality in revusiran-treated patients as compared to those on placebo. We conducted a comprehensive evaluation of the revusiran data and reported the results of our evaluation in August 2017. Following our evaluation, we continue to believe that the decision to discontinue development of revusiran does not affect patisiran, which is under regulatory review for the treatment of hATTR amyloidosis, or any of our other investigational RNAi therapeutic programs in development. 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. In December 2017, we reached alignment with study investigators and the FDA on safety measures and a risk mitigation strategy to enable resumption of dosing in clinical studies with fitusiran, including our Phase 2 OLE study and the ATLAS Phase 3 program, including protocol-specified guidelines and additional investigator and patient education concerning reduced doses of replacement factor or bypassing agent to treat any breakthrough bleeds in fitusiran studies.

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, our clinical trials for fitusiran or cemdisiran, due to the availability of existing approved treatments, as well as other investigational treatments in development. Moreover, given the recent temporary suspension of dosing in our fitusiran studies due to a fatal thrombotic SAE, people with hemophilia may be more reluctant to enroll in the ATLAS Phase 3 program of fitusiran. 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, 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, as noted above, 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. In addition, in October 2016, we made the decision to discontinue our revusiran program. Following reports in the revusiran Phase 2 OLE study of new onset or worsening peripheral neuropathy, the revusiran ENDEAVOUR Phase 3 study DMC assembled in early October 2016 at our request to review these reports and ENDEAVOUR safety data on an unblinded basis. The DMC did not find conclusive evidence for a drug-related neuropathy signal in the ENDEAVOUR trial, but informed us that the benefit-risk profile for revusiran no longer supported continued dosing. We subsequently reviewed unblinded ENDEAVOUR data which revealed an imbalance of mortality in the revusiran arm as compared to placebo. Further, a review by us in 2017 of the ENDEAVOUR results subsequent to the completion of follow-up of the patients post-dosing discontinuation revealed an imbalance in new onset or worsening peripheral neuropathy in the revusiran arm as compared to placebo. We had previously reported, in July 2016, preliminary data from our revusiran Phase 2 OLE study for 12 patients who had reached the 12-month endpoint as of the data transfer date of May 26, 2016. SAEs were observed in 14 patients, one of which, a case of lactic acidosis, was deemed possibly related to the study drug and the patient discontinued treatment. There were a total of seven deaths reported at that time in the revusiran OLE study, all of which were unrelated to the study drug. The majority of the AEs were mild or moderate in severity; injection site reactions, or ISRs, were reported in 12 patients. In August 2015, we reported that three patients had discontinued from the revusiran Phase 2 OLE study due to recurrent localized reactions at the injection site or a diffuse rash; no further discontinuations due to ISRs had occurred as of May 26, 2016.

In our patisiran APOLLO Phase 3 study in patients with polyneuropathy due to hATTR amyloidosis, the most commonly reported AEs that occurred more frequently in patisiran patients were peripheral edema and infusion-related reactions, or IRRs. These were generally mild to moderate in severity and only one patient discontinued from the APOLLO study due to an IRR. Compared to placebo, patisiran treatment was associated with fewer treatment discontinuations and fewer study withdrawals due to AEs. The incidence of SAEs across the patisiran and placebo groups was similar and the SAEs reported in two or more patients in the patisiran group included: diarrhea, cardiac failure, congestive cardiac failure, orthostatic hypotension, pneumonia and atrioventricular block complete. These were all considered unrelated to patisiran, except for one SAE of diarrhea. SAEs occurred with similar frequency in the placebo group, except for diarrhea. Deaths were recorded with a similar incidence across the patisiran and placebo treatment groups and no deaths were considered related to the study drug.

In addition, in our ALN-VSP clinical trial, one patient with advanced pancreatic neuroendocrine cancer with extensive involvement of the liver developed hepatic failure five days following the second dose of ALN-VSP and subsequently

died; this was deemed possibly related to the study drug. As demonstrated by the discontinuation of our revusiran program in October 2016 and the temporary suspension of dosing in September 2017 in our fitusiran studies, the occurrence of SAEs and/or AEs can result in the suspension or termination of clinical trials of a product candidate by us or the FDA or a foreign regulatory authority, or refusal 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 United States, 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;
- 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;
- 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
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

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

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

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, 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 United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. 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 may also encounter unexpected delays or increased

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costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the drugs we are developing may represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these drugs. The lack of policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the FDA's standards, especially regarding drug safety, appear to have become more stringent.

In November 2017, we reported positive complete results from our APOLLO Phase 3 clinical trial and generally encouraging safety data, and in December 2017, we completed the submission of our first NDA and submitted our first MAA for patisiran. In January 2018, we announced that the EMA has accepted the MAA and initiated its review. Patisiran was previously granted an accelerated assessment by the EMA. In early February 2018, we announced that the FDA has accepted our NDA and granted our request for priority review, with an action date of August 11, 2018. We also plan to file for regulatory approval in Japan in mid-2018 and in one or more additional countries by the end of the year. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from patisiran or any product candidate for which we may seek approval in the future. Furthermore, any regulatory approval to market patisiran or any other product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy, 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 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 authorisation, 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 United States and vice versa.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight. If we 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 patisiran and any other drugs we may develop, 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 patisiran or other drug products required as a condition of approval or agreed to by us. Any regulatory approvals that we receive for patisiran or our other product candidates 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 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 United States, 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.

The CMO and manufacturing facilities we use to make our product candidates, including our Cambridge facility, our future 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 are subject to regulatory inspection by the FDA, the EMA and potentially other regulatory authorities in connection with the review of our patisiran NDA and MAA, as well as any subsequent applications for regulatory approval of patisiran filed in other territories. The discovery of any new or previously unknown problems with us 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 Phase 3 clinical and commercial use. In addition, in April 2016, we completed our purchase of a parcel of land in Norton, Massachusetts, where we are constructing a cGMP manufacturing facility for drug substance, including siRNAs and siRNA conjugates, for clinical and 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. Our product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review.

If we or our collaborators, CMOs or service providers fail to comply with applicable continuing regulatory requirements in the United States 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 will 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, patisiran utilizes an intravenous mode of administration that physicians and/or patients may not readily adopt or which may not compete with other potentially available options. In addition, fitusiran represents a new approach to treating hemophilia which may not be readily accepted by patients and their caregivers.

In addition, our estimates regarding the potential market size for patisiran or our other product candidates may be materially different from what we currently expect at the time we commence commercialization, 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.

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

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. These laws and regulations include:

- The U.S. federal Anti-Kickback statute, which prohibits, among other things, persons from 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 False Claims Act, or 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, and which may apply to us by virtue of statements and representations made to customers or third parties, and, 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. 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; and which may apply to us by virtue of statements and representations made to customers or third parties.
- 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 impose requirements relating to the privacy, security, and transmission of individually identifiable health information; and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information.
- The U.S. federal Open Payments requirements were implemented by the Centers for Medicare and Medicaid Services, or CMS, pursuant to the Patient Protection and Affordable Care Act, also referred to as the Affordable Care Act or the PPACA. 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 all transfers of value, including consulting fees, travel reimbursements, research grants, and other payments or gifts with values over \$10 made to physicians and teaching hospitals.
- 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.

If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, 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 establishing our global compliance infrastructure as we prepare for the potential launch of patisiran in 2018 in the United States and the EU. 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 patisiran or our other products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning 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.

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 await potential regulatory approval for patisiran in the U.S. and the EU and several of our other programs move into 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 patisiran, 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 patisiran or any other products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing patisiran or other products to the market, patisiran and such other products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell patisiran or our other products 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. If the price we are able to charge for patisiran or any other products we develop, 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 2.2 percent currently). 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.



We currently expect that some of the drugs we develop may need to be administered under the supervision of a physician or other healthcare professional on an outpatient basis, including patisiran. 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 United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for patisiran or other new drugs that we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. 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.

On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.

A number of other legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription drug benefit legislation that was enacted in 2003 and took effect in January 2006, healthcare reform legislation enacted by certain states, and major healthcare reform legislation that was passed by Congress and enacted into law in the United States in 2010. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

In particular, in March 2010, the PPACA 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. Provisions affecting pharmaceutical companies include 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.

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- 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 percent 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 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 full effects of the U.S. healthcare reform legislation cannot be known until the law is fully implemented through regulations or guidance issued by the 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 United States.

As a result of the 2016 election in the United States, there is great political uncertainty concerning the fate of the PPACA and other healthcare laws. Members of the United States Congress and the Trump Administration have expressed an intent to pass legislation or adopt executive orders to fundamentally change or repeal parts of the PPACA. While Congress has not passed repeal legislation to date, the TCJA includes a provision repealing the individual insurance coverage mandate included in PPACA, effective January 1, 2019. Further, on January 20, 2017, the President signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, the President signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the PPACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces. Congress may consider other legislation to replace elements of the PPACA. The implications of the PPACA, its possible repeal, any legislation that may be proposed to replace the PPACA, or the political uncertainty surrounding any repeal or replacement legislation for our business and financial condition, if any, are not yet clear.

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 United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

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

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 percent 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. 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 any products we may develop.

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

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 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 facilities comply with the relevant guidelines of the City of Cambridge, 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 methods and technologies that we develop under the patent and other intellectual property laws of the United States 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 technology 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 may be required to obtain licenses under third-party patents to market our proposed products or conduct our research and development or other activities. If licenses are not available to us on acceptable terms, we 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 United States 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 included a number of changes to the patent laws of the United States. 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 America Invents Act, which took effect in March 2013, changed United States 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.

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, Cancer Research Technology Limited, Ionis Pharmaceuticals, Inc., or 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 Innovation, and Arbutus. 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 United States 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, reexamination and opposition proceedings, as well as inter partes and post-grant review proceedings introduced by provisions of the America Invents Act, which became available to third party challengers on September 16, 2012, in various patent offices relating to patent rights in the RNAi field. For example, various third parties have initiated oppositions to patents in our McSwiggen, Kreutzer-Limmer and Tuschl II series in the EPO and in other jurisdictions. 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. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need for our siRNA therapeutic candidates. 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. 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 or perform research and development or other activities covered by such patents. For example, Silence Therapeutics plc, or Silence, has filed a claim in the High Court of England and Wales, naming us, our wholly owned subsidiary Alnylam UK Ltd., and The Medicines Company UK Ltd as co-defendants. The claim seeks a declaration that Silence is entitled to supplementary protection certificates, or SPCs, based on a European patent held by Silence, that Silence alleges covers certain of our product candidates. An SPC is an intellectual property right that could extend the life of the Silence patent in relation to a specified product for a period of up to five additional years bringing the potential expiration date to 2028. On October 27, 2017, we, through our affiliate Alnylam UK Ltd., and The Medicines Company UK Ltd filed a claim against Silence Therapeutics GmbH and Silence in the High Court of England and Wales seeking revocation of Silence's patent, as well as a declaration of non-infringement by each of the products of such patent, and costs and interest among other potential remedies. On November 30, 2017, we and The Medicines Company UK Ltd filed our defense to Silence's claim against us denying that the products that are the subject of Silence's claim against us fall under the Silence patent or that it is entitled to an SPC based on that patent. Both cases are expected to be tried in the High Court of England and Wales in December 2018. The Silence claim filed in the High Court of England and Wales has been amended by Silence to assert an additional patent against the defendants. There are also a number of related actions brought by us or Silence in connection with this ongoing intellectual property dispute. Although we believe Silence's patents are invalid and not infringed by our product candidates and that, therefore, Silence would not be entitled to obtain an SPC based on any of our product candidates and would not be entitled to the injunctive relief or monetary damages it seeks, litigation is subject to inherent uncertainty, and a court could ultimately rule against us.

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. 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. We and Dicerna settled the ongoing litigation between us in April 2018. A third party may also claim that we have improperly obtained or used its confidential or proprietary information. For example, in March 2011, Arbutus (formerly Tekmira) filed a civil complaint against us alleging, among other things, misappropriation of its confidential and proprietary information and trade secrets. In November 2012, we settled this litigation and restructured our contractual relationship with Arbutus. In connection with this restructuring, we incurred a \$65.0 million charge to operating expenses during the quarter ended December 31, 2012.

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 UMass, 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 could delay our research and development 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 require us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially acceptable 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 and protecting our RNAi technology and any related 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. For example, in 2013, Arbutus (formerly Tekmira) notified us that it believed it had achieved a \$5.0 million milestone payment under our cross-license agreement relating to the manufacture of ALN-VSP clinical trial material for use in China. We notified Arbutus that we did not believe that the milestone has been achieved under the terms of the cross-license agreement. In August 2013, we initiated binding arbitration proceedings seeking a declaratory judgment that Arbutus had not yet met the conditions of the milestone and was not entitled to payment at the time. The Arbutus arbitration hearing was held in May 2015. On March 9, 2016, the arbitration panel ruled in our favor and as a result, no milestone payment is due to Arbutus at this time. Arbutus did not appeal this ruling.

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 future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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. We believe a number of drugs are currently under development, and 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. For example, we are developing patisiran for the treatment of hATTR amyloidosis. In November 2017, we reported positive complete results from our APOLLO Phase 3 clinical trial and generally encouraging safety data, and in December 2017, we submitted our first NDA and MAA for patisiran. In January 2018, we announced that the EMA has accepted the MAA and initiated its review. Patisiran was previously granted an accelerated assessment by the EMA. In early February 2018, we announced that the FDA has accepted our NDA and granted our request for priority review, with an action date of August 11, 2018. We are aware of other approved products used to treat this disease, including tafamidis, marketed by Pfizer in Europe and certain countries outside the United States, as well as product candidates in various stages of clinical development, including an investigational drug being developed by Ionis. In October and November 2017, Ionis reported positive efficacy data as well as safety data from its Phase 3 clinical trial in hATTR amyloidosis, including thrombocytopenia and renal insufficiency SAEs. In November 2017, Ionis reported that it has filed its NDA and MAA for this investigational drug and in January 2018, reported that the FDA had accepted its NDA for priority review and set a PDUFA date of July 6, 2018. Ionis has licensed Akcea Therapeutics, Inc. to commercialize this product, if approved. In early May 2018, Akcea Therapeutics reported that the FDA has extended the review period for this product and has assigned a new PDUFA goal date of October 6,

2018. In addition, in March 2018, Pfizer announced positive topline results from a Phase 3 study of tafamidis in patients with transthyretin cardiomyopathy. In June 2017, the FDA granted Fast Track designation to tafamidis for transthyretin cardiomyopathy; additionally, in March 2018, the Ministry of Labor Health and Welfare in Japan granted SAKIGAKE designation to tafamidis for this indication. While we believe that patisiran will have a competitive product profile, it is possible it will not compete favorably with these products and product candidates, or others, and even if approved, it may not achieve commercial success. Moreover, positive data and/or the commercial success of competitive products could negatively impact our stock price.

If we 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;

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the availability and cost of manufacturing, marketing and sales capabilities;  
price;  
reimbursement coverage; and  
patent position.

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. 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 Takeda Pharmaceutical Company Limited, or Takeda, Marina Biotech, Inc., Arrowhead Research Corporation, or Arrowhead, and its subsidiary, Calando Pharmaceuticals, Inc., or Calando, Quark Pharmaceuticals, Inc., or Quark, Silence, Arbutus, Sylentis S.A.U., Dicerna, 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, 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, Arrowhead, as the assignee of F. Hoffmann-La Roche Ltd, and Takeda have obtained non-exclusive licenses, and Arrowhead, as the assignee of Novartis Pharma AG, has obtained specific exclusive licenses for 30 gene targets, that include access to certain aspects of our technology that give them the right to compete with us in certain circumstances. 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. Ionis is currently marketing several antisense drugs and has multiple antisense product candidates in clinical trials, including one for the treatment of hATTR amyloidosis that is currently under regulatory review in the United States and the EU. 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 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. 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 due to stock volatility.

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 and in September 2017, following our temporary suspension of dosing in our fitusiran program, our stock also declined, although to a lesser extent. 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. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Sales of additional shares of our common stock, including by us or our directors and officers, could cause the price of our common stock to decline.

Sales of substantial amounts of our common stock in the public market, or the availability of such shares for sale, by us or others, including the issuance of common stock upon exercise of outstanding options, could adversely affect the price of our common stock.

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

Sanofi Genzyme currently holds approximately 11 percent of our outstanding common stock and has the right to increase its ownership up to 30 percent, as well as the right to maintain its then current ownership percentage through the term of our collaboration, subject to certain limitations. This concentration of ownership may harm the market price of our common stock 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 percent of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 percent of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

ITEM 6. EXHIBITS.

- 3.1 Amended and Restated Bylaws of the Registrant, as amended
- 10.1† Amendment No. 2 entered into as of January 6, 2018 to the Master Collaboration Agreement dated as of January 11, 2014, as amended by Amendment No. 1, including certain Regional, Global and Co-Co License Terms attached thereto, by and between the Registrant and Genzyme Corporation
- 10.2† Exclusive License Agreement entered into as of January 6, 2018 by and between the Registrant and Genzyme Corporation
- 10.3† ALN-AT3 Global License Terms entered into as of January 6, 2018 by and between the Registrant and Genzyme Corporation
- 10.4† Manufacturing Services Agreement effective as of March 28, 2018 by and between the Registrant and Agilent Technologies, Inc.
- 31.1 Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
- 31.2 Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
- 32.1 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.
- 32.2 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.
- 101 The following materials from the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, formatted in XBRL (Extensible Business Reporting Language): (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Comprehensive Loss, (iii) the Condensed Consolidated Statements of Cash Flows, and (iv) Notes to Condensed Consolidated Financial Statements.

†Indicates confidential treatment requested as to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Request.

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: May 4, 2018 /s/ John M. Maraganore  
John M. Maraganore, Ph.D.  
Chief Executive Officer  
(Principal Executive Officer)

Date: May 4, 2018 /s/ Manmeet S. Soni  
Manmeet S. Soni  
Senior Vice President, Chief Financial Officer  
(Principal Financial and Accounting Officer)