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 June 30, 2025

OR

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

For the transition period from _____ to _____

Commission File Number 001-36407

ALNYLAM PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware **(State or Other Jurisdiction of Incorporation or Organization)**	**77-0602661** **(I.R.S. Employer Identification No.)**
675 West Kendall Street, Henri A. Termeer Square Cambridge, MA **(Address of Principal Executive Offices)**	**02142** **(Zip Code)**

(617) 551-8200
(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.01 par value per share	ALNY	The Nasdaq Stock Market LLC

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

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

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

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

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

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

At July 25, 2025, the registrant had 131,079,015 shares of Common Stock, $0.01 par value per share, outstanding.

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

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our views with respect to the potential for our approved and investigational RNAi therapeutics and those of our collaborators, including AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO, Leqvio® (inclisiran), Qfitlia™ (fitusiran), zilebesiran, mivelsiran and nucresiran;
- our plans for additional global regulatory filings and the continuing product launches of AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO and our collaborators' plans with respect to Leqvio and Qfitlia;
- our ability to obtain regulatory approval of AMVUTTRA (vutrisiran) for the treatment of ATTR amyloidosis with cardiomyopathy in jurisdictions outside the United States;
- our expectations regarding the potential market size for, and the successful commercialization of, AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO, Leqvio, Qfitlia or any future products;
- our ability to obtain and maintain regulatory approvals and pricing and reimbursement for AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO or any future products, and our collaborators' ability with respect to Leqvio and Qfitlia;
- the progress of our research and development programs, including programs across a broad range of disease areas and indications;
- the potential for improved product profiles to emerge from our technologies and our ability to expand our clinical development pipeline to include additional tissue types and disease indications;
- our current and anticipated clinical trials and expectations regarding the reporting of data from these trials;
- the number and timing of regulatory filings and interactions with, or actions or advice of, regulatory authorities, which may affect the design, initiation, timing, continuation and/or progress of clinical trials, or result in the need for additional preclinical and/or clinical testing or the timing or likelihood of regulatory approvals;
- the status of our manufacturing operations and any delays, interruptions or failures in the manufacture and supply of AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO or any of our product candidates (or Leqvio, Qfitlia or other products or product candidates being developed and commercialized by our collaborators), by our or their contract manufacturers or by us or our collaborators;
- the impact of current and potential healthcare reforms, including those affecting the delivery of or payment for healthcare products and services;
- the impact of any future pandemics or public health emergencies on, among other things, our financial performance, business and operations, including manufacturing, supply chain, research and development activities and pipeline programs, and other potential impacts to our business;
- our progress continuing to build and leverage our global commercial infrastructure;
- the possible impact of any competing products on the commercial success of AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO, Leqvio and Qfitlia, as well as our product candidates, and, our, or with respect to Leqvio or Qfitlia, our collaborators', ability to compete against such products;
- our ability to manage our growth and operating expenses;
- our ability to successfully execute on our *Alnylam P^{5}x25* strategy and our intention to achieve the metrics associated with this strategy, including to become a top-tier biotech company by the end of 2025;
- our ability to achieve sustainable operating profitability beginning in 2025;

- our expectations regarding the length of time our current cash, cash equivalents and marketable debt securities will support our operations based on our current operating plan;
- the ability of the third parties on which we rely for development, manufacture and distribution of our products to meet their obligations to us;
- our ability to maintain our existing collaborations and our expectations regarding potential future research and development funding, licensing fees and milestone and royalty payments that we may receive under existing or future collaboration agreements;
- our ability to obtain, maintain and protect our intellectual property;
- our ability to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors;
- the outcome of litigation, including our patent infringement suits against Pfizer, Inc., BioNTech SE and Moderna, Inc., or of other legal proceedings or government investigations;
- regulatory developments in the U.S. and other jurisdictions;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- our ability to satisfy our payment obligations, and to service the interest on, or to refinance our indebtedness, including our convertible notes, or to make cash payments in connection with any conversion of our convertible notes, to the extent required; and
- our expectations regarding the effect of the capped call transactions and the anticipated market activities of the option counterparties and/or their respective affiliates.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part II, Item 1A, “Risk Factors” and elsewhere in this Quarterly Report on Form 10-Q. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for management to predict all risk factors, nor can we assess the impact of all risk factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You are advised, however, to consult any further disclosure we make in our reports filed with the Securities and Exchange Commission, or SEC.

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

PART I. FINANCIAL INFORMATION
ITEM 1. FINANCIAL STATEMENTS (UNAUDITED)

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

	June 30, 2025	December 31, 2024
ASSETS		
Current assets:		
Cash and cash equivalents	$ 1,113,685	$ 966,428
Marketable debt securities	1,743,900	1,719,920
Marketable equity securities	—	8,156
Accounts receivable, net	567,112	405,308
Inventory	71,688	78,509
Prepaid expenses and other current assets	147,314	116,964
Total current assets	3,643,699	3,295,285
Property, plant and equipment, net	499,791	502,784
Operating lease right-of-use assets	192,401	191,148
Deferred tax assets	104,363	116,863
Restricted investments	68,593	68,593
Other assets	57,172	65,310
Total assets	$ 4,566,019	$ 4,239,983
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 102,393	$ 88,415
Accrued expenses	918,966	793,692
Operating lease liabilities	46,097	41,886
Deferred revenue	15,080	55,481
Liability related to the sale of future royalties	97,523	113,018
Development derivative liability	120,788	93,780
Total current liabilities	1,300,847	1,186,272
Operating lease liabilities, net of current portion	224,445	229,541
Convertible debt	1,026,522	1,024,621
Liability related to the sale of future royalties, net of current portion	1,345,147	1,334,353
Development derivative liability, net of current portion	407,535	393,139
Other liabilities	10,932	4,969
Total liabilities	4,315,428	4,172,895
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.01 par value per share, 5,000 shares authorized and no shares issued and outstanding as of June 30, 2025 and December 31, 2024	—	—
Common stock, $0.01 par value per share, 250,000 shares authorized; 130,977 shares issued and outstanding as of June 30, 2025; 129,294 shares issued and outstanding as of December 31, 2024	1,310	1,293
Additional paid-in capital	7,690,737	7,388,061
Accumulated other comprehensive loss	(29,952)	(34,518)
Accumulated deficit	(7,411,504)	(7,287,748)
Total stockholders' equity	250,591	67,088
Total liabilities and stockholders' equity	$ 4,566,019	$ 4,239,983

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Statements of Operations				
Revenues:				
Net product revenues	$ 672,212	$ 410,088	$ 1,140,750	$ 775,251
Net revenues from collaborations	61,496	227,338	160,681	345,886
Royalty revenue	39,981	22,399	66,447	33,021
Total revenues	773,689	659,825	1,367,878	1,154,158
Operating costs and expenses:				
Cost of goods sold	142,029	67,271	212,212	121,884
Cost of collaborations and royalties	924	1,401	1,782	12,764
Research and development	323,621	294,142	588,743	555,137
Selling, general and administrative	323,314	248,397	563,263	459,194
Total operating costs and expenses	789,888	611,211	1,366,000	1,148,979
(Loss) income from operations	(16,199)	48,614	1,878	5,179
Other (expense) income:				
Interest expense	(40,246)	(33,258)	(78,892)	(68,511)
Interest income	27,486	29,182	56,159	58,827
Other expense, net	(6,399)	(55,705)	(56,099)	(70,249)
Total other expense, net	(19,159)	(59,781)	(78,832)	(79,933)
Loss before income taxes	(35,358)	(11,167)	(76,954)	(74,754)
Provision for income taxes	(30,919)	(5,722)	(46,802)	(8,070)
Net loss	$ (66,277)	$ (16,889)	$ (123,756)	$ (82,824)
Net loss per common share — basic and diluted	$ (0.51)	$ (0.13)	$ (0.95)	$ (0.66)
Weighted-average common shares used to compute basic and diluted net loss per common share	130,628	126,733	130,155	126,435
Statements of Comprehensive Loss				
Net loss	$ (66,277)	$ (16,889)	$ (123,756)	$ (82,824)
Other comprehensive income (loss):				
Unrealized (loss) gain on marketable securities	(343)	(727)	687	(4,295)
Foreign currency translation gain (loss)	7,855	(6,952)	3,771	(7,030)
Defined benefit pension plans, net of tax	53	30	108	63
Total other comprehensive income (loss)	7,565	(7,649)	4,566	(11,262)
Comprehensive loss	$ (58,712)	$ (24,538)	$ (119,190)	$ (94,086)

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

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2024	129,294	$ 1,293	$ 7,388,061	$ (34,518)	$ (7,287,748)	$ 67,088
Exercise of common stock options, net of tax withholdings	423	4	50,981	—	—	50,985
Issuance of common stock under equity plans	594	6	(6)	—	—	—
Stock-based compensation	—	—	57,840	—	—	57,840
Other comprehensive loss	—	—	—	(2,999)	—	(2,999)
Net loss	—	—	—	—	(57,479)	(57,479)
Balance as of March 31, 2025	130,311	1,303	7,496,876	(37,517)	(7,345,227)	115,435
Exercise of common stock options, net of tax withholdings	556	6	81,055	—	—	81,061
Issuance of common stock under equity plans	110	1	(1)	—	—	—
Stock-based compensation	—	—	112,807	—	—	112,807
Other comprehensive income	—	—	—	7,565	—	7,565
Net loss	—	—	—	—	(66,277)	(66,277)
Balance as of June 30, 2025	130,977	$ 1,310	$ 7,690,737	$ (29,952)	$ (7,411,504)	$ 250,591

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

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount				
Balance as of December 31, 2023	125,794	$ 1,259	$ 6,811,063	$ (23,375)	$ (7,009,591)	$ (220,644)
Exercise of common stock options, net of tax withholdings	223	2	24,763	—	—	24,765
Issuance of common stock under equity plans	446	4	(4)	—	—	—
Stock-based compensation	—	—	46,155	—	—	46,155
Other comprehensive loss	—	—	—	(3,613)	—	(3,613)
Net loss	—	—	—	—	(65,935)	(65,935)
Balance as of March 31, 2024	126,463	1,265	6,881,977	(26,988)	(7,075,526)	(219,272)
Exercise of common stock options, net of tax withholdings	1,264	13	140,273	—	—	140,286
Issuance of common stock under equity plans	294	3	10,358	—	—	10,361
Stock-based compensation	—	—	90,096	—	—	90,096
Other comprehensive loss	—	—	—	(7,649)	—	(7,649)
Net loss	—	—	—	—	(16,889)	(16,889)
Balance as of June 30, 2024	128,021	$ 1,281	$ 7,122,704	$ (34,637)	$ (7,092,415)	$ (3,067)

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)

	Six Months Ended June 30,	
	2025	**2024**
Cash flows from operating activities:		
Net loss	$ (123,756)	$ (82,824)
Adjustments to reconcile net loss to net cash provided by operating activities:		
Depreciation and amortization	28,349	28,520
Non-cash interest expense on liability related to the sale of future royalties	71,434	61,103
Stock-based compensation expense	168,392	134,635
Realized and unrealized loss on marketable equity securities	2,306	1,289
Change in fair value of development derivative liability	74,150	64,228
Deferred income taxes	19,374	794
Other	(37,864)	(18,292)
Changes in operating assets and liabilities:		
Accounts receivable, net	(144,347)	10,050
Inventory	17,359	6,816
Prepaid expenses and other assets	(25,992)	(13,775)
Accounts payable, accrued expenses and other liabilities	26,411	69,605
Deferred revenue	(40,400)	(219,506)
Net cash provided by operating activities	35,416	42,643
Cash flows from investing activities:		
Purchases of property, plant and equipment	(23,263)	(20,991)
Purchases of marketable securities	(861,199)	(717,826)
Sales and maturities of marketable securities	856,850	705,137
Proceeds from maturity of restricted investments	58,075	57,875
Purchases of restricted investments	(58,075)	(57,875)
Net cash used in investing activities	(27,612)	(33,680)
Cash flows from financing activities:		
Proceeds from exercise of stock options and other types of equity, net	130,587	158,637
(Repayment of) proceeds from development derivative, net	(32,746)	1,770
Net cash provided by financing activities	97,841	160,407
Effect of exchange rate changes on cash, cash equivalents and restricted cash	41,564	(13,061)
Net increase in cash, cash equivalents and restricted cash	147,209	156,309
Cash, cash equivalents and restricted cash, beginning of period	968,652	814,884
Cash, cash equivalents and restricted cash, end of period	$ 1,115,861	$ 971,193
Supplemental disclosure of cash flows:		
Cash paid for interest	$ 81,497	$ 39,101
Cash paid for taxes	$ 1,098	$ 3,561
Operating lease right-of-use assets obtained in exchange for new operating lease liabilities	$ 8,537	$ 7,793
Supplemental disclosure of noncash investing activities:		
Capital expenditures included in accounts payable and accrued expenses	$ 4,081	$ 1,063

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

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

1. NATURE OF BUSINESS

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

As of June 30, 2025, we have six marketed products, including two products that are commercialized by collaborators, and multiple late-stage investigational programs advancing towards potential commercialization. We currently generate worldwide product revenues from four commercialized products, AMVUTTRA, ONPATTRO, GIVLAARI and OXLUMO, primarily in the United States, or U.S., and Europe.

2. BASIS OF PRESENTATION AND PRINCIPLES OF CONSOLIDATION

The accompanying condensed consolidated financial statements of Alnylam are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP, applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to state fairly the results of operations for the reported periods. Our condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, our audited consolidated financial statements for the year ended December 31, 2024, which were included in our Annual Report on Form 10-K that was filed with the Securities and Exchange Commission on February 13, 2025. 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. Certain prior period amounts in the condensed consolidated financial statements have been reclassified to conform to the current period presentation.

Our significant accounting policies are described in Note 2 of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2024. There have been no material changes to our significant accounting policies during the six months ended June 30, 2025.

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 as of the date of the condensed consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. In our condensed consolidated financial statements, we use estimates and assumptions related to our inventory valuation and related reserves, clinical accruals, liability related to the sale of future royalties, development derivative liability, income taxes, deferred tax asset valuation allowances, revenue recognition, research and development expenses, and stock-based compensation expense. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Liquidity

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of June 30, 2025, will be sufficient to satisfy our near-term capital and operating needs for at least the next 12 months from the filing date of this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

In November 2024, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2024-04, *Induced Conversions of Convertible Debt Instruments,* which clarifies the requirements for determining whether certain settlements of convertible debt instruments should be accounted for as an induced conversion or extinguishment of

convertible debt. The standard is effective for annual reporting periods beginning after December 15, 2025, and interim periods within those annual periods. We are currently evaluating the impact of ASU 2024-04 on our consolidated financial statements and related disclosures.

In November 2024, the FASB issued ASU 2024-03, *Disaggregation of Income Statement Expenses*, which is intended to improve disclosures by requiring additional information about specific expense categories in the notes to the financial statements on an annual and interim basis. The standard will be effective for annual reporting periods beginning after December 15, 2026 and interim reporting periods beginning after December 15, 2027, with early adoption permitted. The standard updates may be applied on either a prospective or retrospective basis. We are currently evaluating the disclosure requirements related to ASU 2024-03.

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which requires entities to disclose disaggregated information about their effective tax rate reconciliation as well as expanded information on income taxes paid by jurisdiction. The disclosure requirements will be applied on a prospective basis, with the option to apply them retrospectively. The standard is effective for annual reporting periods beginning after December 15, 2024, with early adoption permitted. We are currently evaluating the disclosure requirements related to ASU 2023-09.

3. NET PRODUCT REVENUES

Net product revenues, classified based on the geographic region in which the product is sold and by franchise ("TTR", which includes AMVUTTRA and ONPATTRO, and "Rare", which includes GIVLAARI and OXLUMO) consist of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
AMVUTTRA				
United States	$ 361,346	$ 148,463	$ 559,310	$ 278,701
Europe	92,868	56,760	172,956	100,493
Rest of World	37,739	24,886	69,679	46,156
Total	491,953	230,109	801,945	425,350
ONPATTRO				
United States	22,053	22,112	$ 37,625	$ 38,651
Europe	21,246	37,074	47,787	81,764
Rest of World	9,239	18,058	16,615	26,046
Total	52,538	77,244	102,027	146,461
Total TTR	544,491	307,353	903,972	571,811
GIVLAARI				
United States	55,151	41,225	98,945	79,956
Europe	20,966	16,314	39,510	31,629
Rest of World	4,732	4,588	9,362	8,598
Total	80,849	62,127	147,817	120,183
OXLUMO				
United States	16,019	15,744	30,128	29,076
Europe	21,929	20,503	42,913	41,930
Rest of World	8,924	4,361	15,920	12,251
Total	46,872	40,608	88,961	83,257
Total Rare	127,721	102,735	236,778	203,440
Total net product revenues	$ 672,212	$ 410,088	$ 1,140,750	$ 775,251

As of June 30, 2025 and December 31, 2024, net product revenue-related receivables of $474.7 million and $269.9 million, respectively, were included in accounts receivable, net on our condensed consolidated balance sheets.

The following table summarizes balances and activity in each product revenue allowance and reserve category:

(In thousands)	Chargebacks and Rebates	Trade Discounts and Allowances	Returns Reserve and Other Incentives	Total
Beginning balance as of December 31, 2024	$ 350,908	$ 975	$ 9,933	$ 361,816
Provision related to current period sales	302,162	4,956	30,906	338,024
Provision related to prior period sales	(37,200)	—	—	(37,200)
Credit or payments made during the period for current period sales	(123,063)	(3,217)	(11,725)	(138,005)
Credit or payments made during the period for prior period sales	(43,118)	(927)	(6,655)	(50,700)
Total as of June 30, 2025	$ 449,689	$ 1,787	$ 22,459	$ 473,935

4. NET REVENUES FROM COLLABORATIONS

Net revenues from collaborations consist of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Roche	$ 18,267	$ 16,506	$ 35,323	$ 91,186
Regeneron Pharmaceuticals	32,542	207,429	83,581	234,193
Novartis AG	—	2,304	—	16,820
Other	10,687	1,099	41,777	3,687
Total	$ 61,496	$ 227,338	$ 160,681	$ 345,886

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

(In thousands)	As of June 30, 2025	As of December 31, 2024
Receivables included in accounts receivable, net	$ 55,587	$ 102,743
Contract liabilities included in deferred revenue	$ 15,080	$ 55,481

We recognized net revenues from collaborations of $13.0 million and $41.1 million in the three and six months ended June 30, 2025, respectively, and $200.0 million and $228.7 million in the three and six months ended June 30, 2024, respectively, each of which was included in the contract liability balance at the beginning of the applicable period.

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.

Product Collaborations

Roche

On July 21, 2023, or the Effective Date, we entered into a Collaboration and License Agreement, or the Roche Agreement, with F. Hoffmann-La Roche Ltd. and Genentech, Inc., or, collectively, Roche, pursuant to which we and Roche established a worldwide, strategic collaboration for the joint development of zilebesiran. Zilebesiran is our investigational small interfering RNA, or siRNA, therapeutic targeting liver-expressed angiotensinogen, which is currently in Phase 2 clinical development for the treatment of hypertension.

Under the Roche Agreement, we granted to Roche (i) co-exclusive rights to develop zilebesiran worldwide and commercialize zilebesiran in the U.S., referred to as the Co-Commercialization Territory, (ii) exclusive rights to commercialize zilebesiran outside of the U.S., referred to as the Roche Territory, and (iii) non-exclusive rights to manufacture zilebesiran for the development and commercialization of zilebesiran in the Roche Territory.

We lead the global clinical development for zilebesiran. We are responsible for forty percent (40%) and Roche is responsible for the remaining sixty percent (60%) of development costs incurred in the conduct of development activities that support regulatory approval of zilebesiran globally. We and Roche share equally (50/50) all costs incurred in connection with development activities that are conducted to support regulatory approval of zilebesiran solely in the Co-Commercialization

Territory if incremental development activities are needed. Roche is solely responsible for all costs incurred in the conduct of development activities that primarily support regulatory approval in the Roche Territory. Upon regulatory approval, Roche has the exclusive right to commercialize zilebesiran in the Roche Territory and will pay us tiered, low double-digit royalties based on net sales of zilebesiran on a country-by-country basis during the applicable royalty term. We and Roche will co-commercialize zilebesiran in the Co-Commercialization Territory and share equally (50/50) in profits and losses (including commercialization costs).

Roche has the right to terminate the Roche Agreement for any or no reason at all upon prior written notice; however, if the termination occurs after the achievement of the first development milestone and before the achievement of the third development milestone, Roche is required to pay us a termination fee of $50.0 million. In addition, either party may terminate the Roche Agreement for a material breach by, or insolvency of, the other party, subject to a cure period. Unless earlier terminated pursuant to its terms, the Roche Agreement will remain in effect until expiration on a country-by-country basis (a) in the Roche Territory, upon expiration of the applicable royalty term in the applicable country and (b) in the Co-Commercialization Territory, upon expiration of the term of the co-commercialization efforts.

As of the Effective Date, we identified the following promises in the Roche Agreement that were evaluated under the scope of Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers,* or ASC 606: (i) a co-exclusive license to develop zilebesiran worldwide and commercialize zilebesiran within the Co-Commercialization Territory, a non-exclusive license to manufacture zilebesiran in the Roche Territory solely for purposes of developing and commercializing zilebesiran in the Roche Territory, and an exclusive license to commercialize zilebesiran in the Roche Territory, collectively referred to as Roche License Obligation, (ii) development services, including the manufacture of clinical supply, that support regulatory approval of zilebesiran, referred to as the Roche Development Services Obligation, and (iii) a technology transfer of the existing manufacturing process for zilebesiran, referred to as the Roche Technology Transfer Obligation. The three performance obligations under the Roche Agreement are collectively referred to as the Roche Performance Obligations.

We determined that the Roche License Obligation, Roche Development Services Obligation and Roche Technology Transfer Obligation were reflective of a vendor-customer relationship and therefore represented performance obligations within the scope of ASC 606. The Roche License Obligation was considered functional intellectual property and distinct from other promises under the contract as Roche can benefit from the licenses on its own or together with other readily available resources. As the licenses were delivered at the same time, they were considered one performance obligation at contract inception. The Roche Development Services Obligation was considered distinct as Roche could benefit from the development services together with the licenses transferred by us at the inception of the agreement. The development services are not expected to significantly modify or customize the initial intellectual property as zilebesiran was in Phase 2 of clinical development at contract inception. The Roche Technology Transfer Obligation was distinct as Roche can benefit from the manufacturing license transferred by us at the inception of the agreement given the advancements of our RNAi platform and our utilization of third-party contract manufacturing organizations to manufacture zilebesiran. Therefore, each represented a separate performance obligation within the contract with a customer under the scope of ASC 606 at contract inception.

We consider the collaborative activities associated with the co-commercialization of zilebesiran in the U.S. to be a separate unit of account within the scope of ASC Topic 808, *Collaborative Arrangements*, as we and Roche are both active participants in the commercialization activities and are exposed to significant risks and rewards that are dependent on the commercial success of the activities in the arrangement.

Based on the standalone selling prices of each performance obligation as of the Effective Date, we allocated the variable consideration related to the estimated reimbursements for the Roche Development Services Obligation and the Roche Technology Transfer Obligation to each performance obligation as the terms of the variable payment relate specifically to our efforts to satisfy the performance obligation. We allocated the fixed upfront consideration entirely to the Roche License Obligation as the value of the fixed consideration together with the expected value of the remaining development and regulatory milestones, sales-based milestones, and royalties, all of which are either currently constrained at inception or subject to the sales- or usage-based royalty exception, approximates the standalone selling price of the Roche License Obligation. This allocation is consistent with the allocation objective of ASC 606 when considering all of the performance obligations and payment terms in the contract.

The Roche License Obligation was satisfied at a point in time upon transfer of the license to Roche. Control of the licenses was transferred on the Effective Date and Roche could begin to use and benefit from the licenses. Because of this, all consideration allocated to the Roche License Obligation, including the upfront payment, milestones and royalties, is recognized when these amounts are no longer considered fully constrained or when the related sales occur for amounts subject to the sales-or-usage based royalty exception of ASC 606. For the Roche Development Services Obligation, we measure proportional performance over time using an input method based on cost incurred relative to the total estimated cost of the obligation, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the transaction price allocated to the obligation. As all costs in the proportional performance model are allowable for

reimbursement from Roche, and the assumptions used to determine the total estimated cost of the obligation are consistent with the assumptions used to determine the transaction price allocated to the obligation, the revenue recognized for this obligation will approximate 60% of the actual reimbursable cost incurred. Management has applied significant judgment in the process of developing our estimates. We re-evaluate the transaction price as of the end of each reporting period and as of June 30, 2025, the total transaction price was determined to be $1.31 billion.

The following table provides a summary of the transaction price allocated to each performance obligation:

(In thousands)	As of June 30, 2025
Roche License Obligation	$ 375,000
Roche Development Services Obligation	937,533
Roche Technology Transfer Obligation	2,000
	$ 1,314,533

Net revenues from collaborations recognized under the Roche Agreement consist of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Roche License Obligation	$ —	$ —	$ —	$ 65,000
Roche Development Services Obligation	16,690	12,797	32,530	19,948
Other	1,577	3,709	2,793	6,238
Total	$ 18,267	$ 16,506	$ 35,323	$ 91,186

As of June 30, 2025, the aggregate amount of the transaction price allocated to the Roche Performance Obligations that was unsatisfied was $837.3 million, which is expected to be recognized through the term of the Roche Agreement based on our input method model as the services are performed. We incurred research and development costs related to our collaboration with Roche of $31.0 million and $60.7 million, during the three and six months ended June 30, 2025, respectively, and $26.2 million and $44.3 million, during the three and six months ended June 30, 2024, respectively.

Regeneron Pharmaceuticals, Inc.

Overview

In 2019, we entered into a global, strategic collaboration with Regeneron Pharmaceuticals, Inc., or Regeneron, to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic targets expressed in the eye and central nervous system, or CNS, in addition to a select number of targets expressed in the liver, which we refer to as the Regeneron Collaboration. The Regeneron Collaboration is governed by a Master Agreement, referred to as the Regeneron Master Agreement. In connection with the Regeneron Master Agreement, we and Regeneron entered into (i) a co-co collaboration agreement covering the continued development of cemdisiran, our C5 siRNA, currently in development for C5 complement-mediated diseases, as a monotherapy, or the C5 Co-Co Collaboration Agreement, and (ii) a license agreement to evaluate anti-C5 antibody-siRNA combinations for C5 complement-mediated diseases including evaluating the combination of Regeneron's pozelimab and cemdisiran, or the C5 License Agreement. The Master Agreement, the C5 Co-Co Collaboration Agreement and the C5 License Agreement were accounted for as a single arrangement because the agreements were negotiated together.

In November 2022, Regeneron exercised its right under the C5 Co-Co Collaboration Agreement to opt-out of the further development and commercialization of cemdisiran monotherapy. As a result of Regeneron's decision to opt-out, the licenses granted to Regeneron under the C5 Co-Co Collaboration Agreement reverted to us, we had the sole right to continue to develop and commercialize cemdisiran monotherapy, and Regeneron no longer shared in the costs on any monotherapy program. Regeneron remained eligible to receive tiered, double-digit royalties on net sales of cemdisiran as a monotherapy.

In June 2024, we entered into an amended and restated C5 License Agreement, or the Amended C5 License Agreement, which terminated the C5 Co-Co Collaboration Agreement and granted Regeneron a worldwide license to cemdisiran as a monotherapy in addition to the license to cemdisiran in combination with anti-C5 antibodies. Through the Amended C5 License Agreement, Regeneron is now solely responsible for development, manufacturing and commercialization of cemdisiran as a monotherapy and in combination with anti-C5 antibodies. As part of the Amended C5 License Agreement, we provided manufacturing technology transfer services for cemdisiran to Regeneron. Regeneron provided us with an upfront payment of $10.0 million, and we will receive certain milestone payments upon receipt of regulatory approval for cemdisiran as a monotherapy, and tiered double-digit royalties on net sales. The Amended C5 License Agreement did not change our rights to

receive low double-digit royalties and commercial milestones of up to $325.0 million on any potential product sales if cemdisiran is used as part of a combination product.

Under the terms of the Regeneron Collaboration, we continue to work exclusively with Regeneron to discover RNAi therapeutics for eye and CNS diseases for an initial research period of up to seven years, which we refer to as the Initial Research Term. Regeneron has an option to extend the Initial Research Term (referred to as the Research Term Extension Period, and together with the Initial Research Term, the Research Term) for up to an additional five years, for a research term extension fee of $300.0 million. The Regeneron Collaboration also covers a select number of RNAi therapeutic programs designed to target genes expressed in the liver.

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

In connection with the Regeneron Master Agreement, we remain eligible to receive an additional $100.0 million milestone payment upon achievement of certain criteria during early clinical development for an eye program. In addition, we and Regeneron are continuing to advance programs nominated during the Initial Research Term, and Regeneron has the right to nominate up to six additional targets per year during this period. For each of these programs, Regeneron will provide us with $2.5 million in funding at program initiation and an additional $2.5 million at lead candidate identification. If Regeneron exercises the option to extend the research term, Regeneron will retain the right to nominate up to six additional targets per year, and we will remain eligible to achieve $2.5 million in funding at each program initiation and an additional $2.5 million at each lead candidate identification during the Research Term Extension Period.

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

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

Contract Modification

In June 2024, we determined the Amended C5 License Agreement does not meet the requirements to account for the contract modification as a separate contract under ASC 606 because the consideration exchanged for the additional distinct goods and services does not reflect the standalone selling price. Therefore, we have accounted for the Amended C5 License Agreement and Regeneron Master Agreement as a single combined contract. The modification date was determined to be the June 2024 effective date of the Amended C5 License Agreement.

Our performance obligations subsequent to the contract modification included: (i) a research license and research services, collectively referred to as the Research Services Obligation; (ii) a worldwide license to cemdisiran for combination therapies, and manufacturing and development service obligations, collectively referred to as the C5 License Obligation; (iii) a worldwide

license to cemdisiran for monotherapies, referred to as the C5 Monotherapy Obligation; and (iv) a technology transfer of the existing manufacturing process for cemdisiran, referred to as the Regeneron Technology Transfer Obligation.

The Amended C5 License Agreement did not change the Research Services Obligation or the C5 License Obligation, which were both performance obligations at the inception of our global, strategic collaboration with Regeneron prior to the contract modification. The Amended C5 License Agreement resulted in two additional performance obligations, which were the C5 Monotherapy Obligation and the Regeneron Technology Transfer Obligation. The C5 Monotherapy Obligation was considered functional intellectual property and distinct from other promises as Regeneron can benefit from the cemdisiran monotherapy license on its own or together with other readily available resources and the license is separately identifiable from the other promises in the contract. The Regeneron Technology Transfer Obligation was distinct as Regeneron can benefit from the cemdisiran monotherapy license transferred by us without the technology transfer given cemdisiran was in an advanced stage of clinical development and our utilization of third-party contract manufacturing organizations to manufacture cemdisiran. Therefore, the C5 Monotherapy Obligation and the Regeneron Technology Transfer Obligation each represented a separate performance obligation.

The initial transaction price of $191.5 million allocated to the C5 Monotherapy Obligation was recognized immediately as this obligation was satisfied at a point in time upon transfer of the license to Regeneron. Control of the license was transferred in June 2024 as Regeneron could begin to use and benefit from the license on its own or together with other readily available resources to generate economic benefit from the license. The remaining variable consideration allocated to the C5 Monotherapy Obligation, including milestones and royalties, will be recognized immediately when these amounts are no longer considered fully constrained or when the related sales occur for amounts subject to the sales-or-usage based royalty exception of ASC 606. In the three months ended March 31, 2025, we completed our obligations related to the C5 License Obligation and the Regeneron Technology Transfer Obligation.

We continue to perform work in satisfaction of the remaining unsatisfied performance obligation, the Research Services Obligation. For this performance obligation, we measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for each of the identified obligations by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the transaction price allocated to the obligation. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch-up. We re-evaluate the transaction price as of the end of each reporting period and as of June 30, 2025, the total transaction price was determined to be $100.5 million related to this obligation. As of June 30, 2025, the aggregate amount of the transaction price that was unsatisfied was $46.8 million, which is expected to be recognized through the term of the Regeneron Collaboration based on our input method model as the services are performed.

Net revenues from collaborations recognized under the Regeneron Collaboration consist of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Research Services Obligation	$ 12,957	$ 4,000	$ 26,767	$ 18,700
C5 License Obligation	—	8,800	21,458	10,500
C5 Monotherapy Obligation	—	191,520	—	191,520
Regeneron Technology Transfer Obligation	—	—	2,431	—
Other license programs	19,585	3,109	32,925	13,473
Total	$ 32,542	$ 207,429	$ 83,581	$ 234,193

Revenue recognized for the “Other license programs” relates to seven separate programs subject to individual license agreements with Regeneron.

Deferred revenue is classified as either current or noncurrent in the condensed consolidated balance sheets based on the period the revenue is expected to be recognized. The composition of deferred revenue related to the Regeneron Collaboration is as follows:

(In thousands)	As of June 30, 2025
Research Services Obligation	$ 15,080
Total	$ 15,080

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

(In thousands)	As of December 31, 2024
Research Services Obligation	$ 41,156
C5 License Obligation	12,018
Regeneron Technology Transfer Obligation	2,307
Total	$ 55,481

We incurred research and development costs related to the Regeneron Collaboration of $12.5 million and $31.5 million, during the three and six months ended June 30, 2025, respectively, and $14.3 million and $33.0 million, during the three and six months ended June 30, 2024, respectively.

Novartis AG

2013 Collaboration with The Medicines Company

In February 2013, we entered into a license and collaboration agreement with The Medicines Company, or MDCO, pursuant to which we granted to MDCO an exclusive, worldwide license to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9 for the treatment of hypercholesterolemia and other human diseases, including inclisiran. We refer to this agreement, as amended through the date hereof, as the MDCO License Agreement. In 2020, Novartis AG, or Novartis, completed its acquisition of MDCO and assumed all of MDCO's rights and obligations under the MDCO License Agreement. We are entitled to royalties ranging from 10% up to 20% based on annual worldwide net sales of licensed products by Novartis, its affiliates and sublicensees, subject to reduction under specified circumstances.

Vir Biotechnology, Inc.

In March 2025, we and Vir Biotechnology, Inc., or Vir, entered into an amended and restated collaboration and license agreement, or the Amended Vir Agreement, relating to elebsiran (formerly ALN-HBV02 (VIR-2218)). Vir remains solely responsible for development, manufacturing and commercialization of elebsiran. In connection with execution of the Amended Vir Agreement, Vir made a $30.0 million payment, and we remain entitled to receive milestone payments upon the achievement of specified regulatory and commercial milestones, and royalties on the net sales of elebsiran ranging from low-to-mid teen percentages. Because the license rights have already been delivered and we have no other remaining performance obligations under the Amended Vir Agreement, the $30.0 million payment was recognized within net revenues from collaborations during the six months ended June 30, 2025.

Other

In addition to the collaboration agreements discussed above, we have various other collaboration agreements that are not individually significant to our operating results or financial condition at this time. Pursuant to the terms of those agreements, we may be required to pay, or we may receive, additional amounts contingent upon the occurrence of various future events (e.g., upon the achievement of various development and commercial milestones) which in the aggregate could be significant. We may also incur, or be reimbursed for, significant research and development costs. In addition, if any products related to these collaborations are approved for sale, we may be required to pay, or we may receive, royalties on future sales. The payment or receipt of these amounts, however, is contingent upon the occurrence of various future events. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development and commercialization, it is possible we may not receive any such payments under all of our existing collaboration and license agreements, including the agreements described within this note.

5. FAIR VALUE MEASUREMENTS

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

(In thousands)	As of June 30, 2025	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	$ 120,514	$ 120,514	$ —	$ —
U.S. treasury securities	9,912	—	9,912	—
Commercial paper	9,328	—	9,328	—
Marketable debt securities:				
U.S. treasury securities	867,006	—	867,006	—
U.S. government-sponsored enterprise securities	421,651	—	421,651	—
Corporate notes	425,106	—	425,106	—
Commercial paper	25,131	—	25,131	—
Municipal securities	5,006	—	5,006	—
Restricted cash (money market funds)	914	914	—	—
Total financial assets	$ 1,884,568	$ 121,428	$ 1,763,140	$ —
Financial liabilities				
Development derivative liability	$ 528,323	$ —	$ —	$ 528,323

(In thousands)	As of December 31, 2024	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	$ 190,779	$ 190,779	$ —	$ —
U.S. treasury securities	36,428	—	36,428	—
Commercial paper	22,709	—	22,709	—
U.S. government-sponsored enterprise securities	9,952	—	9,952	—
Marketable debt securities:				
U.S. treasury securities	921,627	—	921,627	—
U.S. government-sponsored enterprise securities	396,143	—	396,143	—
Corporate notes	361,739	—	361,739	—
Commercial paper	35,408	—	35,408	—
Municipal securities	5,003	—	5,003	—
Marketable equity securities	8,156	8,156	—	—
Restricted cash (money market funds)	910	910	—	—
Total financial assets	$ 1,988,854	$ 199,845	$ 1,789,009	$ —
Financial liabilities				
Development derivative liability	$ 486,919	$ —	$ —	$ 486,919

As of June 30, 2025 and December 31, 2024, the estimated fair value of our 1% Convertible Senior Notes due 2027, or the Notes, was approximately $1.35 billion and $1.11 billion, respectively. The fair value was determined based on the last actively traded price per $100 of the Notes (Level 2) as of June 30, 2025 and December 31, 2024, respectively.

During the three and six months ended June 30, 2025 and 2024, there were no transfers into or out of Level 3 financial assets or liabilities. The carrying amounts reflected on our condensed consolidated balance sheets for cash, accounts receivable, net, other current assets, accounts payable and accrued expenses approximate fair value due to their short-term maturities.

6. MARKETABLE DEBT SECURITIES

We invest our excess cash balances in marketable debt securities and, at each balance sheet date presented, we classify all of our investments in debt securities as available-for-sale and as current assets as they represent the investment of funds available for current operations. We did not record any impairment charges related to our marketable debt securities during the three and six months ended June 30, 2025 or 2024.

The following tables summarize our marketable debt securities:

	As of June 30, 2025			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 875,716	$ 1,392	$ (190)	$ 876,918
U.S. government-sponsored enterprise securities	421,519	394	(262)	421,651
Corporate notes	424,215	995	(104)	425,106
Commercial paper	34,459	—	—	34,459
Municipal securities	5,000	6	—	5,006
Total	$ 1,760,909	$ 2,787	$ (556)	$ 1,763,140

	As of December 31, 2024			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 957,145	$ 1,377	$ (467)	$ 958,055
U.S. government-sponsored enterprise securities	405,890	575	(370)	406,095
Corporate notes	361,311	769	(341)	361,739
Commercial paper	58,117	—	—	58,117
Municipal securities	5,002	1	—	5,003
Total	$ 1,787,465	$ 2,722	$ (1,178)	$ 1,789,009

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

(In thousands)	As of June 30, 2025	As of December 31, 2024
Marketable debt securities	$ 1,743,900	$ 1,719,920
Cash and cash equivalents	19,240	69,089
Total	$ 1,763,140	$ 1,789,009

7. OTHER BALANCE SHEET DETAILS

Inventory

The components of inventory are summarized as follows:

(In thousands)	As of June 30, 2025	As of December 31, 2024
Raw materials	$ 22,869	$ 23,965
Work in process	43,779	64,978
Finished goods	33,749	26,433
Total inventory	$ 100,397	$ 115,376

As of June 30, 2025 and December 31, 2024, we had $28.7 million and $36.9 million of long-term inventory, respectively, included within other assets in our condensed consolidated balance sheets as we anticipate it being consumed beyond our normal operating cycle.

Cash, Cash Equivalents and Restricted Cash

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

	As of June 30,	
(In thousands)	2025	2024
Cash and cash equivalents	$ 1,113,685	$ 968,492
Total restricted cash included in other assets	2,176	2,701
Total cash, cash equivalents, and restricted cash shown in the condensed consolidated statements of cash flows	$ 1,115,861	$ 971,193

Accumulated Other Comprehensive Loss

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

(In thousands)	Loss on Investment in Joint Venture	Defined Benefit Pension Plans, Net of Tax	Unrealized Gains (Losses) from Debt Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Loss
Balance as of December 31, 2024	$ (32,792)	$ (4,249)	$ 1,544	$ 979	$ (34,518)
Other comprehensive income before reclassifications	—	—	1,580	3,771	5,351
Amounts reclassified from accumulated other comprehensive loss	—	108	(893)	—	(785)
Net other comprehensive income	—	108	687	3,771	4,566
Balance as of June 30, 2025	$ (32,792)	$ (4,141)	$ 2,231	$ 4,750	$ (29,952)

(In thousands)	Loss on Investment in Joint Venture	Defined Benefit Pension Plans, Net of Tax	Unrealized Gains (Losses) from Debt Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive Loss
Balance as of December 31, 2023	$ (32,792)	$ (2,753)	$ 1,548	$ 10,622	$ (23,375)
Other comprehensive loss before reclassifications	—	—	(4)	(7,030)	(7,034)
Amounts reclassified from accumulated other comprehensive loss	—	63	(4,291)	—	(4,228)
Net other comprehensive income (loss)	—	63	(4,295)	(7,030)	(11,262)
Balance as of June 30, 2024	$ (32,792)	$ (2,690)	$ (2,747)	$ 3,592	$ (34,637)

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

8. LIABILITY RELATED TO THE SALE OF FUTURE ROYALTIES

As of June 30, 2025 and December 31, 2024, the carrying value of the liability related to the sale of future royalties was $1.44 billion, net of closing costs of $8.7 million, and $1.45 billion, net of closing costs of $9.1 million, respectively. The carrying value of the liability related to the sale of future royalties approximates fair value as of June 30, 2025 and is based on our current estimates of future royalties expected to be paid over the life of the arrangement, which are considered Level 3 inputs.

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

Carrying value as of December 31, 2024	$	1,447,371
Interest expense		71,434
Payments		(76,135)
Carrying value as of June 30, 2025	$	1,442,670

9. DEVELOPMENT DERIVATIVE LIABILITY

As of June 30, 2025 and December 31, 2024, we recorded $120.8 million and $93.8 million, respectively, within development derivative liability and $407.5 million and $393.1 million, respectively, within development derivative liability, net of current portion on our condensed consolidated balance sheets, based on expected timing of our payments to BXLS V Bodyguard – PCP L.P. and BXLS Family Investment Partnership V – ESC L.P., collectively referred to as Blackstone Life Sciences. The change in fair value due to the remeasurement of the development derivative liability is recorded within other expense, net on our condensed consolidated statements of operations and comprehensive loss.

As of June 30, 2025, the derivative liability is classified as a Level 3 financial liability in the fair value hierarchy. The valuation method incorporates certain unobservable Level 3 key inputs, including (i) the probability and timing of achieving stated development milestones to receive payments from Blackstone Life Sciences, (ii) the probability and timing of achieving regulatory approval and payments to Blackstone Life Sciences, (iii) an estimate of the amount and timing of the royalty payable on net sales of AMVUTTRA, (iv) our cost of borrowing (10%), and (v) Blackstone Life Sciences' cost of borrowing (7%).

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

Carrying value as of December 31, 2024	$	486,919
Change in fair value		74,150
Payments		(32,746)
Carrying value as of June 30, 2025	$	528,323

10. STOCK-BASED COMPENSATION

The following table summarizes stock-based compensation expense included in operating costs and expenses on our condensed consolidated statements of operations and comprehensive loss, and stock-based compensation charges included in additional paid-in capital on our condensed consolidated statements of stockholders' equity (deficit):

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2025	2024	2025	2024
Research and development	$ 49,552	$ 48,115	$ 73,350	$ 67,330
Selling, general and administrative	62,128	41,173	95,042	67,305
Total stock-based compensation expense	111,680	89,288	168,392	134,635
Capitalized stock-based compensation costs	1,127	808	2,255	1,616
Total stock-based compensation charges	$ 112,807	$ 90,096	$ 170,647	$ 136,251

11. NET LOSS PER COMMON SHARE

We compute basic net income (loss) per common share by dividing net income (loss) by the weighted-average number of common shares outstanding. Diluted net income per common share utilizing the treasury stock and if-converted methods is based upon the weighted-average number of common shares and dilutive potential common share equivalents outstanding during the period. For periods in which we have generated a net loss, diluted net loss per common share is the same as basic net loss per common share, as the inclusion of potentially dilutive common shares would be anti-dilutive.

The following table sets forth the potential common shares (prior to consideration of the treasury stock or if-converted methods) excluded from the calculation of diluted net loss per common share because their inclusion would be anti-dilutive:

	As of June 30,	
(In thousands)	2025	2024
Options to purchase common stock, inclusive of performance-based stock options	4,372	6,235
Unvested restricted stock units, inclusive of performance-based restricted stock units	3,055	2,870
Convertible debt	3,616	3,616
Total	11,043	12,721

12. COMMITMENTS AND CONTINGENCIES

Technology License and Other Commitments

We have licensed from third parties the rights to use certain technologies and information in our research processes as well as in any other products we may develop. In accordance with the related license or technology agreements, we are required to make certain fixed payments to the licensor or a designee of the licensor over various agreement terms. Many of these agreement terms are consistent with the remaining lives of the underlying intellectual property that we have licensed. As of June 30, 2025, our commitments over the next five years to make fixed and cancellable payments under existing license agreements were not material.

Legal Matters

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

Patent Infringement Lawsuits

In March 2022, we filed separate lawsuits in the U.S. District Court for the District of Delaware, or the District Court, against (1) Moderna, Inc. and its subsidiaries ModernaTX, Inc. and Moderna US, Inc., collectively referred to as Moderna, which we refer to as the Moderna lawsuit, and (2) Pfizer, Inc. and its subsidiary Pharmacia & Upjohn Co. LLC, collectively referred to as Pfizer, which we refer to as the Pfizer lawsuit, seeking damages for patent infringement in Moderna's and Pfizer's manufacture and sale of their messenger RNA, or mRNA, COVID-19 vaccines. In May 2022, Pfizer added BioNTech SE to the Pfizer lawsuit.

Following claim construction rulings of the District Court in the Moderna lawsuit in 2023, we and Moderna jointly agreed to final judgment of non-infringement of two of our patents, and we appealed the claim construction ruling to the Court of Appeals for the Federal Circuit. The claim construction ruling initially did not affect a third patent in the Moderna lawsuit, but in September 2024 the District Court entered a ruling in which it construed this third patent in the same manner as the other patents, and in October 2024 we and Moderna jointly agreed to a final judgment of non-infringement with respect to the third patent while preserving all rights to appeal.

In October 2024, Moderna filed a motion seeking recovery of fees incurred by Moderna from the time we agreed to a judgment of non-infringement with respect to the first two patents until the time we agreed to a judgment of non-infringement with respect to the third patent, which period runs from approximately September 2023 to October 2024. We opposed the motion in a reply filed on November 6, 2024. The District Court has not yet ruled on the motion. Due to uncertainty as to whether we will be liable for these fees, a loss is not probable or reasonably estimable at this time.

In June 2025, following oral argument, the Court of Appeals for the Federal Circuit affirmed the District Court's claim construction ruling in the Moderna lawsuit. We are currently considering our options with respect to any further action on this ruling.

In the Pfizer lawsuit, the District Court issued an order in April 2025 that effectively placed the Pfizer product outside the coverage of our asserted patents. On May 13, 2025, we and Pfizer filed a joint motion seeking to stay all proceedings with a stipulation to non-infringement, which the District Court granted on the same day. On July 30, 2025, the District Court granted Pfizer's motion for summary judgement of non-infringement and entered final judgment of non-infringement. We are currently evaluating our options, including a potential appeal to the Court of Appeals for the Federal Circuit.

On July 12, 2024, Acuitas Therapeutics, Inc., or Acuitas, filed a declaratory judgment action against us in the District Court, seeking a judgment adding certain Acuitas employees as co-inventors on the patents we have asserted against Pfizer/BioNTech and Moderna in our lawsuits. On September 19, 2024, we filed a motion to dismiss, arguing Acuitas did not have standing to sue and failed to state a claim upon which relief could be granted. On July 1, 2025, the District Court granted our motion to dismiss the complaint without prejudice, finding that the plaintiffs had failed to plead facts sufficient to establish standing.

On December 12, 2024, The Board of Regents of the University of Texas System filed a lawsuit in the U.S. District Court for the Western District of Texas, or the Texas District Court, alleging that we infringe U.S. Patent No. 8,895,717 by making, using and commercializing ONPATTRO in the U.S. On February 5, 2025, we filed a motion to dismiss the case for improper venue and an alternative motion to transfer the case to the U.S. District Court for the District of Massachusetts if the dismissal is not granted. On July 2, 2025, the Texas District Court denied the motions to dismiss and to transfer the case without prejudice, permitting us to refile the motions following the conclusion of venue discovery. In light of the early stage of this matter, a loss is not probable or reasonably estimable at this time.

Indemnifications

In connection with license agreements we may enter with companies to obtain rights to intellectual property, we may be required to indemnify such companies for certain damages arising in connection with the intellectual property rights licensed under the agreements. Under such agreements, we may be responsible for paying the costs of any litigation relating to the license agreements or the underlying intellectual property rights, including the costs associated with certain litigation regarding the licensed intellectual property. We are also a party to a number of agreements entered into in the ordinary course of business, which contain typical provisions that obligate us to indemnify the other parties to such agreements upon the occurrence of certain events, including litigation or other legal proceedings. In addition, we have agreed to indemnify our officers and directors for expenses, judgments, fines, penalties, excise taxes, and settlement amounts paid in connection with any threatened, pending or completed litigation proceedings, in which an officer or director was, is or will be involved as a party, on account of such person's status as an officer or director, or by reason of any action taken by the officer or director while acting in such capacity, subject to certain limitations. These indemnification costs are charged to selling, general and administrative expense.

Our maximum potential future liability under any such indemnification provisions is uncertain. We have reviewed the estimated aggregate fair value of our potential liabilities under all such indemnification provisions and have not recorded any related liability as of June 30, 2025.

13. SEGMENT INFORMATION

We operate in a single segment dedicated to the discovery, development, manufacturing and commercialization of RNAi therapeutics. Consistent with our management reporting, results of our operations are reported on a consolidated basis for purposes of segment reporting. Our Chief Executive Officer, or CEO, as the chief operating decision maker, or CODM, evaluates performance and decides how to allocate resources based on consolidated net income (loss) that is reported on the condensed consolidated statements of operations and comprehensive loss. The measure of segment assets is reported on the condensed consolidated balance sheets as total assets. Please refer to the condensed consolidated financial statements for further

information related to these measures of segment performance. In addition, research and development and selling, general and administrative expenses are significant segment expenses regularly provided to the CEO with the following categories:

Research and Development

(In thousands)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
Clinical research and outside services	$ 140,692	$ 119,496	$ 268,035	$ 245,00
Compensation and related	143,450	134,877	242,637	231,30
Occupancy and all other costs[1]	39,479	39,769	78,071	78,83
Total research and development expense	$ 323,621	$ 294,142	$ 588,743	$ 555,13

Selling, General and Administrative

(In thousands)	Three Months Ended June 30, 2025	Three Months Ended June 30, 2024	Six Months Ended June 30, 2025	Six Months Ended June 30, 2024
Compensation and related	$ 191,233	$ 137,711	$ 322,670	$ 255,052
Consulting and professional services	82,637	66,731	147,324	123,490
Occupancy and all other costs[1]	49,444	43,955	93,269	80,652
Total selling, general and administrative expense	$ 323,314	$ 248,397	$ 563,263	$ 459,194

[1] Occupancy and all other costs includes facilities, information technology, depreciation and certain departmental expenses.

14. SUBSEQUENT EVENTS

On July 4, 2025, President Trump signed H.R. 1, the “One Big Beautiful Bill Act”, or the Act, into law. The legislation includes several changes to federal tax law that are designed to allow for more favorable deductibility of certain business expenses beginning in 2025, including the restoration of immediate expensing of domestic research and development expenditures, reinstatement of 100% bonus depreciation, and more favorable rules for determining the limitation on business interest expense. The Act also includes certain changes to the U.S. taxation of foreign activity, including changes to foreign tax credits, global intangible low-taxed income, foreign-derived intangible income, and base erosion and anti-abuse tax, amongst other changes. These changes are generally effective for tax years beginning after December 31, 2025 and were not reflected in the income tax provision for the period ended June 30, 2025, as enactment occurred after the balance sheet date.

We are currently evaluating the impact on future periods.

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

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with our unaudited condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q.

Overview

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

Our research and development strategy is to target genetically validated genes that have been implicated in the cause or pathway of human disease. We utilize a N-acetylgalactosamine (GalNAc) conjugate approach or lipid nanoparticle (LNP) to enable hepatic delivery of siRNAs. For delivery to the central nervous system, or CNS, and the eye (ocular delivery), we are utilizing an alternative conjugate approach based on a hexadecyl (C16) moiety as a lipophilic ligand. We are also advancing approaches for heart, skeletal muscle and adipose tissue delivery of siRNAs. Our focus is on clinical indications where there is a high unmet need, a genetically validated target, early biomarkers for the assessment of clinical activity in Phase 1 clinical trials, and a definable path for drug development, regulatory approval, patient access and commercialization.

In early 2021, we launched our *Alnylam P^{5}x25* strategy, which focuses on our planned transition to a top-tier biotech company by the end of 2025. With *Alnylam P^{5}x25*, we aim to deliver transformative medicines across a broad range of disease areas and indications, benefiting patients around the world through sustainable innovation and exceptional financial performance, resulting in a leading biotech profile.

We currently have six marketed products and more than 20 clinical programs, including several in late-stage development.

AMVUTTRA is approved in the U.S. for the treatment of hereditary transthyretin-mediated amyloidosis, or hATTR amyloidosis, with polyneuropathy in adults, in the European Union, or EU, and the United Kingdom, or UK, for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, in Japan for the treatment of transthyretin, or TTR, type familial amyloidosis with polyneuropathy, and in multiple additional countries. Regulatory reviews continue in other territories. In March 2025, the United States Food and Drug Administration, or the FDA, approved our supplemental New Drug Application, or sNDA, for AMVUTTRA for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits. In June 2025, the European Commission, or EC, granted approval of AMVUTTRA for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy, following a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency. AMVUTTRA has also been approved by each of the Brazilian Health Regulatory Agency, or ANVISA, the Japanese Health Authority, or PMDA, the UK's Medicines and Healthcare Products Regulatory Agency, or MHRA, and the Colombian Health Authority for the treatment of ATTR amyloidosis with cardiomyopathy.

ONPATTRO is approved in the United States, or U.S., for the treatment of the polyneuropathy of hATTR amyloidosis in adults and has also been approved in the EU for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, in Japan for the treatment of TTR-type familial amyloidosis with polyneuropathy, and in multiple additional countries. In February 2025, ONPATTRO received regulatory approval from ANVISA for the treatment of ATTR amyloidosis with cardiomyopathy.

GIVLAARI is approved in the U.S. for the treatment of adults with acute hepatic porphyria, or AHP, in the EU for the treatment of AHP in adults and adolescents aged 12 years and older, and in several other countries. Regulatory filings for givosiran (the generic name of GIVLAARI) in additional territories are pending or planned during 2025 and beyond.

OXLUMO is approved in the U.S. for the treatment of primary hyperoxaluria type 1, or PH1, to lower urinary and plasma oxalate levels in pediatric and adult patients, and in the EU and the UK for the treatment of PH1 in all age groups. OXLUMO has also been approved in several other countries and regulatory filings for lumasiran (the generic name of OXLUMO) in additional territories are pending or planned during 2025 and beyond.

Leqvio (inclisiran), our fifth product, is being developed and commercialized by our collaborator Novartis AG, or Novartis, and has received marketing authorization from the EC for the treatment of adults with hypercholesterolemia or mixed dyslipidemia and from the FDA as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with

heterozygous familial hypercholesterolemia, or HeFH, or clinical atherosclerotic cardiovascular disease, or ASCVD, who require additional lowering of low-density lipoprotein cholesterol, or LDL-C. In July 2023, the FDA approved an expanded indication for Leqvio to include treatment of adults with high LDL-C and who are at increased risk of heart disease. Leqvio has also been approved in China and Japan, and as of the end of June 2025, Leqvio had been registered in more than 106 countries worldwide and was commercially available in 86 countries.

Qfitlia (fitusiran), our sixth product, is being commercialized by our collaborator, Genzyme Corporation, a Sanofi Company, or Sanofi, and was approved by the FDA in March 2025 for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A or B, with or without factor VIII or IX inhibitors (neutralizing antibodies). Qfitlia is the first and only therapeutic designed to lower antithrombin, a protein that inhibits blood clotting, with the goal of promoting thrombin generation to rebalance hemostasis and prevent bleeds. Regulatory submissions for Qfitlia have also been completed in China and Brazil.

In addition to our marketed products, as part of our *Alnylam P^{5}x25* strategy, we have multiple drivers of future growth, including the development of transformative medicines to treat prevalent disease. In addition to Leqvio, we are advancing zilebesiran, an investigational, subcutaneously administered RNAi therapeutic targeting angiotensinogen in development for the treatment of hypertension. In 2023, we entered into a Collaboration and License Agreement, or the Roche Collaboration and License Agreement, with F. Hoffmann-La Roche Ltd. and Genentech, Inc. or, collectively, Roche, pursuant to which we established a worldwide, strategic collaboration for the joint development and commercialization of zilebesiran. In March 2024, we reported positive topline results from our KARDIA-2 clinical trial, which is designed to evaluate the safety and efficacy of zilebesiran administered biannually as a concomitant therapy in patients whose blood pressure is not adequately controlled by a standard of care antihypertensive medication. We expect to report results from our KARDIA-3 Phase 2 clinical trial, which is designed to evaluate the efficacy and safety of zilebesiran as an add-on therapy in adult patients with high cardiovascular risk and uncontrolled hypertension despite treatment with two to four standard of care antihypertensive medications, in the second half of 2025. We expect to initiate a Phase 3 cardiovascular outcomes clinical trial in the second half of 2025 following our reporting of results from the KARDIA-3 Phase 2 clinical trial.

We are advancing nucresiran (formerly ALN-TTRsc04), an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis. In November 2024, we announced positive results from the ongoing Phase 1 clinical trial of nucresiran in healthy volunteers. These results demonstrated that a single dose of nucresiran at 300 mg or higher resulted in mean reductions of serum TTR of greater than 90% from baseline achieved at Day 15 and were sustained through at least Day 180. We have initiated the TRITON-CM Phase 3 clinical trial of nucresiran in patients with ATTR amyloidosis with cardiomyopathy and expect to initiate the TRITON-PN Phase 3 clinical trial of nucresiran in patients with hATTR polyneuropathy in late 2025.

We are also advancing mivelsiran (formerly ALN-APP), an investigational RNAi therapeutic targeting amyloid precursor protein in development for the treatment of Alzheimer's disease, or AD, and cerebral amyloid angiopathy, or CAA. In July 2025, we presented multiple and single dose data from the Phase 1 clinical trial of mivelsiran in patients with early-onset AD. These data demonstrated that single and multiple doses of mivelsiran were generally well tolerated and demonstrated robust, durable, dose-dependent reductions of soluble amyloid precursor protein beta (sAPPβ) in cerebrospinal fluid. Further lowering of sAPPβ was observed after administration of a second 50 mg dose of mivelsiran. We expect to initiate a Phase 2 clinical trial of mivelsiran in patients with AD in the second half of 2025. In July 2024, we initiated dosing in the cAPPricorn-1 Phase 2 clinical trial of mivelsiran in patients with CAA.

We have additional late-stage investigational programs advancing toward potential commercialization, including cemdisiran for the treatment of complement-mediated diseases, which our collaborator, Regeneron Pharmaceuticals, Inc., or Regeneron, is advancing in combination with pozelimab in Phase 3 clinical trials in myasthenia gravis, geographic atrophy and paroxysmal nocturnal hemoglobinuria.

In further support of our *Alnylam P^{5}x25* strategy and in view of our evolving risk profile, we remain focused on the continued evolution of our global infrastructure, including key objectives such as optimizing our global structure for execution in key markets, enhancing performance consistent with our values, and continuing to strengthen our culture. We continue to build our global compliance program to drive its evolution and enhancement through the launch of new systems and leveraging data analytics to strengthen the efficiency and effectiveness of our program. Building from our global Code of Business Conduct and Ethics, our compliance program is designed to empower our employees and those with whom we work to execute on our strategy consistent with our values and in compliance with applicable laws and regulations, and to mitigate risk. Comprised of components such as risk assessment and monitoring; policies, procedures, and guidance; training and communications; dedicated resources; and systems and processes supporting activities such as third party engagements and investigations and remediation, and our enterprise risk management program; our program and related controls are built to enhance our business processes, structures, and controls across our global operations, and to empower ethical decision making.

Based on our expertise in RNAi therapeutics and broad intellectual property estate, we have formed collaborations with leading pharmaceutical and life sciences companies to support our development and commercialization efforts, including Roche, Regeneron, Sanofi, and Novartis (which acquired our collaborator The Medicines Company, or MDCO, in 2020).

We have incurred significant losses since we commenced operations in 2002 and as of June 30, 2025, we had an accumulated deficit of $7.41 billion. Historically, we have generated losses principally from costs associated with research and development activities, acquiring, filing and expanding intellectual property rights, and selling, general and 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 continued build-out of late-stage clinical and commercial capabilities, including global commercial operations, continued management and growth of our patent portfolio, collaborations and general corporate activities, we may incur additional operating losses. While we are targeting financial self-sustainability by the end of 2025, we will continue to require significant resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We anticipate that our operating results will continue to fluctuate for the foreseeable future, and therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods.

We currently have programs focused on a number of therapeutic areas and, as of June 30, 2025, we generate worldwide product revenues from four commercialized products, AMVUTTRA, ONPATTRO, GIVLAARI and OXLUMO, primarily in the U.S. and Europe. However, our ongoing development and regulatory efforts may not be successful and we may not be able to commence sales of any other products and/or successfully market and sell our existing commercialized products or any other approved products in the future. A meaningful portion of our total revenues in recent years has been derived from collaboration revenues from collaborations with Roche, Regeneron and Novartis. In addition to revenues from the commercial sales of our approved products and potentially from sales of future products, we expect our sources of potential funding for the next several years to continue to be derived in part from existing and new strategic collaborations. Such collaborations include, or may include in the future, license and other fees, equity investments, funded research and development, milestone payments and royalties on product sales by our collaborators.

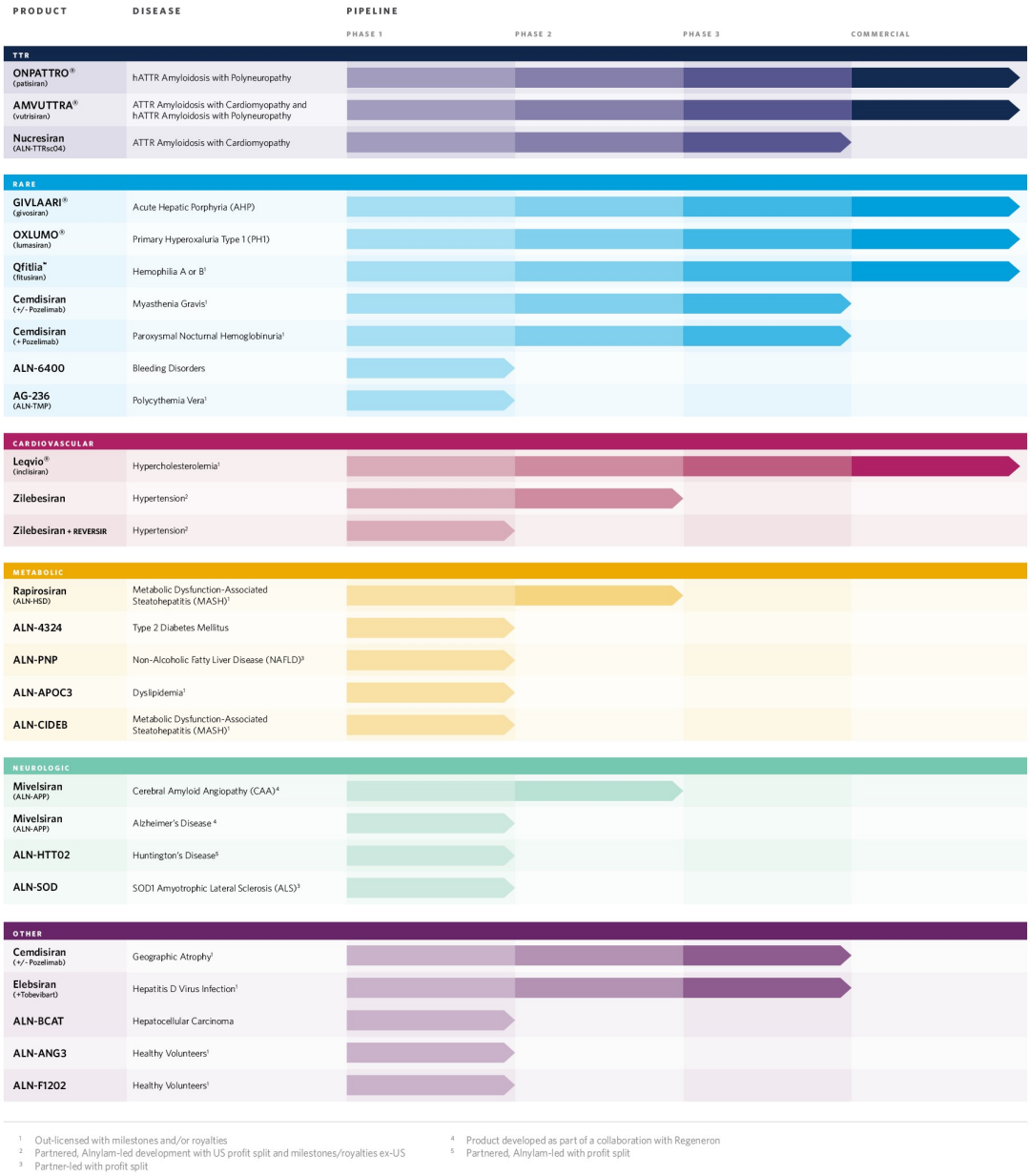
Research and Development

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

Our Product Pipeline

Our broad pipeline includes six approved products and multiple late and early-stage investigational RNAi therapeutics across a broad range of disease areas and indications. We describe our commercial and clinical-stage pipeline in more detail below. The clinical-stage therapeutics described below are in various stages of clinical development and the scientific information included about these therapeutics is preliminary and investigative. These clinical-stage therapeutics have not been approved by the FDA, European Medicines Agency, or EMA, or any other health authority and no conclusions can or should be drawn regarding the safety or efficacy of these investigational therapeutics.

The table below represents our commercial products and late- and early-stage development programs as of July 31, 2025.



During the second quarter of 2025 and recent period, we reported the following updates from our commercially approved products and our late-stage clinical programs:

Commercial

Total TTR: AMVUTTRA & ONPATTRO

- We achieved global net product revenues for AMVUTTRA and ONPATTRO for the second quarter of 2025 of $492.0 million and $52.5 million, respectively.

- Achieved approvals of AMVUTTRA for the treatment of ATTR amyloidosis with cardiomyopathy in numerous global markets.
    - Received regulatory approvals from ANVISA, the EC, the MHRA, and the PMDA.

Total Rare: GIVLAARI & OXLUMO

- We achieved global net product revenues for GIVLAARI and OXLUMO for the second quarter of 2025 of $80.8 million and $46.9 million, respectively.

Late-Stage Clinical Development

- Initiated the TRITON-CM Phase 3 trial of nucresiran in patients with ATTR amyloidosis with cardiomyopathy.
    - Announced that nucresiran received Fast Track Designation from the FDA's Division of Cardiology and Nephrology for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin mediated amyloidosis in adults to reduce mortality, cardiovascular hospitalizations, and urgent heart failure visits.

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 or obtain approval or the desired labeling for the product candidate from regulatory authorities. The success of AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO or any other 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 any potential product candidate or indication, or the period, if any, in which material net cash inflows will commence from any approved product or indication. Any failure to complete any stage of the development of any potential products in a timely manner or successfully launch, market and sell any of our commercially approved products, could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with completing our research and development programs within the planned timeline, or at all, and the potential consequences of failing to do so, are set forth in Part II, Item 1A below under the heading "Risk Factors."

Strategic Collaborations

Our business strategy is to develop and commercialize a broad pipeline of RNAi therapeutic products directed across a broad range of disease areas and indications. 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 collaborations that create significant value for ourselves and our collaborators in the advancement of RNAi therapeutics. We expect these collaborations to provide us with financial support in the form of upfront cash payments, license fees, equity investments, research and development and sales and marketing support and/or funding, milestone payments and/or royalties or profit sharing based on sales of RNAi therapeutics.

Below is a brief description of certain of our key collaborations.

Roche. In July 2023, we entered into the Roche Collaboration and License Agreement, pursuant to which we and Roche established a worldwide, strategic collaboration for the joint development of pharmaceutical products containing zilebesiran. Under the Roche Collaboration and License Agreement, we granted to Roche (i) co-exclusive rights to develop zilebesiran worldwide and commercialize zilebesiran in the U.S., (ii) exclusive rights to commercialize zilebesiran outside of the U.S., and (iii) non-exclusive rights to manufacture zilebesiran for the development and commercialization of zilebesiran outside of the U.S. Roche made an upfront payment of $310.0 million and in April 2024 we achieved the development milestone associated with the dosing of the first patient in the KARDIA-3 Phase 2 clinical trial and received a $65.0 million development milestone payment from Roche. In addition, we are eligible to receive up to an additional $2.45 billion in contingent payments based on the achievement of specified development, regulatory and sales-based milestones. We are responsible for forty percent (40%), and Roche is responsible for sixty percent (60%), of development costs incurred in the conduct of development activities that support regulatory approval of zilebesiran globally. We and Roche share equally (50/50) all costs incurred in connection with development activities that are conducted to support regulatory approval of zilebesiran in the U.S., and Roche is solely responsible for all costs incurred in the conduct of development activities that primarily support regulatory approval outside the U.S. Roche will be solely responsible for costs incurred in connection with commercialization of zilebesiran outside of the U.S. and will pay us tiered, low double digit royalties based on net sales of zilebesiran on a country-by-country basis outside of the U.S. during the royalty term. We and Roche will share equally (50/50) profits and losses (including commercialization costs) of zilebesiran in the U.S.

Regeneron. In April 2019, we entered into a global, strategic collaboration with Regeneron to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic targets expressed in the eye and CNS, in addition to a select number of targets expressed in the liver, which we refer to as the Regeneron Collaboration. The

Regeneron Collaboration is governed by a Master Agreement, referred to as the Regeneron Master Agreement, which became effective in May 2019.

Under the terms of the Regeneron Collaboration, we are working exclusively with Regeneron to discover RNAi therapeutics for eye and CNS diseases for an initial research period of up to seven years, which we refer to as the Initial Research Term. Regeneron has an option to extend the Initial Research Term for up to an additional five years by paying a research term extension fee of $300.0 million. The Regeneron Collaboration also covers a select number of RNAi therapeutic programs designed to target genes expressed in the liver. We retain broad global rights to all of our liver-directed clinical and preclinical pipeline programs that are not part of the Regeneron Collaboration.

Regeneron leads development and commercialization for all programs targeting eye diseases (subject to limited exceptions), entitling us to certain potential milestone and royalty payments pursuant to the terms of a license agreement, the form of which has been agreed upon by the parties. We and Regeneron are alternating leadership on CNS and liver programs, with the lead party retaining global development and commercial responsibility.

In August 2019, in connection with the Regeneron Master Agreement, we and Regeneron entered into (i) a co-co collaboration agreement covering the development of cemdisiran, our C5 siRNA, as a monotherapy for C5 complement-mediated diseases, or the C5 Co-Co Collaboration Agreement, and (ii) a license agreement to evaluate anti-C5 antibody-siRNA combinations for C5 complement-mediated diseases including evaluating the combination of Regeneron's pozelimab and cemdisiran, or the C5 License Agreement.

In June 2024, we entered into an amended and restated C5 License Agreement, or the Amended C5 License Agreement, which terminated the C5 Co-Co Collaboration Agreement and granted Regeneron a worldwide license to cemdisiran as a monotherapy in addition to the license to cemdisiran in combination with anti-C5 antibodies. Through the Amended C5 License Agreement, Regeneron is now solely responsible for development, manufacturing, and commercialization of cemdisiran as a monotherapy and in combination with anti-C5 antibodies. Regeneron provided us with an upfront payment of $10.0 million and we will receive certain milestone payments upon receipt of regulatory approval for cemdisiran as a monotherapy, and tiered, double-digit royalties on net sales. The Amended C5 License Agreement did not change our rights to receive low double-digit royalties and commercial milestones of up to $325.0 million on any potential product sales if cemdisiran is used as part of a combination product.

In May 2024, Regeneron notified us of its decision to opt-out of the further co-development of mivelsiran, an investigational RNAi therapeutic in development for the treatment of hereditary CAA and autosomal dominant Alzheimer's Disease under our co-co collaboration agreement with respect to mivelsiran. As a result of Regeneron's opt-out, we now have full global development and commercialization rights to mivelsiran in all indications, and we are responsible for all development and commercialization costs of mivelsiran other than Regeneron's share of the then-current Phase 1 budget. Regeneron will no longer share potential future profits from sales of mivelsiran with us, although we remain subject to certain financial obligations to Regeneron under the mivelsiran co-co collaboration agreement. We continue to advance multiple other programs with Regeneron.

Sanofi. We formed a broad strategic alliance with Sanofi in 2014. In January 2018, we and Sanofi amended our 2014 collaboration and entered into the Exclusive License Agreement, referred to as the Exclusive TTR License, under which we were granted exclusive rights to pursue the further global development and commercialization of all TTR products, including AMVUTTRA, ONPATTRO and any back-up products, and the ALN-AT3 Global License Terms, referred to as the AT3 License Terms, under which Sanofi has the exclusive right to pursue the further global development and commercialization of Qfitlia and any back-up products. Under the Exclusive TTR License, Sanofi is eligible to receive (i) royalties up to 25% increasing over time, based on annual net sales of ONPATTRO in territories excluding the U.S., Canada and Western Europe, provided royalties on annual net sales of ONPATTRO in Japan were set at 25% beginning at the effective date of the Exclusive TTR License and (ii) tiered royalties on global annual net sales of AMVUTTRA across all indications in the following tiers: 15% of global annual net sales of $0 to $150.0 million; 17.5% of global annual net sales greater than $150.0 million to $300.0 million; 20% of global annual net sales greater than $300.0 million to $500.0 million; 25% of global annual net sales greater than $500.0 million to $1.50 billion; and 30% of global annual net sales in excess of $1.50 billion. In April 2019, we and Sanofi amended and restated the AT3 License Terms to modify certain of the business terms. The material collaboration terms for Qfitlia were unchanged. Under the amended and restated AT3 License Terms, we are eligible to receive tiered royalties on global annual net sales of Qfitlia by Sanofi, its affiliates and its sublicensees. The royalty tiers and amounts that we are eligible to receive on global annual net sales of Qfitlia are the same as the royalty tiers and amounts that we owe to Sanofi on global annual net sales of AMVUTTRA.

Novartis. In February 2013, we entered into an exclusive, worldwide license with MDCO (acquired by Novartis AG in January 2020) pursuant to which MDCO was granted the right to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9 for the treatment of hypercholesterolemia and other human diseases, including Leqvio.

Critical Accounting Policies and Estimates

Our critical accounting policies are described in the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of our Annual Report on Form 10-K for the year ended December 31, 2024, which we filed with the SEC on February 13, 2025. There have been no significant changes to our critical accounting policies since the beginning of this fiscal year.

Results of Operations

The following data summarizes the results of our operations:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Total revenues	$ 773,689	$ 659,825	$ 113,864	17 %	$ 1,367,878	$ 1,154,158	$ 213,720	19 %
Total operating costs and expenses	$ 789,888	$ 611,211	$ 178,677	29 %	$ 1,366,000	$ 1,148,979	$ 217,021	19 %
(Loss) income from operations	$ (16,199)	$ 48,614	$ (64,813)	(133)%	$ 1,878	$ 5,179	$ (3,301)	(64)%
Total other expense, net	$ (19,159)	$ (59,781)	$ 40,622	(68)%	$ (78,832)	$ (79,933)	$ 1,101	(1)%
Provision for income taxes	$ (30,919)	$ (5,722)	$ (25,197)	440 %	$ (46,802)	$ (8,070)	$ (38,732)	480 %
Net loss	$ (66,277)	$ (16,889)	$ (49,388)	292 %	$ (123,756)	$ (82,824)	$ (40,932)	49 %

Discussion of Results of Operations

Revenues

Total revenues consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Net product revenues	$ 672,212	$ 410,088	$ 262,124	64 %	$ 1,140,750	$ 775,251	$ 365,499	47 %
Net revenues from collaborations	61,496	227,338	(165,842)	(73)%	160,681	345,886	(185,205)	(54)%
Royalty revenue	39,981	22,399	17,582	78 %	66,447	33,021	33,426	101 %
Total	$ 773,689	$ 659,825	$ 113,864	17 %	$ 1,367,878	$ 1,154,158	$ 213,720	19 %

Net Product Revenues

Net product revenues, classified based on the geographic region in which the product is sold and by franchise ("TTR", which includes AMVUTTRA and ONPATTRO, and "Rare", which includes GIVLAARI and OXLUMO), consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	2025	2024	$ Change	% Change	2025	2024	$ Change	% Change
AMVUTTRA								
United States	$ 361,346	$ 148,463	$ 212,883	143 %	$ 559,310	$ 278,701	$ 280,609	101 %
Europe	92,868	56,760	36,108	64 %	172,956	100,493	72,463	72 %
Rest of World	37,739	24,886	12,853	52 %	69,679	46,156	23,523	51 %
Total	491,953	230,109	261,844	114 %	801,945	425,350	376,595	89 %
ONPATTRO								
United States	22,053	22,112	(59)	— %	37,625	38,651	(1,026)	(3)%
Europe	21,246	37,074	(15,828)	(43)%	47,787	81,764	(33,977)	(42)%
Rest of World	9,239	18,058	(8,819)	(49)%	16,615	26,046	(9,431)	(36)%
Total	52,538	77,244	(24,706)	(32)%	102,027	146,461	(44,434)	(30)%
Total TTR	544,491	307,353	237,138	77 %	903,972	571,811	332,161	58 %
GIVLAARI								
United States	55,151	41,225	13,926	34 %	98,945	79,956	18,989	24 %
Europe	20,966	16,314	4,652	29 %	39,510	31,629	7,881	25 %
Rest of World	4,732	4,588	144	3 %	9,362	8,598	764	9 %
Total	80,849	62,127	18,722	30 %	147,817	120,183	27,634	23 %
OXLUMO								
United States	16,019	15,744	275	2 %	30,128	29,076	1,052	4 %
Europe	21,929	20,503	1,426	7 %	42,913	41,930	983	2 %
Rest of World	8,924	4,361	4,563	105 %	15,920	12,251	3,669	30 %
Total	46,872	40,608	6,264	15 %	88,961	83,257	5,704	7 %
Total Rare	127,721	102,735	24,986	24 %	236,778	203,440	33,338	16 %
Total net product revenues	$ 672,212	$ 410,088	$ 262,124	64 %	$ 1,140,750	$ 775,251	$ 365,499	47 %

Net product revenues increased during the three and six months ended June 30, 2025, as compared to the same period in 2024, primarily due to growth from AMVUTTRA driven by increased patient demand, mainly in patients with ATTR-CM in the U.S., which was partially offset by a decrease in ONPATTRO due to patient switches to AMVUTTRA, and due to growth from an increased number of patients on GIVLAARI and OXLUMO.

Net Revenues from Collaborations and Royalty Revenue

Net revenues from collaborations and royalty revenue consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Roche	$ 18,267	$ 16,506	$ 1,761	11 %	$ 35,323	$ 91,186	$ (55,863)	(61)%
Regeneron Pharmaceuticals	32,542	207,429	(174,887)	(84)%	83,581	234,193	(150,612)	(64)%
Novartis AG	—	2,304	(2,304)	(100)%	—	16,820	(16,820)	(100)%
Other	10,687	1,099	9,588	*	41,777	3,687	38,090	*
Total net revenues from collaborations	$ 61,496	$ 227,338	$ (165,842)	(73)%	$ 160,681	$ 345,886	$ (185,205)	(54)%
Royalty revenue	$ 39,981	$ 22,399	$ 17,582	78 %	$ 66,447	$ 33,021	$ 33,426	101 %

* Indicates the percentage change period over period is greater than 500%

Net revenues from collaborations decreased during the three months ended June 30, 2025, as compared to the same period in 2024, primarily driven by recognition of $185.0 million of revenue under our collaboration with Regeneron Pharmaceuticals in the three months ended June 30, 2024, as we modified the collaboration in June 2024 and provided Regeneron with an exclusive license to develop, manufacture and commercialize cemdisiran as a monotherapy. Net revenues from collaborations decreased during the six months ended June 30, 2025, as compared to the same period in 2024, primarily driven by:

- recognition of $185.0 million of revenue under our Regeneron Collaboration in the six months ended June 30, 2024; and
- recognition of $65.0 million of milestone revenue under our Roche Collaboration in March 2024 associated with the dosing of the first patient in the zilebesiran KARDIA-3 Phase 2 clinical trial.

Partially offset by:

- recognition of a $30.0 million payment in connection with the amendment to our agreement with Vir Biotechnology, Inc. in March 2025.

Royalty revenue increased during the three and six months ended June 30, 2025, as compared to the same period in 2024, due to increased volume and rate of royalties earned from global net sales of Leqvio by our collaborator, Novartis.

Recognition of our combined net revenues from collaborations and royalty revenue is dependent on a variety of factors, including the level of work reimbursed by collaborators, achievement of milestones under our collaboration agreements, and royalties associated with sales of Leqvio and Qfitlia. We expect net revenues from collaborations will increase in 2025, as compared to 2024, primarily driven by higher anticipated revenues under our Roche Collaboration and License Agreement. We expect our royalty revenue will increase in 2025, as compared to 2024, due to the continued growth of royalties earned from global net sales of Leqvio by our collaborator, Novartis, and royalties earned from global net sales of Qfitlia by our collaborator, Sanofi.

Operating Costs and Expenses

Operating costs and expenses consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Cost of goods sold	$ 142,029	$ 67,271	$ 74,758	111 %	$ 212,212	$ 121,884	$ 90,328	74 %
Cost of goods sold as a percentage of net product revenues	*21.1 %*	*16.4 %*			*18.6 %*	*15.7 %*		
Cost of collaborations and royalties	924	1,401	(477)	(34)%	1,782	12,764	(10,982)	(86)%
Research and development	323,621	294,142	29,479	10 %	588,743	555,137	33,606	6 %
Selling, general and administrative	323,314	248,397	74,917	30 %	563,263	459,194	104,069	23 %
Total	$ 789,888	$ 611,211	$ 178,677	29 %	$ 1,366,000	$ 1,148,979	$ 217,021	19 %

Cost of goods sold

Cost of goods sold, including cost of goods sold as a percentage of net product revenues, increased during the three and six months ended June 30, 2025, as compared to the same periods in 2024, primarily as a result of increased sales of AMVUTTRA and an associated increase in royalties payable on net sales of AMVUTTRA.

We expect our cost of goods sold, including cost of goods sold as a percentage of net product revenues, will increase during 2025, as compared to 2024, primarily as a result of an expected increase in sales of AMVUTTRA and an associated increase in royalties payable on net sales of AMVUTTRA.

Cost of collaborations and royalties

Cost of collaborations and royalties decreased during the three and six months ended June 30, 2025, as compared to the same periods in 2024, primarily due to decreased demand for GalNAc material supplied to our collaborators in support of certain product manufacturing as our collaborators transition to producing the material independently.

We expect cost of collaborations and royalties will continue to decrease during 2025, as compared to 2024, as a result of our collaborators continuing to transition to produce GalNAc material independently.

Research and development

Research and development expenses consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Clinical research and outside services	$ 140,692	$ 119,496	$ 21,196	18 %	$ 268,035	$ 245,006	$ 23,029	9 %
Compensation and related	93,898	86,762	7,136	8 %	169,287	163,971	5,316	3 %
Occupancy and all other costs[1]	39,479	39,769	(290)	(1)%	78,071	78,830	(759)	(1)%
Stock-based compensation	49,552	48,115	1,437	3 %	73,350	67,330	6,020	9 %
Total	$ 323,621	$ 294,142	$ 29,479	10 %	$ 588,743	$ 555,137	$ 33,606	6 %

[1] Occupancy and all other costs includes facilities, information technology, depreciation and certain departmental expenses.

Research and development expenses for the three and six months ended June 30, 2025 increased as compared to the same periods in 2024, which was primarily due to:

- increased clinical trial expenses associated with startup activities for zilebesiran in the Phase 3 cardiovascular outcomes trial and nucresiran in the TRITON-CM Phase 3 trial in patients with ATTR-CM.

Partially offset by:

- decreased expenses within other clinical programs, in particular for zilebesiran in the KARDIA-2 Phase 2 clinical trial due to the wind-down of clinical activities.

Selling, general and administrative

Selling, general and administrative expenses consist of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Compensation and related	$ 129,105	$ 96,538	$ 32,567	34 %	$ 227,628	$ 187,747	$ 39,881	21 %
Consulting and professional services	82,637	66,731	15,906	24 %	147,324	123,490	23,834	19 %
Occupancy and all other costs[1]	49,444	43,955	5,489	12 %	93,269	80,652	12,617	16 %
Stock-based compensation	62,128	41,173	20,955	51 %	95,042	67,305	27,737	41 %
Total	$ 323,314	$ 248,397	$ 74,917	30 %	$ 563,263	$ 459,194	$ 104,069	23 %

[1] Occupancy and all other costs includes facilities, information technology, depreciation and certain departmental expenses.

Selling, general and administrative expenses for the three and six months ended June 30, 2025 increased as compared to the same periods in 2024, primarily due to higher employee compensation costs, including stock-based compensation, and increased marketing investment associated with AMVUTTRA launch in ATTR-CM.

We expect that research and development expenses combined with selling, general and administrative expenses will continue to increase during 2025, as compared to 2024, as we continue to build out our global commercial and compliance

infrastructure, launch our current commercial products into new markets, prepare for future commercial product launches, including the continued launch of AMVUTTRA for the treatment of ATTR amyloidosis with cardiomyopathy, advance our product candidates, including collaborated programs, into later-stage development, advance and develop our platform and preclinical pipeline, 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 based on our determination regarding the probability of vesting for performance-based awards.

Other (Expense) Income

Other (expense) income consists of the following:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Interest expense	$ (40,246)	$ (33,258)	$ (6,988)	21 %	$ (78,892)	$ (68,511)	$ (10,381)	15 %
Interest income	27,486	29,182	(1,696)	(6)%	56,159	58,827	(2,668)	(5)%
Other expense, net								
Realized and unrealized losses on marketable equity securities	(1,350)	(1,367)	17	(1)%	(2,306)	(1,289)	(1,017)	79 %
Change in fair value of development derivative liability	(15,259)	(55,642)	40,383	(73)%	(74,150)	(64,228)	(9,922)	15 %
Other	10,210	1,304	8,906	*	20,357	(4,732)	25,089	**
Total	$ (19,159)	$ (59,781)	$ 40,622	(68)%	$ (78,832)	$ (79,933)	$ 1,101	(1)%

* Indicates the percentage change period over period is greater than 500%

** Not meaningful

Total other expense decreased during the three months ended June 30, 2025, as compared to the same period in 2024, primarily due to decreased loss associated with the change in fair value of the development derivative liability as a result of valuation updates during the three months ended June 30, 2024 driven by the regulatory approval of AMVUTTRA for the treatment of ATTR amyloidosis with cardiomyopathy. Total other expense decreased during the six months ended June 30, 2025, as compared to the same period in 2024, primarily due to increased net realized and unrealized foreign currency transaction gains, which was partially offset by increased interest expense associated with the liability related to the sale of future royalties and increased loss associated with the change in fair value of the development derivative liability.

Provision for Income Taxes

Provision for income taxes was as follows:

	Three Months Ended June 30,				Six Months Ended June 30,			
(In thousands, except percentages)	**2025**	**2024**	**$ Change**	**% Change**	**2025**	**2024**	**$ Change**	**% Change**
Provision for income taxes	$ (30,919)	$ (5,722)	$ (25,197)	440 %	$ (46,802)	$ (8,070)	$ (38,732)	480 %

Our provision for income taxes relates to foreign and state income taxes. The provision for income taxes increased during the three and six months ended June 30, 2025, as compared to the same periods in 2024, which primarily relates to foreign income taxes due to income generated in Switzerland, as well as state income taxes in the U.S. We expect to utilize net operating losses in Switzerland to offset taxable income and current taxes resulting in a deferred income tax provision. We continue to maintain a full valuation allowance against our net deferred tax assets in the U.S. and certain deferred tax assets in Switzerland.

We calculate our provision for income taxes during interim reporting periods by applying an estimate of the annual effective tax rate for the full year to pretax income or loss excluding unusual or infrequent occurring discrete items. As a result, we may experience significant fluctuations in the effective book tax rate (that is, our tax expense divided by pre-tax book income) from period to period.

Liquidity and Capital Resources

The following table summarizes our cash flow activities:

(In thousands)	Six Months Ended June 30, 2025	2024
Net cash provided by (used in):		
Operating activities	$ 35,416	$ 42,643
Investing activities	$ (27,612)	$ (33,680)
Financing activities	$ 97,841	$ 160,407

Operating activities

Net cash provided by operating activities decreased during the six months ended June 30, 2025, compared to the same period in 2024, primarily due to increased employee compensation and decreased cash received from our collaborators, partially offset by stronger cash receipts from increased product sales.

Investing activities

Net cash used in investing activities decreased during the six months ended June 30, 2025, compared to the same period in 2024, primarily due to the timing of sales, maturities, and purchases of our marketable securities.

Financing activities

Net cash provided by financing activities decreased during the six months ended June 30, 2025, compared to the same period in 2024, primarily due to lower net proceeds from the issuance of common stock in connection with stock option exercises, as well as higher net payments to BXLS V Bodyguard – PCP L.P. and BXLS Family Investment Partnership V – ESC L.P. for the development derivative liability.

Additional Capital Requirements

We currently have programs focused in many therapeutic areas and, as of June 30, 2025, have six marketed products, including two products commercialized by our collaborators. However, our ongoing development efforts may not be successful and we may not be able to commence sales of any other products in the future. In addition, we may incur additional operating losses as a result of planned expenditures for research and development activities relating to our research platform, our drug development programs, including clinical trial and manufacturing costs, the continued build-out of late-stage clinical, manufacturing, commercial and compliance capabilities, including global operations, continued management and growth of our intellectual property including our patent portfolio, collaborations and general corporate activities.

Our expected working and other capital requirements are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 in "Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations." As of June 30, 2025, other than the changes disclosed in the "Notes to Condensed Consolidated Financial Statements" and "Liquidity and Capital Resources" section in this Quarterly Report on Form 10-Q, there have been no other material changes to our expected working and other capital requirements as described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of June 30, 2025, will be sufficient to satisfy our near-term capital and operating needs for at least the next 12 months from the filing date of this Quarterly Report on Form 10-Q. However, due to numerous factors described in more detail under the caption Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q, we may require significant additional funds earlier than we currently expect in order to continue to commercialize our approved products, and to develop, conduct clinical trials for, manufacture and, if approved, commercialize additional product candidates.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Financial market risks related to interest rates are described in our Annual Report on Form 10-K for the year ended December 31, 2024. As of June 30, 2025, there have been no significant changes to the financial market risks described as of December 31, 2024. We do not currently anticipate any other near-term changes in the nature of our financial market risk exposures or in management's objectives and strategies with respect to managing such exposures.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Executive Vice President, Chief Financial Officer (principal financial officer), evaluated the effectiveness of our disclosure controls and

procedures as of June 30, 2025. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934, as amended, or 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 our 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 June 30, 2025, our Chief Executive Officer and Executive Vice President, Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control

There were no changes in our internal control over financial reporting during the quarter ended June 30, 2025 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 12, Commitments and Contingencies, 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

Investing in our securities involves a high degree of risk. You should carefully consider the following risk factors in addition to the other information set forth or incorporated by reference in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and the related notes and "Management's Discussion of Financial Condition and Results of Operations," in evaluating our company and our business. If any of the following risks, or any additional risk not currently known to us or that we currently deem immaterial, actually occurs, our business, prospects, operating results or financial condition could be materially and adversely affected. In these circumstances, the trading price of our common stock could decline, and you may lose all or part of your investment.

SUMMARY OF MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties, discussed in more detail in the following section. These risks include, among others, the following key risks:

Business Related Risks – Risks Related to Our Financial Results

- The marketing and sale of our approved products, including AMVUTTRA for ATTR amyloidosis with cardiomyopathy, or any future products for which we or our collaborators receive regulatory approval may be unsuccessful or less successful than anticipated.
- We have a history of losses and may not become and remain profitable.
- We will require substantial funds to continue our research, development and commercialization activities.

Risks Related to Our Dependence on Third Parties

- We may be unable to maintain existing or enter into new collaborations with other companies that can provide business and scientific capabilities and funds for the development and commercialization of certain of our product candidates.
- If any collaborator materially amends, terminates or fails to perform its obligations under agreements with us, the development and commercialization of certain of our product candidates could be delayed or terminated.
- We expect to incur significant costs as we continue to grow our manufacturing capabilities and resources and develop manufacturing expertise; in the meantime, we rely, and expect to continue to rely, on third parties to manufacture our products.
- We rely on third parties to conduct our clinical trials, and if such third parties fail to fulfill their obligations, our development plans may be adversely affected.

Risks Related to Managing Our Operations

- If we are unable to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors, our ability to implement our business plan may be adversely affected.
- We may have difficulty expanding our operations successfully as we continue our evolution from a U.S.- and Europe-based company primarily involved in discovery, preclinical testing and clinical development into a global company that develops and commercializes multiple drugs in multiple geographies.

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

- Any product candidate we or our collaborators develop may fail in development or experience significant delays.
- If any of our current or future products or product candidates causes undesirable side effects or has other unexpected adverse properties, such side effects or properties could delay or prevent regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.
- We or our collaborators may be unable to obtain regulatory approval for our or our collaborated product candidates, and, as a result, we or our collaborators may be unable to commercialize such product candidates.

- Even if we or our collaborators obtain regulatory approvals, our products will be subject to ongoing regulatory oversight.
- We may incur significant liability if enforcement authorities allege or determine that we are engaging in commercial activities with respect to our unapproved product candidates or promoting our commercially approved products in a way that violates applicable regulations.
- Even if we or our collaborators receive regulatory approval to market our product candidates, the market may not be receptive to such product candidates upon their commercial introduction.
- We are a multi-product commercial company and expect to continue to invest significant financial and management resources to continue to build our marketing, sales, market access and distribution capabilities and further establish our global infrastructure, and our efforts may not be successful.
- Any products we currently market or may develop in the future may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives.

Risks Related to Patents, Licenses and Trade Secrets

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

Risks Related to Competition

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

Risks Related to Our Common Stock

- Our stock price has been and may in the future be volatile, and an investment in our common stock could suffer a decline in value.

Risks Related to Our Convertible Notes

- We may not have sufficient cash flow from our business to pay our indebtedness.
- We may not have the ability to raise the funds necessary to settle for cash conversions of our 1% Convertible Senior Notes due 2027, or the Notes, or to repurchase the Notes for cash upon a fundamental change.
- The conditional conversion feature of the Notes, if triggered, may adversely affect our liquidity.

Risks Related to Our Business

Risks Related to Our Financial Results

The marketing and sale of our approved products, including AMVUTTRA for ATTR amyloidosis with cardiomyopathy, or any future products for which we or our collaborators receive regulatory approval may be unsuccessful or less successful than anticipated.

Although we have commercially launched four products and have two additional products being commercialized by our collaborators, we cannot predict whether we will successfully market and sell our approved products, including AMVUTTRA,

which was launched in the U.S. for the treatment of ATTR amyloidosis with cardiomyopathy following FDA approval in March 2025.

To execute our business plan of building a profitable, top-tier biotech company by the end of 2025 and achieving the metrics associated with our *Alnylam P^{5}x25* strategy, in addition to successfully launching, marketing and selling our approved products, we will need to successfully:

- execute product development activities and continue to leverage new technologies related to both RNAi and to the delivery of siRNAs to the relevant tissues and cells, including the liver, CNS, eye, lung, adipose and muscle;
- build and maintain a strong intellectual property portfolio;
- gain regulatory acceptance for the development and commercialization of our product candidates and successfully market our approved products, as well as any other products we commercialize;
- attract and retain customers for our products;
- enter into and maintain successful collaborations; and
- manage our spending as our costs and expenses increase due to, among other things, an increase in the number and size of our clinical trials, and the expansion of our commercialization activities.

If we are unsuccessful in accomplishing the objectives set forth above, we may not be able to develop product candidates, successfully launch and commercialize our approved products or any future products, raise capital, if needed, repay our indebtedness, achieve profitability or continue our operations.

We have a history of losses and may not become and remain profitable.

We have experienced significant operating losses since our inception. As of June 30, 2025, we had an accumulated deficit of $7.41 billion. Although to date we have launched four products in the U.S., EU and various other countries globally, and expect to launch our commercially approved products, including AMVUTTRA in patients with ATTR amyloidosis with cardiomyopathy, in additional countries during the remainder of 2025 and in subsequent years, and have two marketed products being commercialized by our collaborators, we may not achieve or sustain profitability or positive cash flow from operations. For the three and six months ended June 30, 2025, we recognized $672.2 million and $1.14 billion in net product revenues from sales of AMVUTTRA, ONPATTRO, GIVLAARI and OXLUMO. We may continue to incur annual operating losses and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics, and aim to achieve sustainable operating profitability by the end of 2025. While we believe our current cash, cash equivalents and marketable debt securities, as well as the revenue we expect to generate from product sales and under our existing collaborations, including royalties on sales of Leqvio and Qfitlia, should enable us to achieve sustainable operating profitability by the end of 2025, we will depend on our ability to generate product, collaboration and royalty revenues to achieve this goal. In addition to revenues derived from sales of our current and future, if any, commercially approved products, we anticipate that a portion of any revenues we generate over the next several years will continue to be from collaborations with pharmaceutical and biotechnology companies, including Roche, Regeneron, Sanofi and Novartis, and we cannot be certain that we will be able to maintain our existing collaborations, secure and maintain new collaborations, meet our obligations under collaboration agreements, or achieve any milestones that we may be required to meet or achieve to receive payments under our existing or new collaborations. Moreover, we cannot be certain that our collaborators, including Roche, Regeneron, Novartis and Sanofi, will continue to successfully execute their obligations under our collaboration agreements and generate collaboration and royalty revenues for us.

To sustain profitability, we will need to succeed in discovering, developing and commercializing novel product candidates with significant market potential. This will require us to build upon the success we have had in a range of challenging activities, including continued platform innovation, preclinical testing and clinical trial stages of development, obtaining regulatory approval and reimbursement for our novel product candidates and manufacturing, marketing and selling our approved products. We may not be able to sustain or increase profitability on a quarterly or annual basis. If we cannot 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 and commercialize additional product candidates or continue our operations.

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

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

Our future capital requirements and the period for which our existing resources will support our operations may vary from what we currently expect. We have based our expectations on a number of factors, many of which are difficult to predict or are outside of our control, including:

- progress in our research and development programs, including programs across a broad range of disease areas and indications, as well as what may be required by regulatory authorities to advance these programs;
- the timing, receipt and amount of milestone, royalty, research and development funding and other payments, if any, from present and future collaborators, if any, including milestone, royalty and research and development funding payments from Roche with respect to the development and commercialization of zilebesiran, as well as royalty payments from Novartis and Sanofi related to the commercialization of Leqvio and Qfitlia, respectively;
- our ability to establish and maintain existing and additional collaborations and/or new business initiatives;
- the potential for improved product profiles to emerge from our new technologies and our ability to successfully advance our delivery efforts in extrahepatic tissues;
- the resources, time and costs required to successfully initiate and complete our preclinical studies 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 our approved products for commercial sale;
- the impact of any future pandemics or public health emergencies or the ongoing conflicts in the Middle East and Ukraine on the initiation or completion of preclinical studies or clinical trials and the supply of our products or product candidates;
- the resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;
- the costs associated with legal activities, including litigation and government investigations, arising in the course of our business activities and our ability to prevail or reach a satisfactory result in any such legal disputes and investigations;
- the timing, receipt and amount of sales milestones and royalties, if any, from our approved products commercialized by our collaborators and our product candidates commercialized by our collaborators, if and when approved; and
- the outcome of the global regulatory review process and commercial success of our products, including AMVUTTRA for the treatment of ATTR amyloidosis with cardiomyopathy, and products for which we are entitled to receive royalties, including Leqvio and Qfitlia.

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

The terms of any financing we may be required to pursue in the future may adversely affect the holdings or the rights of our stockholders. If we raise additional funds by issuing equity securities, 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 our existing stockholders.

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

Although we sold a portion of the royalty stream from the global sales of Leqvio by Novartis, we are entitled to retain the remaining portions of the future royalties on Leqvio, and any negative developments related to Leqvio could have a material adverse effect on our receipt of those future royalties.

In April 2020, we sold to BX Bodyguard Royalties L.P. (an affiliate of The Blackstone Group Inc.), or Blackstone Royalties, 50% of the royalties payable to us with respect to net sales by Novartis, its affiliates or sublicensees of Leqvio under the MDCO License Agreement. If Blackstone Royalties does not receive royalty payments in respect of global sales of Leqvio equaling at least $1.00 billion by December 31, 2029, Blackstone Royalties' interest in Leqvio royalties will increase to 55% (and our interest will decrease to 45%) effective January 1, 2030. As a result, any factor that has an adverse impact on sales of

Leqvio could affect our ability to meet the $1.00 billion repayment threshold in this timeframe, which in turn would have a negative impact on the percentage of the Leqvio royalty stream that we are entitled to retain.

Factors that could have an adverse impact on Leqvio sales include:

- competitors may develop new therapies or alternative formulations of products for HeFH and ASCVD;
- lack of acceptance of Leqvio by patients, the medical community or third party payors;
- any negative developments relating to Leqvio, such as safety, efficacy, or reimbursement issues;
- any disputes concerning patents or proprietary rights, or under license and collaboration agreements;
- foreign currency exchange rate fluctuations; and
- adverse regulatory or legislative developments that limit or prohibit the sale of Leqvio, such as restrictions on the use of Leqvio or safety-related label changes, including enhanced risk management programs.

If the revenues generated by sales of Leqvio are lower than expected, we may not receive royalties in the amount we are currently anticipating, and our business, prospects, operating results and financial condition could be materially and adversely affected.

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

Our condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the U.S., or GAAP. The preparation of these condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

Further, from time to time we issue financial guidance relating to our expectations regarding our combined product sales, collaboration and royalty revenues, and GAAP and non-GAAP combined research and development and selling, general and administrative expenses, which guidance is based on estimates and the judgment of our management. If, for any reason, our product sales, revenues and/or expenses differ materially from our guidance, we may have to adjust our publicly announced financial guidance. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline.

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

As of June 30, 2025, we had $2.86 billion in cash, cash equivalents and marketable securities. We historically have invested these amounts in money market funds, certificates of deposit, commercial paper, corporate notes, U.S. government-sponsored enterprise securities and U.S. treasury securities through highly rated financial institutions. 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 financial condition. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would decline. The market risks associated with our investment portfolio may have an adverse effect on our operating results, liquidity and financial condition.

Volatility in foreign currency exchange rates could have a material adverse effect on our operating results.

Our revenue from outside of the U.S. is expected to increase as our products, whether commercialized by us or our collaborators, gain marketing approval in such jurisdictions. We are exposed to foreign exchange risk as certain of our expenses and liabilities are required to be paid in currencies other than the U.S. dollar. Our primary foreign currency exposure relates to movements in the Japanese yen, Euro and British pound. If the U.S. dollar weakens against a specific foreign currency, our revenues will increase, having a positive impact on net income, but our overall expenses will increase, having a negative impact. Conversely, if the U.S. dollar strengthens against a specific foreign currency, our revenues will decrease, having a negative impact on net income, but our overall expenses will decrease, having a positive impact. The exchange rates between the U.S. dollar and the other foreign currencies to which we are exposed have fluctuated significantly in response to international political conditions, general economic conditions and other factors beyond our control. In addition, the current presidential administration has enacted or proposed to enact certain economic and trade policies, including with respect to tariffs, that could impact the global economy and further increase the volatility of foreign exchange rates. Any future volatility in foreign exchange rates is likely to impact our operating results and financial condition.

Changes in tax laws could adversely affect our business, prospects, operating results and financial condition.

Our business is subject to numerous international, federal, state, and other governmental laws, rules, and regulations that may adversely affect our operating results, including taxation and tax policy changes, tax rate changes, new tax laws, or revised tax law interpretations, which individually or in combination may cause our effective tax rate to increase. In the U.S., the rules dealing with federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, prospects, operating results and financial condition.

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

We may incur additional tax liabilities related to our operations.

We are subject to income tax in the U.S. and the foreign jurisdictions in which we operate. Significant judgment is required in determining our worldwide tax liabilities, and our effective tax rate is derived from the applicable statutory tax rates and relative earnings in each taxing jurisdiction. We record liabilities for uncertain tax positions that involve significant management judgment as to the application of law. Domestic or foreign taxing authorities may disagree with our interpretation of tax law as applied to our and our subsidiaries' operations or with the positions we may take with respect to particular tax issues on our tax returns. Consequently, tax assessments or judgments in excess of accrued amounts that we have estimated in preparing our financial statements may materially and adversely affect our reported effective tax rate or our cash flows. Further, other factors may adversely affect our effective tax rate, including changes in the mix of our profitability from country to country, tax effects of stock-based compensation (which depend in part on the price of our stock and, therefore, are beyond our control), and changes in tax laws or regulations. For example, the OECD Global Anti-Base Erosion Model have influenced tax laws in countries in which we operate, including the implementation of minimum taxes. Changes to these or other laws and regulations or their interpretations could materially and adversely impact our effective tax rate or cash flows.

Risks Related to Our Dependence on Third Parties

If we are unable to maintain our existing collaborations, or enter into new collaborations with companies that can provide business and scientific capabilities and funds for the development and commercialization of our product candidates, it may have a negative impact on our business, prospects, operating results and financial condition.

We do not currently have adequate capacity or capabilities to advance all opportunities arising from our growing pipeline of RNAi therapeutics. Accordingly, we have entered into collaborations with third party collaborators we believe can provide such capacity and capabilities in certain territories and/or for certain product candidates, and we intend to enter into additional such collaborations in the future. Specifically, we currently have active collaborations with, among other companies, Roche, Regeneron, Sanofi and Novartis covering various products and product candidates in our pipeline.

In such collaborations, we expect our current, and may expect any future, collaborators to provide substantial capabilities in clinical development, regulatory affairs, and/or marketing, sales and distribution. Under certain of our collaborations, we also expect our collaborators to develop, market and/or sell certain of our product candidates in certain territories or globally, and we have limited or no control over the development, sales, marketing and distribution activities of these collaborators. Our future revenues may depend on the success of the efforts of these third parties. For example, we will rely entirely on (i) Regeneron for the development and commercialization of all programs targeting eye diseases (subject to limited exceptions), and potentially other CNS and liver programs; (ii) Novartis for the development and commercialization of Leqvio worldwide; (iii) Sanofi for the commercialization of Qfitlia worldwide; and (iv) Roche for the commercialization of zilebesiran outside of the U.S. In the case of each collaboration referenced in clauses (i)-(iv) above, we are entitled to royalties, and in some instances commercial milestone payments, on the sales of the applicable product. If our collaborators are not successful in their development and/or commercialization efforts, our future revenues from the relevant product or product candidate may be adversely affected. For example, in December 2020 Novartis received a complete response letter, or CRL, from the FDA stating that the FDA could not approve the NDA by the Prescription Drug User Fee Act, or PDUFA, action date due to unresolved inspection-related conditions at a third party manufacturing facility. While Leqvio was ultimately approved by the FDA in December 2021, the resolution of the CRL resulted in a delay in the payment of an approval milestone and potential U.S. royalties. As discussed above, under our agreement with Blackstone Royalties, if the revenues generated by the royalties received by Blackstone Royalties from us with respect to Leqvio sales do not reach a certain level by the end of 2029, Blackstone Royalties will be entitled to a higher royalty percentage beginning in 2030, which would have a negative impact on the percentage of the Leqvio royalty stream that we are entitled to retain.

We may not be successful in entering into future collaborations on terms favorable to us due to various factors, including our ability to demonstrate improved product profiles from our new technologies, our ability to successfully demonstrate proof-of-concept for our technology in humans in certain tissues or disease areas, our ability to demonstrate the safety and efficacy of our specific product candidates, our ability to manufacture or have third parties manufacture RNAi therapeutics, the strength of our intellectual property portfolio and/or concerns around challenges or potential challenges to our intellectual property portfolio. Even when we succeed in securing such new collaborations, we may not be able to maintain them, or they may not be successful, 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, sales of an approved drug are lower than we expected, or our collaborator changes its strategic focus or otherwise determines not to move forward with a product or product candidate or to continue its collaboration with us.

Furthermore, any delay in entering into new collaboration agreements would have the potential to prevent or delay the development and commercialization of certain product candidates, or reduce the competitiveness such product candidates if they ultimately reach the market, which in turn could adversely affect our business, prospects, operating results and financial condition.

For certain product candidates, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaborations with Roche, Regeneron, Sanofi and Novartis. We may not, however, be able to enter into additional collaborations for certain other programs, and the terms of any collaboration agreements 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 or other resources to develop these product candidates or other product candidates on our own, or to bring such product candidates to market. In these circumstances, we will not be able to generate revenues from these product candidates, and this will substantially harm our business, prospects, operating results and financial condition.

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

Our dependence on collaborators for capabilities and funding means that our business could be adversely affected if any collaborator materially amends or terminates its collaboration agreement with us, in whole or in part, 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 our 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, under certain circumstances, our collaborators may have additional termination rights for convenience with respect to the collaboration as a whole or a particular program under the collaboration. For example, in August 2024, we announced that Regeneron had opted out of further co-development and co-commercialization of mivelsiran for portfolio prioritization reasons. As a result of Regeneron's opt-out, we have full development and commercialization rights to mivelsiran in all indications but we are responsible for funding further development and commercialization of mivelsiran, including the ongoing Phase 2 development program, without funding from Regeneron. Regeneron will be eligible to receive low double-digit royalties on sales of mivelsiran, if approved. It is possible that Regeneron will choose not to exercise its option to extend the Initial Research Term under our collaboration. In these circumstances, we would not receive the research term extension fee, and we and Regeneron would not nominate additional targets to be added to the collaboration.

Our collaboration agreement with Roche requires that Roche pay us a milestone payment at the initiation of a Phase 3 clinical trial of zilebesiran, which we refer to as the Phase 3 initiation milestone. In the event that Roche determines to terminate our collaboration prior to the initiation of a Phase 3 clinical trial of zilebesiran, whether because of data from the earlier clinical development of zilebesiran or for any other reason, we would not receive the Phase 3 initiation milestone, which could have a material adverse effect on our operating results and financial condition and make it more difficult for us to achieve operating profitability in 2025. In these circumstances, we would also need to determine whether to continue the clinical development of zilebesiran in the absence of funding and other support from Roche.

Our agreement with Novartis relating to the development and commercialization of inclisiran worldwide may be terminated by Novartis at any time upon four months' prior written notice, provided if the agreement is terminated by Novartis for convenience, Novartis must grant a license to us under certain technology developed in the course of its (or MDCO's) activities under the agreement, subject to a royalty to be negotiated between the parties. Moreover, any adverse actions by Novartis with respect to, or disputes with Novartis regarding, the MDCO License Agreement could adversely impact our ability to comply with our obligations under our agreements with Blackstone Royalties. If we were to lose a commercialization collaborator, we would have to attract a new collaborator (potentially on less favorable terms for us than we have with our existing collaborator) or develop expanded sales, distribution and marketing capabilities internally, which would require us to invest significant 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 the affected product or product candidate, it could delay our development of product candidates, result in the need for additional company resources to develop the impacted product candidate(s), 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 adversely affect how we are perceived in the business and financial communities.

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

- pursue alternative technologies or develop alternative products, either on its own or jointly with others, that may be competitive with the products on which it is collaborating with us or which could affect its commitment to its 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 commercial rights, choose to devote fewer resources to the marketing of our products, if any are approved for marketing, than it does for products developed or commercialized outside of our collaboration.

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

We expect to incur significant costs as we continue to grow our manufacturing capabilities and resources and develop manufacturing expertise; in the meantime, we rely, and expect to continue to rely, on third parties to manufacture our products and product candidates. The loss of these or future third-party suppliers, or their inability to provide us with sufficient supply, could harm our business.

We have been expanding our manufacturing capabilities, and in order to continue to commercialize our approved products, continue to develop our current product candidates, apply for regulatory approvals and, if approved, commercialize future products, we will need to continue to develop our internal manufacturing capabilities and/or contract or otherwise arrange for any necessary external manufacturing capabilities. During 2020, we completed construction and qualification of our manufacturing facility in Norton, Massachusetts where we manufacture drug substances for early-stage clinical development and have the possibility to manufacture drug substances for late-stage clinical development and commercial use, in the future.

At the present time, we only have the capacity to manufacture limited quantities of clinical trial drug substance ourselves, and otherwise we continue to rely on third party CMOs to manufacture additional drug substance, and we rely on third party CMOs for all of our drug product requirements for clinical and commercial use. There are a limited number of CMOs worldwide with the expertise to manufacture our siRNA therapeutic products, and we currently rely on a limited number of CMOs in North America, Europe and Asia to manufacture our products and product candidates. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our CMOs to meet our delivery time requirements or provide adequate amounts of material to meet our needs, and if our CMOs fail to do these things it could delay our clinical trials and potentially put our commercial supply at risk, as well as result in additional expense to us. To fulfill our future requirements, we will likely need to contract with additional CMOs, and such alternative suppliers may be limited, not be readily available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner, or at all.

In addition to the manufacture of 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 or other drug delivery technologies. In some cases, the delivery technology we utilize is 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 limited experience in such scale-up and manufacturing, requiring us to depend on a limited number of third parties, who might not be able to deliver in a timely manner, or at all. Failure by manufacturers to properly manufacture our delivery technology and/or formulate our siRNAs for delivery could result in unusable product, supply delays and drug shortages. Furthermore, competition for supply from our manufacturers from other companies, a breach by such manufacturers of their contractual obligations or a dispute with such manufacturers would disrupt our clinical and/or commercial supply, cause delays in our discovery and development efforts, and result in additional expense to us.

In developing manufacturing capabilities by building our own manufacturing facilities, we have incurred substantial expenditures, and expect to incur significant additional expenditures in the future. Also, we have had to, and will likely need to continue to, recruit, hire, and train qualified employees to staff our facilities. If we are unable to manufacture sufficient quantities of material or if we encounter problems with our facilities in the future, we may also need to secure alternative suppliers, and such alternative suppliers may not be available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner, or at all. Given our dependence on a limited number of CMOs to supply our

commercial products and clinical candidates, and the ongoing utilization of our own facilities, any delay or setback in the manufacture of our products could impede ongoing clinical and commercial supply, which could materially and adversely impact our business, prospects, operating results and financial condition. In addition, to the extent we or our collaborators rely on CMOs to supply our product candidates, any delays or disruptions in supply could have a material adverse impact on the research and development activities and potential commercialization of our or our collaborators' product candidates.

The manufacturing processes for our products and any other product candidates that we may develop is subject to the FDA and foreign regulatory authority approval processes and we will need to meet, and will need to contract with CMOs that can meet, all applicable FDA and foreign regulatory authority requirements on an ongoing basis. The failure of any CMO to meet required regulatory authority requirements could result in the delayed submission of regulatory applications, or delays in receiving regulatory approval for any of our or our current or future collaborators' product candidates. For example, in April 2022, due to an amendment to our vutrisiran NDA submission to address a pending inspection classification at a third-party secondary packaging and labeling facility, the FDA extended the review timeline of the NDA. 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.

Additionally, in January 2024, the U.S. House of Representatives introduced the BIOSECURE ACT (H.R. 7085), which was subsequently amended on May 15, 2024 and passed by the U.S. House of Representatives on September 9, 2024, and the Senate advanced a substantially similar bill (S.3558), both of which would prohibit U.S. federal executive agencies from contracting with any entity where the biotechnology equipment or services of a "biotechnology company of concern" would be used in the performance of that contract. Generally, a "biotechnology company of concern" is a biotechnology company that is subject to the jurisdiction, direction, control, or operates on behalf of a foreign adversary's government and poses a risk to the national security of the U.S. The final language, pathway and timing for either of these bills or their provisions to become law remain uncertain and, although the bill was passed in the House on September 9, 2024, the Senate did not pass the bill before the end of the 118th Congress's term. Nonetheless, if these bills are re-introduced in the House and Senate and become law, or similar laws are passed, they would have the potential to severely restrict our ability to purchase services or products from, or otherwise collaborate with, certain Chinese "biotechnology companies of concern" without losing the ability to contract with, or otherwise receive reimbursement from, the U.S. government. We do business with companies in China and it is possible some of our contractual counterparties could be impacted by the legislation described above and alternative arrangements may need to be made.

The current presidential administration has substantially altered prior U.S. government international trade policy and has commenced activities to renegotiate, or potentially terminate, certain existing bilateral or multi-lateral trade agreements and treaties with foreign countries. In addition, the administration has initiated or is considering imposing tariffs on certain foreign goods, and has announced plans to impose or increase tariffs of 25% or more on pharmaceuticals, including pharmaceutical products and components manufactured outside of the U.S. Related to this action, certain foreign governments, including China, have instituted or are considering imposing reciprocal tariffs on certain U.S. goods. It remains unclear what the current administration or foreign governments will or will not do with respect to tariffs or other international trade agreements and policies. A trade war or other governmental action related to tariffs or international trade agreements or policies has the potential to disrupt our research activities, affect our suppliers, increase the cost of materials purchased to manufacture our products, impact our ability to sell our products outside the U.S. or to sell our products outside the U.S. at competitive prices and/or to affect the U.S. or global economy or certain sectors thereof and, thus, could adversely impact our business. Although it remains unclear whether and to what extent any such tariffs will ultimately be adopted or implemented, or the effect that any such actions would have on us, our third party CMOs or our industry, any unfavorable tariffs may increase our cost of goods sold.

If the third parties we engage to supply materials or manufacture product candidates or products for preclinical testing or clinical or commercial supply should cease to do so for any reason, we would likely experience delays in advancing these preclinical tests and clinical trials and/or interruptions in commercial supply while we identify and qualify replacement suppliers or manufacturers, and we may be unable to obtain replacement supplies on terms that are favorable to us, or at all. If we are not able to obtain adequate supplies of our product candidates or products or the substances used to manufacture them, it could materially and adversely impact our business, prospects, operating results or financial condition.

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

- we or our collaborators may not be able to initiate or continue clinical trials of product candidates that are under development;
- we or our collaborators may be delayed in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;

- we may lose the cooperation of our collaborators;
- our facilities and those of our CMOs, and our products could be the subject of inspections by regulatory authorities that could have a negative outcome and result in supply delays;
- 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 the clinical and commercial demands for our products and product candidates.

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

We rely on independent clinical investigators, CROs, and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our clinical trials. We have contracted with, and we plan to continue to contract with, certain third parties to provide certain services for our clinical trials, including site selection, enrollment, monitoring, auditing and data management services. These investigators and CROs are not our employees, and we have limited control over the amount of time and resources they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw their time and resources away from our programs. Although we depend heavily on these parties, we control only limited aspects of their activity and therefore we cannot be assured that these third parties will adequately perform 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 GCP requirements, which are regulations and guidelines enforced by the FDA and foreign regulatory authorities for our product candidates in clinical development, and to implement timely corrective action to address 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 in a timely manner or at all, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA, PMDA or other foreign regulatory authorities may require us to take additional action or perform additional clinical trials before approving our marketing applications. We cannot be certain that upon inspection by a regulatory authority in the future, such regulatory authority will determine that any of our clinical trials comply with GCP requirements.

If our third-party service providers cannot adequately and timely fulfill their obligations to us for any reason, or if the quality and accuracy of our clinical trial data is compromised due to failure by a third party service provider to adhere to our protocols or regulatory requirements or if a third party service provider otherwise fails to meet deadlines, our development plans and/or regulatory reviews for marketing approvals may be delayed or terminated. As a result, our business, prospects, operating results and financial condition would be harmed, and our stock price would likely be negatively impacted.

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, sales and medical staff. The loss of the services of any members of our senior management could significantly delay or prevent the achievement of product development and commercialization, and other business objectives, and adversely impact our stock price. Our employment arrangements with our key personnel are terminable without notice. We do not carry key person life insurance on any of our employees.

We have grown our workforce significantly over the past several years and anticipate additional employee growth in the future, and 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 to attract and reward qualified individuals than we do. If we are not able to attract and retain highly qualified sales and marketing, research, development, and other professionals, it would negatively impact our ability to commercialize our approved products and any future products and to support our growing research and development and global commercialization efforts and initiatives, which would have an adverse effect on our ability to implement our future business plans.

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

As we continue the commercial launches of our approved products, including the launch of AMVUTTRA in ATTR amyloidosis with cardiomyopathy, and increase the number of product candidates we are developing, we will need to continue to expand our operations in the U.S. and further develop our operations in the EU and other geographies, including Asia and

Latin America. To date, we have received regulatory approval for four products, which we have launched in multiple geographies globally, and we continue to expand the reach of these products with additional regulatory filings and launches.

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

The use of social media presents risks and challenges.

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

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

We are increasingly dependent on our information technology systems and infrastructure for our business. We collect, store and transmit sensitive information including intellectual property, proprietary business information, including highly sensitive clinical trial data, and personal information in connection with our business operations. The secure maintenance of this information is critical to our operations and business strategy. Some of this information could be subject to information breaches, unauthorized access, human error, computer viruses, denial-of-service attacks, malicious code, spam attacks, phishing, ransomware or other forms of social engineering and other events that could impact the security, reliability, confidentiality, integrity and availability of our systems, including by third parties with a wide range of motives and expertise, including organized criminal groups, nation-states, “hacktivists,” patient groups, rogue current or former employees and others. Cyber-attacks can be designed to collect sensitive or proprietary information, manipulate, destroy or corrupt data, systems or applications, or accounts, to steal money or extort money through the use of so-called “ransomware”, and to disable the functioning or use of applications or technology assets. Cyber-attacks are of ever-increasing levels of sophistication, and despite our security measures, our information technology and infrastructure may be vulnerable to such attacks or may be breached, including due to employee error or malfeasance. The risk of cyber-attacks is increased with employees working remotely, as remote work increases our vulnerability to cybersecurity-related events such as phishing attacks and other security threats. Cybersecurity requires ongoing investment and diligence against evolving threats and is subject to federal and state regulation relating to the protection of confidential information. We may be required to expend significant additional resources to modify our protective measures, to investigate and remediate vulnerabilities or other exposures, to make required notifications, to restore our systems and fully recover from a cyber-attack, or to update our technologies and digital properties to comply with industry and regulatory standards, but we may not have adequate personnel, financial or other resources to fully meet these threats and evolving standards. We will also be required to effectively and efficiently govern, manage and ensure timely enhancements to our systems, including in their design, architecture and interconnections as well as their organizational and technical protections.

The pervasiveness of cybersecurity incidents in general and the risks of cyber-crime are complex and continue to evolve. Although we are making significant efforts to maintain the security and integrity of our information systems and are exploring various measures to manage the risk of a security breach or disruption, there can be no assurance that our security efforts and measures will be effective or that attempted security breaches or disruptions would not be successful or damaging. Despite the implementation of security measures, our internal computer systems and those of our contractors, consultants and collaborators are vulnerable to damage or interruption from computer viruses, unauthorized or inappropriate access or use, natural disasters, pandemics or public health emergencies, terrorism, war (including the ongoing conflicts in Ukraine and the Middle East), and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss of preclinical trial data, data from completed or ongoing clinical trials for our product candidates, or manufacturing data could result in delays in our regulatory filings and development efforts, as well as delays in the commercialization of our products, and significantly increase our costs. To the extent that any disruption, security breach or unauthorized or inappropriate use or access to our systems were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, including but not limited to patient, employee or vendor information, we could incur notification obligations to affected individuals and government agencies, face potential lawsuits from patients, collaborators, employees, stockholders or other third parties, and incur liability under foreign, federal and state laws that protect the privacy and security of personal information, and the development and potential commercialization of our products and product candidates could be delayed. Such events may ultimately result in financial losses that are either not insured or are not fully covered through any insurance we maintain.

In addition, our increased use of cloud technologies heightens these third party risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber-attacks could disrupt our operations and result in misappropriation, corruption, or loss of confidential or proprietary information. Although we require certain third party service providers to maintain certain minimum security levels and adopt certain security procedures by policy, we cannot ensure the universal or consistent compliance with these policies across our service providers, or that our policies and procedures will be adequate to address the evolving threat environment and identify and provide controls for all of the risks in a particular service provider's environment.

Risks Related to Our Industry

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

Any product candidate we or our collaborators develop may fail in development or experience significant delays.

Our business depends upon the successful development and commercialization of our product candidates. These product candidates are in various stages of development and must satisfy rigorous standards of safety and efficacy before they can be approved for sale by the FDA or foreign regulatory authorities. Nonclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete, is uncertain as to outcome, and the historical failure rate for product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Failure to advance our product candidates through clinical development could impair our ability to ultimately commercialize products, which could materially harm our business and long-term prospects.

Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses, and earlier results, both nonclinical and clinical, may not be indicative of future clinical trial results. Many 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, prospects, operating results and financial condition. Moreover, clinical data are often susceptible to varying interpretations, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their product candidate. Moreover, certain of our product candidates employ novel delivery technologies that have yet to be extensively evaluated in human clinical trials and proven safe and effective.

In addition, from time to time, we report interim, topline, and preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change. Interim or preliminary data from a clinical trial may not be predictive of final results from the clinical trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and treatment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Additionally, several of our planned and ongoing clinical trials utilize an "open-label" trial design. In an "open-label" clinical trial, both the patient and investigator know whether the patient is receiving the investigational product candidate or, if the trial includes multiple arms, either an existing approved drug or placebo. Most typically, open-label clinical trials test only

the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Accordingly, open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a blinded, controlled environment with a placebo or active control.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in trial design, dose selection issues, patient enrollment criteria, operational challenges, site implementation challenges, biostatistical plans and failure to demonstrate favorable safety or efficacy traits.

If our product candidates experience any such problems, we may not have the financial resources necessary to continue development of the affected product candidate or any of our other product candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected product candidate or any of our other product candidates.

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 extend our clinical development timelines and 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 have the potential to be promising;
- delays in filing IND applications or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or institutional review boards/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 institutional review board or ethics committee, or the FDA or comparable foreign regulatory authorities regarding the scope or design of our clinical trials;
- problems in engaging institutional review boards or ethics committees to oversee clinical trials or problems in obtaining or maintaining institutional review board or ethics committee approval of clinical trials;
- delays in enrolling patients and volunteers into clinical trials, and variability in the number and types of patients and volunteers available for clinical trials, including as a result of a pandemic or public health emergency or the ongoing conflicts in Ukraine and the Middle East;
- disruptions caused by man-made or natural disasters or pandemics, epidemics or public health emergencies or other business interruptions;
- high drop-out rates for patients and volunteers in clinical trials;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours;
- inadequate supply or quality of product candidate materials or other materials necessary for the conduct of our clinical trials or disruption or delays in clinical supply due to a future pandemic or public health emergency;
- serious and unexpected drug-related side effects experienced by patients taking our approved products, participants in our clinical trials or individuals using drugs similar to our products or product candidates;
- poor or disappointing effectiveness of our product candidates during clinical trials;
- the imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or manufacturing concerns or after an inspection of our clinical trial operations or trial sites;
- 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 GLP, 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;

- delays in reaching a consensus with regulatory agencies on trial design;
- interpretations of data by the FDA or foreign regulatory authorities that differ from ours;
- lack of adequate funding to continue the clinical trial; or
- diminished revenue potential of the applicable program due to competition.

Clinical trials must be conducted in accordance with the legal requirements, regulations or guidelines of the FDA and regulatory authorities outside the U.S. We could encounter delays if a clinical trial is suspended or terminated by us, by the FDA or any other regulatory authority, or if the institution review boards of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval.

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. Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis is subject to a number of factors. Clinical trials are expensive and require significant operational resources. Delays in patient enrollment or unforeseen drop-out rates may result in increased costs and longer development times.

Patient enrollment is 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, the eligibility criteria for the clinical trial, the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion, and factors we may not be able to control, such as potential pandemics. We or our collaborators may experience difficulty enrolling our clinical trials due to the availability of existing approved treatments, as well as other investigational treatments in development. For example, we may experience delays in recruiting and enrolling patients, and in particular treatment-naive patients, for our Phase 3 clinical trial of nucresiran for the treatment of ATTR amyloidosis with cardiomyopathy because there are multiple approved therapies on the market and multiple investigational therapies in ongoing clinical trials for that indication. Delays or difficulties in patient enrollment, or difficulties retaining trial participants, including as a result of the availability of existing approved treatments or other investigational treatments, safety concerns, or the impact of pandemics or other public health emergencies, can result in increased costs, longer development times or termination of a clinical trial.

If any of our current or future products or product candidates causes undesirable side effects or has other unexpected adverse properties, such side effects or properties could delay or prevent regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

There can be no assurance that our products or product candidates will not cause undesirable side effects. For example, results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. If any product candidates we develop are associated with unacceptable side effects or deaths, we may need to abandon the development of such product candidates or limit development to certain uses or subpopulations in which the unacceptable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. Furthermore, the occurrence of such adverse events could result in the suspension or termination of clinical trials of a product candidate by us, our collaborators, institutional review boards or ethics committees, or the FDA or a foreign regulatory authority, and may negatively impact the clinical and/or regulatory timelines of the impacted product candidates. For example, our Phase 1 clinical trial of mivelsiran for Alzheimer's Disease remains on partial clinical hold in the U.S. due to findings observed in non-clinical chronic toxicology studies. While our clinical development of mivelsiran has not been impacted by the partial clinical hold because of the dose levels at which it applies, it is possible that the partial clinical hold could have an impact if our development plans change or that future partial or full clinical holds on mivelsiran or our other product candidates could impact our ability to advance the clinical development of such product candidate on our expected timelines or at all.

In addition, the occurrence of serious adverse events could also result in refusal by the FDA or a foreign regulatory authority to approve a particular product candidate for any or all indications of use, or in limitations in the label of any approved product. Even if we are able to demonstrate that any future serious adverse events are not product-related and regulatory authorities do not order us to cease further development of our product candidates, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate, the commercial prospects of such product candidates may be

harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

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

Any product candidates we or our collaborators develop are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, pricing, advertising, promotion and distribution of drugs. Failure to obtain marketing approval for a product candidate we may develop will prevent us from commercializing the product candidate in a given jurisdiction. Securing regulatory approval requires the submission of extensive nonclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authorities. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that the product candidates we and our collaborators are developing will not obtain the regulatory approvals necessary for us or our collaborators to begin commercialization, or that approved products, including AMVUTTRA, will not obtain regulatory approval to be sold for an additional, broader indication than the indication for which it is currently approved. For example, although AMVUTTRA has been approved by the FDA, EC, PMDA, MHRA and certain other regulatory authorities for the treatment of ATTR-CM, regulatory authorities in other jurisdictions have not yet granted approval for this expanded indication. It is also possible that the FDA or other regulatory authorities may determine that the data generated in clinical trials for a product candidate is not sufficient to support the approval of an application for regulatory approval. For example, although we reported positive results from the APOLLO-B Phase 3 clinical trial of patisiran in patients with ATTR amyloidosis with cardiomyopathy, in October 2023, the FDA issued a CRL in response to our sNDA for patisiran, indicating the sNDA could not be approved in its present form.

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 in a predictable or uniform manner and can change over time. Any analysis we perform of data from nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We or our collaborators may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because there may be approved treatments for some of the diseases for which we or our collaborators may seek approval, or treatments in development which will be approved by the time we or our collaborators file for approval, in order to receive regulatory approval, we or they may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases are not only safe and effective, but safer and/or more effective than other products.

Interruption or delays in the operations of the FDA, EMA and comparable foreign regulatory agencies may impact the review, inspection and approval timelines for our or our collaborated product candidates. During the COVID-19 public health emergency, the FDA worked to ensure timely reviews of applications for medical products in line with its user fee performance goals and conducted mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. In addition, during the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In December 2020, the FDA issued a CRL regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the PDUFA action date due to unresolved facility inspection-related conditions. In July 2021, Novartis announced that the resubmission to the FDA of the inclisiran NDA to address the complete response letter was filed, and the FDA approved Leqvio (the trade name under which inclisiran is marketed in the U.S.) in December 2021. This delay in the approval of Leqvio resulted in delayed milestone and royalty revenue to us. Any similar interruption or delay by the FDA, EMA or comparable foreign regulatory authorities could have a material adverse effect on our or our collaborators' efforts to obtain regulatory approval for our or our collaborators' product candidates, which could have a material adverse effect on our business, prospects, operating results or financial condition.

Inadequate funding for the FDA and other government agencies and/or potentially shifting priorities under the current presidential administration could hinder the FDA's and/or those other government agencies' ability to hire and retain key leadership and other personnel, prevent new products and services from being developed and/or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products, to provide feedback on clinical trials and development programs, to meet with or engage in other informal interactions with sponsors and to otherwise review regulatory submissions can be affected by a variety of factors, including government budget and funding

levels; the ability to hire and retain key personnel and accept the payment of user fees; and statutory, regulatory, and policy changes, among other factors. Average review times at the agency may fluctuate as a result. In addition, government funding of other government agencies or of government programs that provide research funding on which our operations may rely directly or indirectly via third party research and development projects associated with our product development programs, is subject to the political process, which is inherently fluid and unpredictable. The failure for such funding to be furnished or to be furnished in a timely manner could impact our ongoing research and development initiatives.

Since the start of the current presidential administration in 2025, U.S. policy changes have been implemented at a rapid pace and additional changes are likely. It is difficult to predict how executive actions that may be taken under the current administration may affect the FDA's ability to exercise its regulatory authority. Any disruptions at the FDA and other agencies that impose constraints on the FDA's ability to engage in routine oversight and product review activities may slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies or to otherwise respond to regulatory submissions, which would adversely affect our business. For example, the current administration has discussed several changes to the reach and oversight of the FDA, which could affect its relationship with the pharmaceutical industry, transparency in decision making and ultimately the cost and availability of prescription drugs. The FDA may pursue legislative, regulatory or policy changes regarding the standards or processes for approving our products or product candidates that we may be unable to satisfy. Additionally, over the last several years, the U.S. government has shut down multiple times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. For example, the current administration previously announced plans to reduce the number of federal employees by establishing voluntary termination programs, by position eliminations or by involuntary terminations. Reductions in workforce, particularly in the review or inspection divisions, could extend NDA review timelines, delay or prevent pre-approval inspections, and limit opportunities for FDA feedback on pending applications. A significant reduction in the FDA's workforce or budget, changes in the FDA's regulatory and oversight priorities or activities, or a prolonged government shutdown could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

The FDA or foreign regulatory authorities may request additional clinical or other data or information in connection with the regulatory review of our or our collaborators' product candidates, including by issuing a complete response letter that may require that we or our collaborators submit additional clinical or other data or impose other conditions that must be met in order to secure final approval of our or our collaborators' NDA applications, including potentially requiring a facility inspection. Even if such data and information are submitted, or any such inspection is completed, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

We may seek a Fast Track, Priority Review, or Breakthrough Therapy designation or similar designations outside the U.S. for some of our product candidates. Product candidates that receive one or more of these designations may be eligible for, among other things, a priority regulatory review. Each of these designations is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for Fast Track, Priority Review, and/or Breakthrough Therapy designation, the FDA or similar regulatory authorities may disagree and instead determine not to make such designation. The receipt of one or more of these designations for a product candidate does not guarantee a faster development process, review or approval compared to products developed or considered for approval under conventional assessment procedures and does not assure ultimate approval by the FDA or similar regulatory authorities. In addition, even if one or more of our products or product candidates qualifies for Fast Track, Priority Review, and/or Breakthrough Therapy designation, the FDA or similar regulatory authorities may later decide to withdraw such designation if it determines that the product or product candidate no longer meets the conditions for qualification.

Any delay or failure in obtaining required approvals for our product candidates or our collaborated product candidates could have a material adverse effect on our ability to generate revenues from any product candidate for which we or our collaborators may seek approval in the future. For example, as a result of the CRL from the FDA in response to our sNDA for patisiran as a treatment for ATTR amyloidosis with cardiomyopathy, our ability to generate product revenues for patisiran has been negatively impacted.

Furthermore, even if we or our collaborators receive approval of an NDA or foreign marketing application for a product candidate, the FDA or the applicable foreign regulatory agency may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-market clinical trials. The FDA or the applicable foreign regulatory agency also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any of these restrictions or commitment could limit an approved product's market opportunity and have a negative impact on our business, prospects, operating results and financial condition and our stock price. For example, if a foreign regulatory agency approves vutrisiran for the treatment of ATTR amyloidosis with cardiomyopathy with a more limited label than we are seeking, it could limit the scope of the commercial opportunity for vutrisiran in such jurisdiction.

In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy, or REMS, as part of its review of an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved

drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. In the EU, we or our collaborators 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 our products and affect reimbursement by third-party payors.

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

Our marketed products and any product candidates for which we obtain approval are subject to extensive and ongoing regulatory oversight. If we or our collaborators 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 in any such case our business would be seriously harmed.

Our six marketed products, including two products that are commercialized by collaborators, and any product candidates for which we or our collaborators may ultimately receive marketing authorization, are subject to ongoing regulatory requirements governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, import, export, recordkeeping, and reporting. Ongoing FDA requirements include, among other things, submission of safety and other post-marketing information and reports, registration and listing, continued compliance with GMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians, and GCP requirements for any clinical trials that we conduct post-approval. In addition, we are conducting, and intend to continue to conduct, clinical trials for our product candidates, and we intend to seek approval to market our product candidates, in jurisdictions outside of the U.S., and therefore will be subject to, and must comply with, regulatory requirements in those jurisdictions.

Our products are subject to continuing regulatory oversight following approval, including the review of adverse drug experiences and clinical results that are reported after our drug products are made commercially available. This includes results from any post-marketing tests or surveillance to monitor the safety and efficacy of our approved products or other products required as a condition of approval or otherwise agreed to by us. Products are more widely used by patients once approval has been obtained and therefore side effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre-approval clinical trials or nonclinical studies. The subsequent discovery of previously unknown or underestimated problems with a product could result in:

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

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

The CMO and manufacturing facilities we use to make our approved products and certain of our current product candidates, including our Cambridge facility, our Norton facility, as well as facilities at Agilent and other CMOs, will also be subject to periodic review and inspection by the FDA and other regulatory agencies. For example, Agilent and our Cambridge-based facility were subject to regulatory inspection by the FDA and the EMA in connection with the review of our applications for regulatory approval for ONPATTRO and GIVLAARI, and may be subject to similar inspection in connection with any subsequent applications for regulatory approval of one or more of our products filed in other territories. The discovery of any new or previously unknown problems with our or our CMO's manufacturing processes or facilities, may result in restrictions on the CMO or facility or the products manufactured at such facility, including delay in approval or withdrawal of an approved product from the market. For example, due to a routine inspection by the FDA at a CMO facility that resulted in a pending inspection classification, we amended our regulatory submission for vutrisiran for the treatment of hATTR-amyloidosis with polyneuropathy in adults, which delayed our PDUFA goal date and AMVUTTRA's initial NDA approval with the FDA. 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 this material for us. Reliance on CMOs entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the applicable CMO for regulatory compliance.

If we or our collaborators, CMOs or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or a foreign jurisdiction in which we seek to market our products, we or they may be subject to, among other things, fines, warning or untitled 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, fines, injunctions, civil penalties and criminal prosecution.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our approved products and any product candidates we may develop and adversely affect our business, financial condition, results of operations and prospects.

The U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding *Chevron* doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rule-making process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business could be materially harmed.

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

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. Although physicians are generally permitted, based on their medical judgment, to prescribe products for indications other than those approved by the applicable regulatory agency, manufacturers are prohibited from promoting their products for such off-label uses. If a regulatory agency determines that our promotional materials, or other activities constitute off-label promotion, it could request that we modify our promotional materials or other activities, conduct corrective advertising, or subject us to regulatory enforcement actions, such as the issuance of a warning or untitled letter, injunction, seizure, civil fines and criminal penalties. It also is possible that other federal, state, or foreign enforcement authorities might take action if they believe that the alleged improper promotion led to the submission and payment of claims for an off-label use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions, and have to divert significant management resources from other matters.

Even if we or our collaborators receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which could adversely affect our business, prospects, operating results and financial condition.

It may be difficult for us to convince the medical community and third-party payors to accept and use our products, or to provide favorable reimbursement.

The factors we believe will materially affect market acceptance of our products 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, dosing regimen 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 our product candidates we develop are intended to treat and the relative risks, benefits and costs of those treatments.

For example, AMVUTTRA is administered through a subcutaneous injection and may not compete favorably with other available options for the treatment of ATTR amyloidosis with cardiomyopathy, including VYNDAQEL/VYNDAMAX, which is marketed by Pfizer and administered in pill form, and ATTRUBY, which is marketed by BridgeBio and administered in pill form, or other available options for the treatment of hATTR amyloidosis with polyneuropathy in adults, including WAINUA, which is marketed by AstraZeneca and Ionis, and administered subcutaneously, or VYNDAQEL/VYNDAMAX, which is marketed by Pfizer in several countries and administered in pill form. In addition, Qfitlia represents a new approach to treating hemophilia, which may not be readily accepted by physicians and patients and their caregivers.

We are a multi-product commercial company and expect to continue to invest significant financial and management resources to continue to build our marketing, sales, market access and distribution capabilities and further establish our global infrastructure. If we are not able to continue to develop and scale these capabilities, we may not be able to successfully commercialize our products and product candidates.

We received our first product approval in August 2018 and have established capabilities for marketing, sales, market access and distribution over the last several years. We currently expect to rely on third parties to launch and market certain of our product candidates in certain geographies, if approved. However, we are commercializing AMVUTTRA, ONPATTRO, GIVLAARI and OXLUMO, and intend to commercialize other product candidates, if approved, on our own globally in major markets. Accordingly, we have developed internal marketing, sales, market access and distribution capabilities as part of our core product strategy initially in the U.S., Europe and Japan, with expansion ongoing globally, which has required, and will continue to require, significant financial and management resources. For those products for which we will perform marketing, sales, market access and distribution functions ourselves we could face a number of additional risks, including:

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

In addition, the current Secretary of the Department of Health & Human Services, Robert F. Kennedy, Jr., has expressed interest in banning direct-to-consumer advertising for prescription drugs. Although a ban on direct-to-consumer advertising would require legislative action, the FDA may implement regulatory or policy changes that materially limit our ability and that of our third-party contractors to promote our products to consumers, which could materially impact our business.

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

The patient populations suffering from ATTR amyloidosis with cardiomyopathy, hATTR amyloidosis with polyneuropathy, AHP and PH1 have not been established with precision. If the actual number of patients suffering from these diseases is smaller than we estimate, or if we fail to raise awareness of these diseases and diagnosis is not improved, our business, prospects, operating results and financial condition may be adversely affected.

Our estimates regarding the potential market size for AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO or any future products that we may commercialize, may be materially different from the actual market size, including as a result of the indication approved by regulatory authorities, which could result in significant changes in our business plan and may have a material adverse effect on our business, prospects, operating results and financial condition. If we are unable to accurately estimate the number of patients suffering from a disease for which we successfully commercialize a product or we were not able to raise awareness of these diseases and improve diagnosis, it could have a material adverse effect on our business, prospects, operating results or financial condition, and it will be more difficult or impossible to achieve profitability.

Any products we currently market or may develop in the future may become subject to unfavorable pricing regulations or healthcare reform initiatives, thereby harming our business, prospects, operating results and financial condition.

The regulations that govern marketing approvals, coverage, pricing and reimbursement for new drugs vary widely from country to country and are subject to change. 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 authorization 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. It is also possible to obtain regulatory approval for a product in a particular country, but then be subject to price regulations or price controls that delay our commercial launch of the product and/or 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.

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.

In the U.S., healthcare and pharmaceutical pricing are subject to both government and public scrutiny and calls for reform, and the U.S. government continues to propose executive, legislative and regulatory changes designed to control costs and reexamine drug pricing and payment models. Specifically, there have been several recent U.S. Congressional inquiries into prescription drugs, and proposed and enacted federal and state legislation and regulations designed to, among other things, bring more transparency to drug pricing, reduce the cost and reimbursement of prescription drugs under third-party payor programs, and alter the nature and operation of manufacturer patient support programs. These developments could, directly or indirectly, affect our ability to sell AMVUTTRA, ONPATTRO, GIVLAARI, OXLUMO or future products, if approved, at a favorable price.

At the federal level, for example, the Inflation Reduction Act, or IRA, includes several provisions that impact our business to varying degrees. For example, the IRA may require us to pay rebates if we increase the net cost of a Medicare Part B or Part D drug faster than the rate of inflation. In addition, our cost-sharing responsibility for any approved product covered by Medicare Part D could be significantly greater under the IRA Part D benefit structure compared to the pre-IRA benefit design. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties or a potential excise tax. The effect of the IRA on our business and the healthcare industry in general continues to evolve and we may continue to discover additional adverse impacts on our company or our industry. The IRA is anticipated to have significant effects on the pharmaceutical industry and may reduce the prices we can charge and reimbursement we can receive for our products, among other effects.

The current presidential administration issued an executive order in April 2025 with multiple directives aimed at lowering drug prices, including refining the Medicare drug price negotiation program established by the IRA; accelerating competition for high-cost prescription drugs by accelerating approval of generics and biosimilars and facilitating the process for re-classifying prescription drugs as over-the-counter drugs and increasing drug importation. In addition, in May 2025, the current presidential administration issued another executive order that directed government agencies and officials to identify most-favored-nation pricing targets for prescription drugs (and looked to pharmaceutical manufacturers to make significant progress towards delivering target prices to patients), prevent foreign countries from disproportionately shifting the cost of global pharmaceutical research and development to the U.S., and facilitate direct-to-consumer purchasing programs for pharmaceutical manufacturers to sell their products to patients at the most-favored-nation price. Many of these reform initiatives will require additional legal and/or administrative action to implement. There is uncertainty regarding the nature or impact of any drug or broader healthcare reform implemented by the current presidential administration through executive or administrative action or by Congress, and the extent to which any such action will be subject to litigation or other challenges. It is unclear how any such healthcare reform measures will impact our business. While frameworks like the IRA aim to control costs, their implementation under the current administration could introduce further regulatory changes, such as additional price restrictions on products we sell to Medicare or other government purchasers. Any such developments could adversely affect reimbursement, competitive dynamics, and our business. We continue to monitor legislative reforms and assess their potential impact on our operations, but we cannot predict their ultimate effect on our business. Additionally, the current presidential administration may propose policy changes that create additional uncertainty for our business. These may include new price restrictions on products we sell to Medicare or other government purchasers, or other regulatory changes impacting reimbursement or competitive dynamics in multisource markets.

At the state level, governments have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing. Some of these measures include upper payment limits on state-regulated payors; regulating product access, copayment assistance, and marketing; imposing drug price, cost, and marketing disclosure and transparency requirements; permitting importation from other countries; and encouraging bulk purchasing. For example, on January 5, 2024, the FDA authorized Florida's Agency for Health Care Administration's drug importation proposal, the first step toward Florida facilitating importation of certain prescription drugs from Canada. We cannot predict how further developments of or changes to these policies and rules will affect our business. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the demand for our products or put pressure on our product pricing. We cannot predict what healthcare reform initiatives may be adopted in the future in the U.S. or other foreign countries. Further federal, state and foreign legislative and regulatory developments are likely, with expected increased pressure on drug pricing. Such reforms could have a material and adverse effect on our anticipated revenues for one or more of our approved products or other product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our business, prospects, operating results and financial condition and our ability to develop drug candidates.

If we are unable to achieve and maintain coverage and adequate reimbursement from third-party payors for AMVUTTRA or our other products, the commercial success of these products may be severely hindered.

Successful commercialization of AMVUTTRA and our other products will depend in part on the extent to which coverage and adequate reimbursement are available from third-party payors, including governmental healthcare programs such as Medicare and Medicaid, commercial health insurers and managed care organizations, and whether and how quickly we can obtain such coverage and reimbursement. Third-party payors determine which medications they will cover and establish reimbursement levels. Reimbursement decisions by third-party payors depend upon a number of factors, including, among other things, each third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- appropriate and medically necessary for the specific condition or disease;
- cost effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval from third-party payors is often a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data, including results from pharmacoeconomic studies, to each third-party payor. No uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. and coverage and reimbursement for products can differ significantly from payor to payor. There could be significant delays in obtaining coverage and there is no guarantee that we will be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement, and any coverage we do obtain could be more limited than the purposes for which the product is approved by the FDA or foreign regulatory authorities. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that further changes in these rules and regulations are likely.

Cost containment is a primary concern of the U.S. healthcare industry and elsewhere as well as for governmental authorities. Third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for medical products and services. Third-party payors may deny reimbursement for covered products if they determine that a medical product was not used in accordance with third-party payor coverage policies, such as required procedures for cost-effective diagnosis methods, and may establish other conditions that must be met before the third-party payor will provide coverage for use of AMVUTTRA or one of our other products. For example, insurers may establish a "step-edit" system that requires a patient to first use a lower price alternative product prior to becoming eligible for reimbursement of a higher price product. Third-party payors also may refuse to reimburse for products deemed to be experimental, or that are prescribed for an unapproved indication. It is also possible that a third-party payor may consider AMVUTTRA or our other products as substitutable by less expensive therapies and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our products, pricing of existing drugs may limit the amount that can be charged for our products. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payors may also deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. Further, third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication, and it is possible that AMVUTTRA or our other products will not be included on the formularies of certain third-party payors.

In addition, some third-party payors challenge the prices charged for medical products and may impose price controls or require that we provide them with predetermined discounts from list prices. In the U.S., we have entered into value-based agreements, or VBAs, and are negotiating additional VBAs with commercial health insurers. The goal of these agreements is to ensure that we are paid based on the ability of our commercially approved products to deliver results in the real-world setting comparable to those demonstrated in our clinical trials, and the agreements are structured to link the performance of our approved products in real-world use to financial terms. Partnering with payors on these agreements is also intended to provide more confidence regarding the value of our products and help accelerate coverage decisions for patients. If the payment we receive for our products, or the reimbursement provided for such products, is inadequate in light of our significant 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 more substantial 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 2.4% currently) absent a significant value driver. Our patient access philosophy could also negatively impact the revenues we are able to generate from the sale of one or more of our products in the future.

Insurers are increasingly adopting programs and policies that limit access to medications and increase out-of-pocket costs for patients. In the U.S., to help patients access and afford our approved product(s), we may utilize programs to assist them, including patient assistance programs and co-pay coupon programs for eligible patients. It is possible that changes in insurer policies regarding co-pay coupons (such as co-pay accumulator and maximizer programs) and patient assistance programs

(such as alternative funding programs) and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these co-pay coupon programs and patient support programs, which could result in fewer patients using affected products, and therefore could have a material adverse effect on our sales, business, and financial condition.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. In particular, governments in certain markets such as in EU, the U.K., Japan, and China, provide healthcare at low (or zero) direct costs to consumers at the point of care, and thus have significant power as large single payors to regulate prices or impose other cost control mechanisms. In addition, the emphasis on managed care in the U.S. has increased, and we expect will continue to exert downward pressure on pharmaceutical pricing. Coverage policies, third-party reimbursement rates and pharmaceutical pricing regulations may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Levels of reimbursement may also decrease in the future, and future legislation, regulation or reimbursement policies of third-party payors may adversely affect the reimbursement available for and the pricing for AMVUTTRA or our other products, which in turn, could negatively impact the demand for AMVUTTRA or our other products. If providers are not adequately reimbursed for AMVUTTRA or our other products, they may reduce or discontinue purchases of them, which would have a significant negative impact on our business, prospects, operating results and financial condition.

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

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, and anti-corruption laws, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, the UK Bribery Act 2010, and other applicable anti-bribery and anti-money laundering laws. Anti-corruption laws are interpreted broadly and prohibit companies and their officers, directors, employees, agents, contractors, and other third-party representatives from directly or indirectly authorizing, promising, offering, providing, soliciting, or receiving payments or anything else of value in order to improperly influence the acts or decisions of recipients in the public or private sector or to secure any other improper advantage to obtain or retain business. From time to time, we may engage third parties to conduct clinical trials outside of the U.S., to sell our products abroad, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of agents, contractors, and third-party representatives acting on our behalf, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial fines and penalties, reputational harm, and other adverse consequences.

We remain focused on these laws and the activities they regulate and maintain a global compliance program designed to empower our business to operate in compliance with their requirements.

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

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

In some countries, including Member States of the EU, or Japan, the pricing of prescription drugs may be subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, governments and other stakeholders can put considerable pressure on prices and reimbursement levels, including as part of cost containment measures. Moreover, political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. We cannot be sure that such prices and reimbursement will be acceptable to us or our collaborators. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the

country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our collaborators and the potential profitability of our approved products or any future products in those countries would be negatively affected. We could also suffer impact from tightening pricing controls on account of greater competition from less expensive generic or biosimilar products once patent or other exclusivity expires. Certain governments have adopted policies to switch prescribed products to generic versions to reduce costs.

If we or our collaborators, CMOs or service providers fail to comply with healthcare laws and regulations, including but not limited to those related to fraud and abuse, we or they could be subject to enforcement actions, which could negatively impact our ability to develop, market and sell our products and may harm our reputation.

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our existing and future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain our business or financial arrangements and relationships through which we market, sell, and distribute our products. In the United States, these laws include, without limitation, federal and state fraud and abuse laws, transparency laws and patient data privacy and security laws and regulations, including but not limited to the following:

- The U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce either the referral of an individual for, or the purchase or ordering of, a good or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. Violations are subject to civil and criminal fines and penalties, imprisonment, and exclusion from government healthcare programs.
- The U.S. federal false claims laws, including the FCA, which generally prohibit, individuals or entities from knowingly presenting or causing to be presented, claims for payment for good or services by government-funded programs such as Medicare or Medicaid that are false or fraudulent. 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. Penalties are three times the amount of the claims in question plus civil monetary penalties.
- The federal civil monetary penalties laws, which generally impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or Medicaid beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or Medicaid. Conduct regulated by the federal civil monetary penalties law often overlaps with other healthcare laws, including the federal Anti-Kickback Statute.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which in addition to privacy and security protections applicable to healthcare providers and other entities, prohibits executing, or attempting to execute, a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters.
- Federal "sunshine" requirements imposed on drug, device, and medical supply manufacturers when payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to HHS information regarding any "transfer of value" made or distributed to healthcare providers and organizations. Failure to submit timely, accurate and complete information may result in civil monetary penalties.
- Federal price reporting laws, which, among other requirements, require manufacturers to calculate, report, and certify in a timely manner complex pricing and other product data to government programs, where such reported data may be used in the calculation of reimbursement and/or discounts on approved products; and to pay rebates or offer discounts on pharmaceutical products.
- Federal statutory and regulatory requirements applicable to pricing and sales of products to federal government agencies.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- The Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products prior to approval or for unapproved indications and regulates the distribution of samples.
- 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 and 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 price transparency and government reimbursement programs patient data privacy and security.

- European privacy laws including Regulation 2016/679, known as the General Data Protection Regulation, or the EU GDPR, and the EU GDPR as transposed into the laws of the UK, the UK GDPR, collectively referred to as the GDPR, and the e-Privacy Directive (2002/58/EC), and the national laws implementing each of them, as well as the Public and Electronic Communications Regulations 2003 in the UK and the privacy laws of Japan, Brazil and other territories.
- The California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, or, collectively, the CCPA, that, among other provisions, gives California residents rights to their personal information and imposes various privacy and security obligations on regulated businesses. Furthermore, comprehensive privacy laws similar to the CCPA and consumer health data laws have been enacted in more than twelve other states and proposed in nearly one third of all states. Washington's law regulating consumer health data contains a private right of action. The effects of the CCPA and other state privacy laws, and the creation of new regulatory bodies, such as the California Privacy Protection Agency, increases the cost and complexity of operating our business and our exposure to regulatory investigations, enforcement, fines, and penalties, any of which could negatively impact our business and operations. Failure to comply with these obligations could result in damage to our reputation and legal liability, censures, penalties and fines, disgorgement of profits, restitution to customers, remediation, the issuance of cease-and-desist orders, or injunctive or other equitable relief against us, which individually or in the aggregate could negatively impact our financial results. Depending on the nature of the violation, we may be required to offer restitution or remediation to customers, and the cost of doing so could exceed our loss reserves.

Analogous state and foreign laws and regulations, such as state anti-kickback, anti-bribery and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers, as well as other state laws that require companies to comply with specific compliance standards, restrict financial interactions between companies and healthcare providers, require companies to report information related to payments to healthcare providers, marketing expenditures or pricing or require the licensing or registration of sales representatives.

If our operations are found to be in violation of any of the aforementioned requirements, we may be subject to penalties, including civil or criminal penalties (including individual imprisonment), criminal prosecution, monetary damages, the curtailment or restructuring of our operations, 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 HHS, or the OIG, any of which could materially and adversely affect our business, prospects, operating results or financial condition. We remain focused on enhancing our global compliance infrastructure as we prepare for the launch of our products in additional countries, assuming regulatory approvals. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. For additional information, see the Risk Factor captioned "We may incur significant liability if enforcement authorities allege or determine that we are engaging in commercial activities with respect to our unapproved product candidates or promoting our commercially approved products in a way that violates applicable regulations." Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

If we or our collaborators, CMOs or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our approved products, or any future products, successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others, civil and criminal penalties, up to and including criminal prosecution resulting in fines, exclusion from healthcare reimbursement programs and imprisonment.

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

Activities we undertake related to commercializing our drug products could create risk under laws such as the federal Anti-Kickback Statute and/or the federal False Claims Act, or FCA, with the potential for significant liability, including civil and administrative penalties, criminal sanctions, and potential exclusion from participation in government programs. Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny, with related legal risk.

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

The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for "special category data," which includes health, biometric and genetic information of data subjects located in the EEA and UK. Further, GDPR provides a broad right for EEA Member States to create supplemental national laws, such as laws relating to the

processing of health, genetic and biometric data, which could further limit our ability to use and share such data or could cause our costs to increase, and harm our business and financial condition.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States and the UK, which may deviate slightly from the GDPR, may result in fines of up to 4% of total global annual revenue, or €20.0 million (£17.5 million under the UK GDPR), whichever is greater, and in addition to such fines, we may be the subject of litigation and/or adverse publicity, which could have a material adverse effect on our reputation and business. As a result of the implementation of the GDPR, we are required to implement a number of measures to ensure compliance with the data protection regime. The GDPR (i) requires us to inform data subjects of how we process their personal data and how they can exercise their rights, (ii) requires us to ensure we have a valid legal basis to process personal data (if this is consent, the requirements for obtaining consent carries a higher threshold), (iii) requires us to appoint a data protection officer where sensitive personal data (i.e., health data) is processed on a large scale, (iv) introduces mandatory data breach notification requirements throughout the EEA and UK, (v) requires us to maintain records of our processing activities and document data protection impact assessments where there is high risk processing, (vi) imposes additional obligations on us when we are contracting with service providers, requires (vii) appropriate technical and organizational measures to be put in place to safeguard personal data and (viii) requires us to adopt appropriate privacy governance including policies, procedures, training and data audit.

Significantly, the GDPR imposes strict rules on the transfer of personal data out of the EEA and UK to the U.S. or other regions that have not been deemed to offer "adequate" privacy protections. In the past, companies in the U.S. were able to rely upon the EU-U.S., UK-U.S. and the Swiss-U.S. Privacy Shield frameworks as a basis for lawful transfer of personal data from the EU and the UK to the U.S. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C-311/18 (Data Protection Commissioner v Facebook Ireland and Maximillian Schrems, or Schrems II) invalidated the EU-U.S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U.S. The CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the EC are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case-by-case basis to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as the EU, and required businesses to adopt supplementary measures if such standard is not met. Subsequent guidance published by the European Data Protection Board, or EDPB, in June 2021 described what such supplementary measures must be, and stated that businesses should avoid or cease transfers of personal data if, in the absence of supplementary measures, equivalent protections cannot be afforded. On June 4, 2021, the EC published new versions of the SCCs, which seek to address the issues identified by the CJEU's Schrems II decision and provide further details regarding the transfer assessments that the parties are required to conduct when implementing the new SCCs. However, there continue to be concerns about whether the SCCs and other mechanisms will face additional challenges. Similarly, in September 2020, the Swiss data protection authority determined the Swiss-U.S. Privacy Shield framework was no longer a valid mechanism for Swiss-U.S. data transfers and raised questions about the validity of the SCCs as a mechanism for transferring personal data from Switzerland. While SCCs provide an alternative to our Privacy Shield certification for EU-U.S. data flows, the decision (and certain regulatory guidance issued in its wake) casts doubt on the legality of EU-U.S. data flows in general. Any inability to transfer, or burdensome restrictions on the ability to transfer, personal data from the EU to the U.S. in compliance with applicable data protection laws may impede our ability to conduct clinical trials and may adversely affect our business, prospects, operating results and financial condition. The UK is not subject to the EC's new SCCs but has published its own transfer mechanism, the International Data Transfer Agreement or International Data Transfer Addendum, which enables transfers from the UK. On March 25, 2022, the EC and the U.S. announced a political agreement on a new "Trans-Atlantic Data Privacy Framework" to replace the invalidated Privacy Shield. The framework introduced new binding safeguards to address the concerns raised by the CJEU in Schrems II. On July 10, 2023, the EC announced that it had adopted its adequacy decision for that data privacy framework, labelled the EU-U.S. Data Privacy Framework. The adequacy decision concluded that the U.S. ensures an adequate level of protection for personal data transferred from the EU to US companies under the new framework, and the EC stated that as a result personal data can flow safely from the EU to US companies participating in the framework, without having to put in place additional data protection safeguards. The EU-U.S. Data Privacy Framework is subject to periodic reviews, to be conducted by the EC, together with other European data protection authorities and U.S. authorities, with the first review to take place within a year of adoption of the adequacy decision. A case has been lodged with and remains pending before the EU courts challenging the validity of the EU-U.S. Data Privacy Framework.

EEA Member States have adopted implementing national laws to implement the GDPR which may partially deviate from the GDPR and the competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country, and we do not expect to operate in a uniform legal landscape in the EU. In addition, the UK Government has now introduced a Data Protection and Digital Information Bill, or the UK Bill, into the UK legislative process. The aim of the UK Bill is to reform UK's data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime. The anticipated UK general election in 2024 could postpone passage of the UK Bill.

We are subject to the supervision of local data protection authorities in those jurisdictions in which we are monitoring the behavior of individuals in the EEA or UK (i.e., undertaking clinical trials). We depend on a number of third parties in relation

to the provision of our services, a number of which process personal data of EU and/or UK individuals on our behalf. With each such provider we enter or intend to enter into contractual arrangements under which the provider is contractually obligated to only process personal data according to our instructions, and conduct or intend to conduct diligence to ensure that they have sufficient technical and organizational security measures in place.

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

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

Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending and services, and any inability on our part to effectively adapt to such changes could substantially affect our business, prospects, operating results and financial condition.

Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. Certain of these automatic cuts have been implemented resulting in reductions in Medicare payments to physicians, hospitals, and other healthcare providers, among other things. Under federal legislation, including the Bipartisan Budget Act of 2018, these reductions, while temporarily altered due to the COVID-19 pandemic, have resumed as of July 1, 2022 and will stay in effect through 2032 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, the American Rescue Plan Act of 2021 increased the budget deficit such that additional sequestration was required under the Statutory Pay-As-You-Go Act of 2010, which led to a further payment reduction, up to 4%, that was to take effect in January 2022, although implementation of the reduction was delayed until 2025. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for our approved products or any of our product candidates for which we may obtain regulatory approval, or the frequency with which our products or any future product is prescribed or used. It is uncertain how current and future reforms, including any new legislation enacted during the current presidential administration, in these areas will influence the future of our business operations and financial condition.

Previous actions taken by Congress to reduce spending, disagreements in Congress over government funding levels, high-levels of government debt, and the Medicare Trustees' warnings about the programs' sustainability as presently structured suggest that uninterrupted/continued growth in funding for relevant programs is not guaranteed. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell our approved products and any other products we may develop.

If we fail to comply with our obligations under the 340B Drug Pricing Program and other U.S. governmental pricing programs, we could be subject to legal consequences, including penalties, sanctions and fines, which could have a material adverse effect on our business, prospects, operating results and financial condition.

We participate in the 340B Drug Pricing Program, Medicaid Drug Rebate Program, and a number of other federal and state government programs in the U.S. Participation in some of these programs is required in order to obtain reimbursement of our drug products under Medicaid or Medicare Part B. These programs generally require that we provide discounts or pay rebates to certain payors when our products are dispensed to beneficiaries of these programs. To support the calculation of these discounts and rebates, these programs may also impose periodic and special price and product data reporting requirements. Changes to our obligations under these government pricing programs occur frequently and program requirements are often ambiguous. Pricing calculations are complex, vary across programs and may be subject to evolving interpretations by legislative and regulatory bodies and the courts. We may be or become subject to penalties for noncompliance, including, but not limited to, civil monetary penalties, exposure under the federal false claims act, and termination from the government program, as a result

of our failure to comply with obligations under these programs, including if we fail to provide timely, complete and accurate information to the government, to pay the correct rebates, or to offer the correct discounted pricing. In addition, potential policy changes by the current presidential administration may introduce additional uncertainty for our business. These could include changes to the level of scrutiny applied by the Health Resources and Services Administration to enforce non-compliance with the 340B Drug Pricing Program, new price restrictions on products we sell to Medicaid, Medicare or other government purchasers, or other regulatory changes impacting reimbursement or competitive dynamics in multisource markets. Any such policy shifts could significantly impact our business and operations.

Increasingly, states are enacting legislation requiring manufacturers to report drug pricing information. However, states have not always clearly defined their reporting requirements, resulting in manufacturers failing to properly disclose the required pricing information. Complying with federal and state programs and future changes to these programs can be complex and cost-and resource-intensive, and could have a material adverse effect on our business, prospects, operating results and financial condition.

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, prospects, operating results and financial condition.

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

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements or insider trading violations, which could significantly harm our business, prospects, operating results and financial condition.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with governmental regulations, including healthcare fraud and abuse and anti-kickback laws and regulations in the U.S. and abroad, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. As discussed in the Risk Factor above captioned "If we or our collaborators, CMOs or service providers fail to comply with healthcare laws and regulations, or legal obligations related to privacy, data protection and information security, we or they could be subject to enforcement actions, which could negatively impact our ability to develop, market and sell our products and may harm our reputation," these laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including improper trading based upon, material information obtained in the course of clinical trials or other material non-public information, which could result in regulatory sanctions and serious harm to our reputation. We maintain a global compliance program and remain focused on its evolution and enhancement. Our program includes efforts such as risk assessment and monitoring, fostering a speak-up culture encouraging employees and third parties to raise good faith questions or concerns, and defined processes and systems for reviewing and remediating allegations and identified potential concerns. It is not always possible, however, to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, prospects, operating results and financial condition, including the imposition of significant fines or other sanctions.

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

Our research, development and manufacturing activities involve the use of hazardous materials, chemicals and various radioactive compounds. We maintain quantities of various flammable and toxic chemicals in our facilities in Cambridge and Norton that are required for our research, development and manufacturing activities. We are subject to federal, state and local

laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Cambridge and Norton facilities comply with the relevant guidelines of the City of Cambridge, the town of Norton, the Commonwealth of Massachusetts and the Occupational Safety and Health Administration of the U.S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Risks Related to Patents, Licenses and Trade Secrets

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

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

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we may rely on third-party collaborators to file patent applications relating to proprietary technology that we develop jointly as part of collaborations. The process of obtaining patent protection is expensive and time-consuming. If we or our 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 milestone and/or royalty payments to us from third party licensors and could have a material adverse effect on our business.

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

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

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

We license patent rights from third-party owners. If such owners do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, our competitive position and business, prospects, operating results and financial condition 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, Ionis, Arbutus, and Dicerna. We may also 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 we have 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, operating results and financial condition. 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 growing scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of RNAi patents and have licensed many of these patents from third parties on an exclusive basis. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics.

Specifically, we have a portfolio of patents, patent applications and other intellectual property covering, among other things: 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 continues to mature, patent applications are being fully processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference, re-examination and opposition proceedings, as well as pre- and post-grant review proceedings in various patent offices relating to patent rights in the RNAi field. In addition, third parties may challenge the validity of our patents. We expect that challenges will be raised relating to 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, prospects, operating results and financial condition if we are not successful in defending the patentability and scope of our pending and issued patent claims. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business, prospects, operating results and financial condition and on 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 products marketed by us or our licensees, our late-stage therapeutic candidates being developed by us or our collaborators, including zilebesiran and fitusiran, as well as our other pipeline products. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for siRNA drugs we wish to develop. In addition, there may be issued and pending patent applications that may be asserted against us in a court proceeding or otherwise based upon the asserting party's belief that we may need such patents for our siRNA therapeutic candidates or marketed products, or to further

develop and commercialize future products, or to continue to develop candidates in our pipeline that are being developed by us or our collaborators. 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 or at all and/or a court rules that we need such patent rights that have been asserted against us, we may be unable to market our products, including AMVUTTRA, ONPATTRO, GIVLAARI or OXLUMO, or to perform research and development or other activities covered by such patents. For example, on December 12, 2024, the Board of Regents of the University of Texas System, or the University of Texas, filed a lawsuit in the United States District Court for the Western District of Texas, alleging that we infringe one of the University of Texas' patents by making, using and commercializing ONPATTRO in the U.S.

If we become involved in intellectual property litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, and in the case of such litigation or proceedings against us, substantial liability for damages or be required to stop our product development and commercialization efforts.

Third parties may sue us for infringing their patent rights. For example, on December 12, 2024, the Board of Regents of the University of Texas System, or the University of Texas, filed a lawsuit in the United States District Court for the Western District of Texas, alleging that we infringe one of the University of Texas' patents by making, using and commercializing ONPATTRO in the U.S. In February 2025, we filed a motion to dismiss for improper venue and an alternative motion to transfer the case to the U.S. District Court for the District of Massachusetts. On July 2, 2025, the Court denied the motions to dismiss without prejudice, permitting us to refile the motions following the conclusion of venue discovery. Third parties may also claim that we have improperly obtained or used their confidential or proprietary information.

Furthermore, third parties may challenge the inventorship of our patents or licensed patents. For example, in March 2011, The University of Utah, or Utah, filed a complaint against us, Max Planck Gesellschaft Zur Foerderung Der Wissenschaften e.V. and Max Planck Innovation, together, Max Planck, Whitehead, MIT and the University of Massachusetts, claiming that a professor of Utah was the sole inventor, or in the alternative, a joint inventor of certain of our in-licensed patents. Utah was seeking correction of inventorship of the Tuschl patents, unspecified damages and other relief. After several years of court proceedings and discovery, the court granted our motions for summary judgment and dismissed Utah's state law damages claims. During the pendency of this litigation, 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.

On July 12, 2024, Acuitas Therapeutics Inc., or Acuitas, filed a declaratory judgment action against us in the U.S. District Court for the District of Delaware, seeking a judgment adding certain Acuitas employees as co-inventors on the patents we have asserted against Pfizer/BioNTech and Moderna in our lawsuits described below. On September 19, 2024, we filed a motion to dismiss arguing that Acuitas did not have standing to sue and failed to state a claim upon which relief could be granted. On July 1, 2025, the District Court granted our motion to dismiss the complaint without prejudice, finding that Acuitas had failed to plead facts sufficient to establish standing.

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. In March 2022, we filed separate lawsuits in United States District Court for the District of Delaware against (1) Moderna and certain of its subsidiaries and (2) Pfizer and one of its subsidiaries, seeking damages for patent infringement in the parties' manufacture and sale of their messenger RNA, or mRNA, COVID-19 vaccines. In May 2022, Pfizer joined BioNTech SE to the Pfizer lawsuit and filed counterclaims. Following claim construction rulings of the District court in the Moderna lawsuit in 2023, we and Moderna jointly agreed to a final judgment of non-infringement of two of our patents, and we appealed the claim construction ruling to the Court of Appeals for the Federal Circuit. The claim construction ruling initially did not affect a third patent in the Moderna lawsuit, but in September 2024, the District Court entered a ruling in which it construed this third patent in the same manner as the other patents, and in October 2024, we and Moderna jointly agreed to final judgment of non-infringement with respect to the third patent while preserving all rights to appeal. In October 2024, Moderna filed a motion seeking recovery of fees incurred by them from the time we agreed to a judgment of non-infringement with respect to the first two patents until the time we agreed to a judgment of non-infringement with respect to the third patent, which period runs from approximately September 2023 to October 2024. We opposed the motion in a reply on November 6, 2024. The court has yet to rule on the motion. In June 2025, following oral argument, the Court of Appeals for the Federal Circuit affirmed the District Court's claim construction ruling. We are currently considering our options with respect to any further action on this ruling.

In the Pfizer lawsuit, the District Court issued an order in April 2025 that effectively placed the Pfizer product outside the coverage of our asserted patents. On May 13, 2025, we and Pfizer filed a joint motion seeking to stay all proceedings with a stipulation to non-infringement, which the District Court granted on the same day. On July 30, 2025, the District Court granted Pfizer's motion for summary judgment of non-infringement and entered final judgment of non-infringement. We are currently evaluating our options, including a potential appeal to the Court of Appeals for the Federal Circuit.

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 all claims in the litigation between us.

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 such intellectual property rights, even if resolved in our favor, could be substantial, and litigation would divert our management's efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation or legal proceeding could delay our research, development and commercialization efforts and limit our ability to continue our operations.

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

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

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license or render the license non-exclusive, which could result in us being unable to develop, manufacture, market and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, we could incur significant costs and/or disruption to our business and distraction of our management defending against any breach of such licenses alleged by the licensor. For example, in June 2018, Ionis sent us a notice claiming that it was owed technology access fees, or TAFs, based on rights granted and amounts paid to us in connection with the January 2018 amendment of our collaboration agreement with Sanofi and the related Exclusive TTR License and AT3 License Terms. Following arbitration proceedings, the panel ruled in favor of each party on certain TAF associated claims and awarded Ionis compensation of $41.2 million for a TAF on certain rights we received in the Sanofi restructuring.

Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we will be required to pay on sales of each of our approved products or future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in such products. Therefore, even if we successfully develop and commercialize products, we may be unable to 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, potential collaborators, employees, consultants, scientific advisors, CMOs, 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, other third parties 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 business, prospects, operating results and financial condition.

Risks Related to Competition

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

- substantially greater financial, technical and human resources than we have;
- more extensive experience in preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;
- multiple 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 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 have developed products. In addition, there are a number of drugs currently under development and that may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. These drugs may be more effective, safer, less expensive, have more convenient administration or be marketed and sold more effectively, than any products we develop and commercialize.

For example, AMVUTTRA for the treatment of ATTR amyloidosis with cardiomyopathy, competes with VYNDAQEL/VYNDAMAX (tafamidis), which is marketed by Pfizer, and ATTRUBY (acoramidis), which is marketed by BridgeBio, both of which are approved to treat ATTR amyloidosis with cardiomyopathy. While we believe AMVUTTRA has a competitive profile for the treatment of patients with ATTR amyloidosis with cardiomyopathy, both VYNDAQEL/VYNDAMAX and ATTRUBY are administered in pill form and are available in the U.S. at lower list prices than AMVUTTRA, which may impact our ability to compete favorably with these products and may result in AMVUTTRA not achieving commercial success. We are also aware of other product candidates in clinical development for the treatment of ATTR amyloidosis with cardiomyopathy, including WAINUA (eplontersen), which is being developed by Ionis and AstraZeneca plc, or AstraZeneca, and is in Phase 3 clinical development; nexiguran ziclumeran (formerly NTLA-2001), which is being developed by Intellia Therapeutics, Inc. and Regeneron and is in Phase 3 clinical development; ALN-2220 (formerly NI006), which is being developed by Neurimmune AG and Alexion Pharmaceuticals, Inc. (a subsidiary of AstraZeneca) and is in Phase 3 clinical development; coramitug (NNC-6019-0001), which is being developed by Novo Nordisk and is in Phase 2 clinical development; and AT0-2, which is being developed by Attralus, Inc. and is in Phase 2 clinical development. We expect to face competition from any of these and potentially other additional new drugs that enter the market to treat patients with ATTR amyloidosis with cardiomyopathy.

AMVUTTRA and ONPATTRO are also approved in certain jurisdictions for the treatment of certain patients with hATTR amyloidosis with polyneuropathy. We are aware of other approved products used to treat this disease, including WAINUA (eplontersen), VYNDAQEL/VYNDAMAX (tafamidis), and TEGSEDI (inotersen), which is marketed by Ionis. There are also product candidates in various stages of clinical development for the treatment of hATTR amyloidosis patients with polyneuropathy, including ATO-02, which is in Phase 2 clinical development, and nexiguran ziclumeran (formerly NTLA-2001), which is in Phase 1 clinical development. It is possible that AMVUTTRA and/or ONPATTRO may not compete favorably with these products and product candidates, or others, and, as a result, may not achieve commercial success.

We are aware of approved products and product candidates in various stages of clinical development for the treatment of PH1 that would compete with OXLUMO, our RNAi therapeutic approved in the U.S. and EU for the treatment of this disease, including Novo Nordisk's RIVFLOZA (nedosiran), which was approved for the treatment of PH1 in September 2023 and launched in the U.S. in early 2024. RIVFLOZA is a once-monthly subcutaneous RNAi therapy that was developed by Dicerna. In April 2020, we and Dicerna granted each other a non-exclusive cross-license to our respective intellectual property related to lumasiran and Dicerna's nedosiran. In addition, several companies have investigational drugs in clinical development for the treatment of PH1, including Biocodex, Inc. in collaboration with M8 Pharmaceuticals, Inc., and YolTech Therapeutics.

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

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

- reimbursement coverage; and
- patent position.

Our competitors may develop or commercialize products with significant advantages over any products we or our collaborators develop based on any of the factors listed above or on other factors. In addition, our competitors may enter into collaborations with or receive funding from larger pharmaceutical or biotechnology companies, providing them with an advantage over us and our collaborators. Our competitors may therefore be more successful in commercializing their products than we or our collaborators are, which could adversely affect our competitive position and business, prospects, operating results and financial condition. Competitive products may make any products we or our collaborators 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 our ability to execute on our business plan. Furthermore, we and our collaborators 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 and our collaborators are targeting could make our or our collaborators' product candidates noncompetitive, obsolete or uneconomical.

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

In addition to the competition we face from competing drugs in general, we and our collaborators 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 with synthetic, exogenously-introduced genes designed to produce siRNA-like molecules within cells. Companies working on chemically synthesized siRNAs include, but are not limited to, Arrowhead and its collaborators, Takeda Pharmaceutical Company Ltd., Janssen Pharmaceutics, Inc., GlaxoSmithKline plc, and Amgen Inc.; Quark Pharmaceuticals, Inc.; Roche; Silence Therapeutics plc and its collaborators, AstraZeneca, Jiangsu Hansoh Pharmaceuticals Group Co., Ltd., and Mallinckrodt plc; Arbutus; Sylentis; Novo Nordisk and its collaborators, Aro Biotherapeutics Company, Boehringer Ingelheim and Eli Lilly and Company; and our collaborators Regeneron, Sanofi and Vir. In addition, we granted licenses or options for licenses to Ionis, Benitec Biopharma Ltd., Arrowhead, Arbutus, Quark, Sylentis and other companies 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 we do. In addition, as a result of agreements that we have entered into, Takeda has obtained a non-exclusive license, and Arrowhead, as the assignee of Novartis, has obtained specific exclusive licenses for 30 gene targets, that include access to certain aspects of our technology.

We and our collaborators also compete with companies working to develop antisense-based drugs. Similar to RNAi therapeutics, antisense drugs target mRNAs in order to suppress the activity of specific genes. Akcea Therapeutics, Inc., a wholly owned subsidiary of Ionis, has received marketing approval for an antisense drug, inotersen, for the treatment of adult hATTR amyloidosis patients with stage 1 or stage 2 polyneuropathy. Several antisense drugs developed by Ionis have been approved and are currently marketed, including WAINUA (eplontersen), and Ionis has multiple antisense product candidates in clinical trials. Ionis is also developing antisense drugs using ligand-conjugated GalNAc technology licensed from us, and these drugs have been shown to have increased potency at lower doses in clinical and preclinical studies, compared with antisense drugs that do not use such licensed GalNAc technology. The development of antisense drugs 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. If our competitors develop safe and effective means to deliver siRNAs to the relevant cell and tissue types, our ability to successfully commercialize a competitive product would be adversely affected. In addition, third parties are expending substantial resources to discover and develop a safe and effective means of delivering siRNAs into the relevant cell and tissue types, including both private companies and academic laboratories. Some of our competitors have substantially greater resources than we do, and if our competitors negotiate exclusive access to delivery solutions developed by third parties, we may be unable to successfully commercialize our product candidates.

Risks Related to Our Common Stock

Our stock price has been and may in the future be volatile, and an investment in our common stock could suffer a decline in value.

Our stock price has been and may in the future be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme price and volume volatility that has often been unrelated to the operating

performance of particular companies. The market price of our common stock in the future could be significantly and adversely affected by many factors, including:

- the information contained in our quarterly earnings releases and other public announcements, including updates regarding our or our collaborators' commercialized products or product candidates, our net product and collaboration revenues and operating expenses for completed periods and financial guidance regarding future periods;
- the success of existing or new competitive products or technologies;
- regulatory actions with respect to our or our collaborators' products or product candidates;
- announcements by us or our competitors of significant acquisitions, collaborations, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of our or our collaborators' product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our or our collaborators' development programs;
- results of clinical trials of our competitors' product candidates;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our or our collaborators' efforts to develop additional product candidates or products;
- actual or anticipated changes in financial results or development timelines;
- announcement or expectation of financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by any of the securities analysts that cover us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including the extent to which such conditions are impacted by administrative and policy decisions globally and in the U.S.; and
- the other factors described in this "Risk Factors" section.

In the past, securities class action litigation has often been brought against companies following declines in the market price of their securities. This risk is especially relevant for biopharmaceutical companies, which have experienced significant stock price volatility in recent years. We may be the target of securities litigation that could result in substantial costs and divert our management's attention and resources, which could cause serious harm to our business, prospects, operating results and financial condition. We maintain liability insurance; however, if any costs or expenses associated with litigation exceed our insurance coverage, we may be forced to bear some or all of these costs and expenses directly, which could be substantial. In addition, we have obligations to indemnify third parties, including our officers and directors, in connection with certain litigation, and those obligations may not be covered by insurance.

Sales of a substantial number of shares of our common stock, including by us, our officers or directors, or our significant stockholders, into the public market could cause the price of our common stock to decline.

A small number of our stockholders beneficially own a substantial amount of our common stock. As of June 30, 2025, our seven largest stockholders beneficially owned in excess of 50% of our outstanding shares of common stock. If we, our officers or directors, or our significant stockholders sell substantial amounts of our common stock in the public market, or there is a perception that such sales may occur, the market price of our common stock could be adversely affected. Sales of common stock by our significant stockholders might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

Anti-takeover provisions in our governing 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 or members of our board of directors.

Provisions in our certificate of incorporation and our bylaws may delay or prevent an acquisition of us or a change in the current members of our management or the members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of our board of directors are not elected at one time;
- establish a prohibition on actions by our stockholders by written consent;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors;
- allow the authorized number of our directors to be changed only by resolution of our board of directors.
- limit who may call a special meeting of stockholders;
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws;
- limit the manner in which stockholders can remove directors from our board of directors; and
- establish advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings.

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

Risks Related to Our Convertible Notes

We may not have sufficient cash flow from our business to pay our indebtedness.

As of June 30, 2025, we had $1.04 billion in total aggregate principal amount of Notes issued and outstanding. The interest rate for the Notes is fixed at 1.00% per annum and is payable semi-annually in arrears on March 15 and September 15 of each year. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the Notes, or to make cash payments in connection with any conversions of Notes, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt and make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional debt financing or equity capital on terms that may be onerous or highly dilutive. Our ability to refinance any future indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

In addition, our indebtedness, combined with our other financial obligations and contractual commitments, could have other important consequences. For example, it could:

- make us more vulnerable to adverse changes in general U.S. and worldwide economic, industry and competitive conditions and adverse changes in government regulation;
- limit our flexibility in planning for, or reacting to, changes in our business and our industry;
- place us at a disadvantage compared to our competitors who have less debt;
- limit our ability to borrow additional amounts to fund acquisitions, for working capital and for other general corporate purposes; and
- make an acquisition of our company less attractive or more difficult.

Any of these factors could harm our business, prospects, operating results and financial condition. In addition, if we incur additional indebtedness, the risks related to our business and our ability to service or repay our indebtedness would increase.

We may not have the ability to raise the funds necessary to settle for cash conversions of the Notes or to repurchase the Notes for cash upon a fundamental change.

Holders of the Notes have the right to require us to repurchase their Notes upon the occurrence of a fundamental change (as defined in the indenture governing the Notes) at a repurchase price equal to 100% of the principal amount of the Notes to be

repurchased, plus accrued and unpaid interest, if any. Upon conversion of the Notes, unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional share), we will be required to make cash payments in respect of the Notes being converted. We may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of Notes surrendered or Notes being converted. In addition, our ability to repurchase the Notes or to pay cash upon conversions of the Notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase Notes at a time when the repurchase is required by the indenture governing such notes or to pay any cash payable on future conversions of the Notes as required by such indenture would constitute a default under such indenture. A default under the indenture governing the Notes or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the Notes or make cash payments upon conversions.

The conditional conversion feature of the Notes, if triggered, may adversely affect our liquidity.

In the event the conditional conversion feature of the Notes is triggered, holders of the Notes will be entitled to convert the Notes at any time during specified periods at their option. If one or more holders elect to convert their Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock (other than paying cash in lieu of delivering any fractional share), we would be required to settle a portion or all of our conversion obligation through the payment of cash, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the Notes as a current liability, rather than long-term liability, which would result in a material reduction of our net working capital.

Transactions relating to the Notes may affect the value of our common stock.

The conversion of some or all of the Notes would dilute the ownership interests of existing stockholders to the extent we satisfy our conversion obligation by delivering shares of our common stock upon any conversion of such Notes. The Notes may become in the future convertible at the option of their holders under certain circumstances. If holders of the Notes elect to convert their notes, we may settle our conversion obligation by delivering to them a significant number of shares of our common stock, which would cause dilution to our existing stockholders.

In addition, in connection with the issuance of the Notes, we entered into the Capped Calls with certain financial institutions, or the Option Counterparties. The Capped Calls are generally expected to reduce potential dilution to our common stock upon any conversion or settlement of the Notes and/or offset any cash payments we are required to make in excess of the principal amount of converted Notes, with such reduction and/or offset subject to a cap.

In connection with establishing their initial hedges of the Capped Calls, the Option Counterparties or their respective affiliates entered into various derivative transactions with respect to our common stock and/or purchased shares of our common stock concurrently with or shortly after the pricing of the Notes.

From time to time, the Option Counterparties or their respective affiliates may modify their hedge positions by entering into or unwinding various derivative transactions with respect to our common stock and/or purchasing or selling our common stock or other securities of ours in secondary market transactions prior to the maturity of the Notes (and are likely to do so following any conversion of the Notes, any repurchase of the Notes by us on any fundamental change repurchase date, any redemption date, or any other date on which the Notes are retired by us, in each case, if we exercise our option to terminate the relevant portion of the Capped Calls). This activity could cause a decrease and/or increased volatility in the market price of our common stock.

We do not make any representation or prediction as to the direction or magnitude of any potential effect that the transactions described above may have on the price of the Notes or our common stock. In addition, we do not make any representation that the Option Counterparties will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

We are subject to counterparty risk with respect to the Capped Calls.

The Option Counterparties are financial institutions, and are subject to the risk that any or all of them might default under the Capped Calls. Our exposure to the credit risk of the Option Counterparties will not be secured by any collateral. Past global economic conditions have resulted in the actual or perceived failure or financial difficulties of many financial institutions. If an Option Counterparty becomes subject to insolvency proceedings, we will become an unsecured creditor in those proceedings with a claim equal to our exposure at that time under the Capped Calls with such Option Counterparty. Our exposure will depend on many factors but, generally, an increase in our exposure will be correlated to an increase in the market price and in the volatility of our common stock. In addition, upon a default by an Option Counterparty, we may suffer adverse tax consequences and more dilution than we currently anticipate with respect to our common stock. We can provide no assurances as to the financial stability or viability of the Option Counterparties.

The accounting method for convertible debt securities that may be settled in cash, such as the Notes, could have a material effect on our reported financial results.

The accounting method for reflecting the Notes on our condensed consolidated balance sheet, accruing interest expense for the Notes and reflecting the underlying shares of our common stock in our reported diluted earnings per share may adversely affect our reported earnings and financial condition.

The Notes are reflected as a liability on our condensed consolidated balance sheets, with the initial carrying amount equal to the principal amount of the Notes, net of issuance costs. The issuance costs were treated as a debt discount for accounting purposes, which is being amortized into interest expense over the term of the Notes. As a result of this amortization, the interest expense that we expect to recognize for the Notes for accounting purposes will be greater than the cash interest payments we will pay on the Notes, which will result in lower reported net income or higher reported net loss, as the case may be.

In addition, the shares of common stock underlying the Notes are reflected in our diluted earnings per share using the "if-converted" method, in accordance with ASU 2020-06. Under this method, diluted earnings per share is generally calculated assuming that all the Notes were converted solely into shares of common stock at the beginning of the reporting period, unless the result would be anti-dilutive. The application of the if-converted method may reduce our reported diluted earnings per share to the extent we are profitable in the future, and accounting standards may change in the future in a manner that may adversely affect our diluted earnings per share.

Furthermore, if any of the conditions to the convertibility of the Notes is satisfied, then we may be required under applicable accounting standards to reclassify the liability carrying value of the Notes as a current, rather than a long-term, liability. This reclassification could be required even if no holders actually convert their Notes and could materially reduce our reported working capital.

ITEM 5. OTHER INFORMATION

Adoption of 10b5-1 Trading Plans by Our Officers and Directors

During our fiscal quarter ended June 30, 2025, certain of our officers (as defined in Rule 16a-1(f) under the Exchange Act) and directors entered into contracts, instructions or written plans for the purchase or sale of our securities that are intended to satisfy the conditions specified in Rule 10b5-1(c) under the Exchange Act for an affirmative defense against liability for trading in securities on the basis of material nonpublic information. We refer to these contracts, instructions, and written plans as "Rule 10b5-1 trading plans" and each as a "Rule 10b5-1 trading plan." We describe the material terms of these Rule 10b5-1 trading plans below.

Dennis A. Ausiello, M.D., Director

On May 15, 2025, Dennis A. Ausiello, a member of our board of directors, entered into a Rule 10b5-1 trading plan that provides that Dr. Ausiello, acting through a broker, may sell up to an aggregate of 31,448 shares of our common stock received upon the exercise of options granted to Dr. Ausiello as director compensation, subject to adjustments for stock splits, stock combinations, stock dividends and other similar changes to our common stock. Sales of shares under the plan may only occur if the market price of our common stock is above specified prices from August 13, 2025 to May 1, 2026. The plan is scheduled to terminate on May 1, 2026, subject to earlier termination upon the sale of all shares subject to the plan, upon termination by Dr. Ausiello or the broker, or as otherwise provided in the plan.

Colleen F. Reitan, Director

On June 10, 2025, Colleen F. Reitan, a member of our board of directors, entered into a Rule 10b5-1 trading plan that provides that Ms. Reitan, acting through a broker, may sell up to an aggregate of 18,000 shares of our common stock received upon the exercise of options granted to Ms. Reitan as director compensation, subject to adjustments for stock splits, stock combinations, stock dividends and other similar changes to our common stock. Sales of shares under the plan may only occur if the market price of our common stock is above specified prices from September 9, 2025 to May 15, 2026. The plan is scheduled to terminate on May 15, 2026, subject to earlier termination upon the sale of all shares subject to the plan, upon termination by Ms. Reitan or the broker, or as otherwise provided in the plan.

Tolga Tanguler, Chief Commercial Officer

On May 27, 2025, Tolga Tanguler, our Chief Commercial Officer, entered into a Rule 10b5-1 trading plan that provides that Mr. Tanguler, acting through a broker, may sell up to an aggregate of 3,474 shares of our common stock received upon the settlement of awards granted to Mr. Tanguler as equity incentive compensation, subject to adjustments for stock splits, stock combinations, stock dividends and other similar changes to our common stock. Sales of shares under the plan may only occur from August 29, 2025 to May 10, 2026. The plan is scheduled to terminate on May 10, 2026, subject to earlier termination upon the sale of all shares subject to the plan, upon termination by Mr. Tanguler or the broker, or as otherwise provided in the plan.

ITEM 6. EXHIBITS

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.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)

#	Filed herewith.
+	This certification will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

SIGNATURES

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

ALNYLAM PHARMACEUTICALS, INC.

Date: July 31, 2025

/s/ Yvonne L. Greenstreet, M.D.

Yvonne L. Greenstreet, M.D.
Chief Executive Officer
(Principal Executive Officer)

Date: July 31, 2025

/s/ Jeffrey V. Poulton

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

EXHIBIT 31.1

CERTIFICATION

I, Yvonne L. Greenstreet, M.D., certify that:

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

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

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

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

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

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

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

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

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

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

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

Dated: July 31, 2025

/s/ Yvonne L. Greenstreet, M.D.

Yvonne L. Greenstreet, M.D.
Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Jeffrey V. Poulton, certify that:

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

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

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

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

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

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

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

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

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

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

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

Dated: July 31, 2025

/s/ Jeffrey V. Poulton

Jeffrey V. Poulton
Executive Vice President, Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT

TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Alnylam Pharmaceuticals, Inc. (the "Company") for the quarter ended June 30, 2025 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Yvonne L. Greenstreet, M.D., Chief Executive Officer of the Company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: July 31, 2025

/s/ Yvonne L. Greenstreet, M.D.

Yvonne L. Greenstreet, M.D.
Chief Executive Officer

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

EXHIBIT 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT

TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Alnylam Pharmaceuticals, Inc. (the "Company") for the quarter ended June 30, 2025 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jeffrey V. Poulton, Executive Vice President, Chief Financial Officer, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: July 31, 2025

/s/ Jeffrey V. Poulton

Jeffrey V. Poulton
Executive Vice President, Chief Financial Officer

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