UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

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

For the quarterly period ended September 30, 2022

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 x 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 x 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	x	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 x

At October 21, 2022, the registrant had 123,028,234 shares of Common Stock, $0.01 par value per share, outstanding.

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

TABLE OF CONTENTS

	PAGE NUMBER
PART I. FINANCIAL INFORMATION	
ITEM 1. FINANCIAL STATEMENTS (Unaudited)	
CONDENSED CONSOLIDATED BALANCE SHEETS AS OF SEPTEMBER 30, 2022 AND DECEMBER 31, 2021	5
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS FOR THE THREE AND NINE MONTHS ENDED SEPTEMBER 30, 2022 AND 2021	6
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY FOR THE THREE AND NINE MONTHS ENDED SEPTEMBER 30, 2022 AND 2021	7
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS FOR THE NINE MONTHS ENDED SEPTEMBER 30, 2022 AND 2021	9
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS	10
ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS	29
ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK	40
ITEM 4. CONTROLS AND PROCEDURES	40
PART II. OTHER INFORMATION	
ITEM 1. LEGAL PROCEEDINGS	41
ITEM 1A. RISK FACTORS	41
ITEM 6. EXHIBITS	78
SIGNATURES	79

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our views with respect to the potential for approved and investigational RNAi therapeutics, including ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA, Leqvio® (inclisiran), fitusiran and zilebesiran;
- our plans for additional global regulatory filings and the continuing product launches of ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA and our partner's plans with respect to Leqvio;
- risks related to the direct or indirect impact of the novel coronavirus, or COVID-19, global pandemic, emerging or future variants of COVID-19 or any future pandemic, such as the scope and duration of the pandemic, government actions and restrictive measures implemented in response, the effectiveness of vaccination and booster vaccination campaigns, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by our products, or in patient enrollment in clinical trials, potential clinical trial, regulatory review and inspection or supply chain disruptions, and other potential impacts to our business;
- our expectations regarding potential market size for, and the successful commercialization of, ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA, Leqvio or any future products;
- our ability to obtain and maintain regulatory approvals and pricing and reimbursement for ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA or any future products, and our partners' ability with respect to Leqvio and fitusiran;
- the progress of our research and development programs, including programs in both rare and prevalent diseases;
- our future ability to successfully expand the indications for ONPATTRO, AMVUTTRA and OXLUMO;
- the potential for improved product profiles to emerge from our new technologies, including our IKARIA and GEMINI platforms and our ability to successfully advance our delivery efforts in extrahepatic tissues;
- our current and anticipated clinical trials and expectations regarding the reporting of data from these trials;
- any impact of the on-going conflict in Ukraine and the imposition of related government sanctions on our business and operations, including disruptions to our clinical trials;
- the timing of regulatory filings and interactions with or actions or advice of regulatory authorities, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing or the timing or likelihood of regulatory approvals;
- the status of our manufacturing operations and any delays, interruptions or failures in the manufacture and supply of ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA or any of our product candidates (or other products or product candidates being developed and commercialized by our partners), by our or their contract manufacturers or by us or our partners;
- our progress continuing to build and leverage our global commercial infrastructure;
- the possible impact of any competing products on the commercial success of ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA and Leqvio, as well as our product candidates, and, our, or with respect to Leqvio or fitusiran, our partners', ability to compete against such products;
- our ability to manage our growth and operating expenses;
- our views and plans with respect to our 5-year *Alnylam P^{5}x25* strategy and our intentions to achieve the metrics associated with this strategy, including to become a top five biotech company by the end of 2025;
- our belief that our current cash balance should enable us to achieve a self-sustainable profile without the need for future equity financing;
- our expectations regarding the length of time our current cash, cash equivalents and marketable equity and debt securities will support our operations based on our current operating plan;
- our dependence on third parties for development, manufacture and distribution of products;

- our expectations regarding our corporate collaborations, including potential future licensing fees and milestone and royalty payments under existing or future agreements;
- 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 and to successfully execute on our *Alnylam P^{5}x25* strategy;
- the outcome of litigation, including our patent infringement suits against Pfizer, Inc., BioNTech SE and Moderna, Inc., or other legal proceedings or of any current or future government investigation, including the investigation related to the subpoena received on or about April 9, 2021 pertaining to our marketing and promotion of ONPATTRO in the United States, or U.S.;
- regulatory developments in the U.S. and foreign countries;
- the impact of laws and regulations;
- developments relating to our competitors and our industry;
- our ability to satisfy our payment obligations, remain in compliance with covenants under our debt agreements 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 the Notes, to the extent required;
- our expectations regarding the effect of the capped call transactions and regarding the anticipated market activities of the option counterparties and/or their respective affiliates; and
- other risks and uncertainties, including those listed under the caption Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q.

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

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

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

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

	September 30, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 1,073,228	$ 819,975
Marketable debt securities	1,169,050	1,548,617
Marketable equity securities	23,051	66,972
Accounts receivable, net	184,513	198,571
Inventory	115,489	86,363
Prepaid expenses and other current assets	125,516	88,078
Total current assets	2,690,847	2,808,576
Property, plant and equipment, net	514,821	501,958
Operating lease right-of-use assets	218,802	231,675
Restricted investments	49,389	40,891
Other assets	61,396	60,204
Total assets	$ 3,535,255	$ 3,643,304
LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY		
Current liabilities:		
Accounts payable	$ 40,572	$ 73,426
Accrued expenses	510,579	395,174
Operating lease liability	41,581	40,548
Deferred revenue	144,208	149,483
Liability related to the sale of future royalties	35,851	37,079
Total current liabilities	772,791	695,710
Operating lease liability, net of current portion	266,323	281,347
Deferred revenue, net of current portion	132,930	152,360
Convertible debt	1,015,975	—
Long-term debt	—	675,697
Liability related to the sale of future royalties, net of current portion	1,231,873	1,151,024
Other liabilities	183,001	98,963
Total liabilities	3,602,893	3,055,101
Commitments and contingencies (Note 14)		
Stockholders' (deficit) equity:		
Preferred stock, $0.01 par value per share, 5,000 shares authorized and no shares issued and outstanding as of September 30, 2022 and December 31, 2021	—	—
Common stock, $0.01 par value per share, 250,000 shares authorized; 122,991 shares issued and outstanding as of September 30, 2022; 120,182 shares issued and outstanding as of December 31, 2021	1,230	1,202
Additional paid-in capital	6,336,771	6,058,453
Accumulated other comprehensive loss	(43,783)	(33,259)
Accumulated deficit	(6,361,856)	(5,438,193)
Total stockholders' (deficit) equity	(67,638)	588,203
Total liabilities and stockholders' (deficit) equity	$ 3,535,255	$ 3,643,304

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Statements of Operations				
Revenues:				
Net product revenues	$ 232,267	$ 167,044	$ 632,654	$ 463,624
Net revenues from collaborations	29,297	20,136	64,267	121,328
Royalty revenue	2,742	453	5,462	800
Total revenues	264,306	187,633	702,383	585,752
Operating costs and expenses:				
Cost of goods sold	36,507	28,091	94,002	81,370
Cost of collaborations and royalties	4,609	4,572	23,549	21,110
Research and development	245,371	194,572	620,976	563,106
Selling, general and administrative	235,859	142,075	560,314	434,257
Total operating costs and expenses	522,346	369,310	1,298,841	1,099,843
Loss from operations	(258,040)	(181,677)	(596,458)	(514,091)
Other (expense) income:				
Interest expense	(41,084)	(40,274)	(126,055)	(106,205)
Other (expense) income, net	(30,233)	17,715	(120,873)	28,454
Loss on the extinguishment of debt	(76,586)	—	(76,586)	—
Total other expense, net	(147,903)	(22,559)	(323,514)	(77,751)
Loss before income taxes	(405,943)	(204,236)	(919,972)	(591,842)
Benefit from (provision for) income taxes	23	(278)	(3,691)	(2,522)
Net loss	$ (405,920)	$ (204,514)	$ (923,663)	$ (594,364)
Net loss per common share - basic and diluted	$ (3.32)	$ (1.72)	$ (7.62)	$ (5.04)
Weighted-average common shares used to compute basic and diluted net loss per common share	122,166	119,141	121,158	118,005
Statements of Comprehensive Loss				
Net loss	$ (405,920)	$ (204,514)	$ (923,663)	$ (594,364)
Other comprehensive (loss) income:				
Unrealized loss on marketable securities	(2,053)	(64)	(11,004)	(312)
Foreign currency translation gain	460	1,857	377	9,530
Defined benefit pension plans, net of tax	34	58	103	174
Total other comprehensive (loss) income	(1,559)	1,851	(10,524)	9,392
Comprehensive loss	$ (407,479)	$ (202,663)	$ (934,187)	$ (584,972)

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

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

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount				
Balance as of December 31, 2021	120,182	$ 1,202	$ 6,058,453	$ (33,259)	$ (5,438,193)	$ 588,203
Exercise of common stock options, net of tax withholdings	524	5	28,054	—	—	28,059
Issuance of common stock under equity plans	23	—	—	—	—	—
Stock-based compensation expense	—	—	30,051	—	—	30,051
Other comprehensive loss	—	—	—	(4,806)	—	(4,806)
Net loss	—	—	—	—	(240,341)	(240,341)
Balance as of March 31, 2022	120,729	1,207	6,116,558	(38,065)	(5,678,534)	401,166
Exercise of common stock options, net of tax withholdings	192	2	13,890	—	—	13,892
Issuance of common stock under equity plans	71	1	8,089	—	—	8,090
Stock-based compensation expense	—	—	34,453	—	—	34,453
Other comprehensive loss	—	—	—	(4,159)	—	(4,159)
Net loss	—	—	—	—	(277,402)	(277,402)
Balance as of June 30, 2022	120,992	1,210	6,172,990	(42,224)	(5,955,936)	176,040
Exercise of common stock options, net of tax withholdings	1,657	17	153,259	—	—	153,276
Issuance of common stock under equity plans	342	3	—	—	—	3
Stock-based compensation expense	—	—	129,133	—	—	129,133
Purchase of capped calls related to convertible debt	—	—	(118,611)	—	—	(118,611)
Other comprehensive loss	—	—	—	(1,559)	—	(1,559)
Net loss	—	—	—	—	(405,920)	(405,920)
Balance as of September 30, 2022	122,991	$ 1,230	$ 6,336,771	$ (43,783)	$ (6,361,856)	$ (67,638)

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

ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY
(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, 2020	116,427	$ 1,164	$ 5,644,074	$ (43,622)	$ (4,585,369)	$ 1,016,247
Exercise of common stock options, net of tax withholdings	614	6	47,028	—	—	47,034
Issuance of common stock under equity plans	280	3	(3)	—	—	—
Stock-based compensation expense	—	—	56,295	—	—	56,295
Other comprehensive income	—	—	—	6,905	—	6,905
Net loss	—	—	—	—	(200,291)	(200,291)
Balance as of March 31, 2021	117,321	1,173	5,747,394	(36,717)	(4,785,660)	926,190
Exercise of common stock options, net of tax withholdings	993	10	75,439	—	—	75,449
Issuance of common stock under equity plans	282	3	7,715	—	—	7,718
Stock-based compensation expense	—	—	32,928	—	—	32,928
Other comprehensive income	—	—	—	636	—	636
Net loss	—	—	—	—	(189,559)	(189,559)
Balance as of June 30, 2021	118,596	1,186	5,863,476	(36,081)	(4,975,219)	853,362
Exercise of common stock options, net of tax withholdings	883	9	71,490	—	—	71,499
Issuance of common stock under equity plans	1	—	—	—	—	—
Stock-based compensation expense	—	—	33,695	—	—	33,695
Other comprehensive income	—	—	—	1,851	—	1,851
Net loss	—	—	—	—	(204,514)	(204,514)
Balance as of September 30, 2021	119,480	$ 1,195	$ 5,968,661	$ (34,230)	$ (5,179,733)	$ 755,893

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

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

	Nine Months Ended September 30,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (923,663)	$ (594,364)
Non-cash adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	30,157	36,192
Amortization and interest accretion related to operating leases	30,508	32,051
Non-cash interest expense on liability related to the sale of future royalties	79,621	87,197
Stock-based compensation	187,882	121,135
Realized and unrealized loss (gain) on marketable equity securities	40,108	(61,273)
Loss on extinguishment of debt	76,586	—
Change in fair value of development derivative liability	70,776	19,654
Other	20,607	15,568
Changes in operating assets and liabilities:		
Accounts receivable, net	7,672	(42,350)
Inventory	(15,158)	(15,655)
Prepaid expenses and other assets	(47,194)	(48,765)
Accounts payable, accrued expenses and other liabilities	89,152	48,738
Operating lease liability	(31,718)	(29,586)
Deferred revenue	(24,632)	(60,094)
Net cash used in operating activities	(409,296)	(491,552)
Cash flows from investing activities:		
Purchases of property, plant and equipment	(50,424)	(54,486)
Purchases of marketable securities	(1,253,584)	(973,146)
Sales and maturities of marketable securities	1,626,848	1,172,100
Proceeds from maturity of restricted investments	89,951	25,975
Purchases of restricted investments	(98,451)	(26,140)
Other investing activities	(5,075)	(4,198)
Net cash provided by investing activities	309,265	140,105
Cash flows from financing activities:		
Proceeds from exercise of stock options and other types of equity, net	202,646	201,227
Proceeds from convertible debt, net	1,016,888	—
Repayment of term loan	(762,107)	—
Purchases of capped calls related to convertible debt	(118,611)	—
Proceeds from the sale of future royalties	—	500,000
Proceeds from development derivative	23,500	16,100
Proceeds from term loan facility	—	250,000
Other financing activities	—	(12,500)
Net cash provided by financing activities	362,316	954,827
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(9,049)	(5,968)
Net increase in cash, cash equivalents and restricted cash	253,236	597,412
Cash, cash equivalents and restricted cash, beginning of period	822,153	499,046
Cash, cash equivalents and restricted cash, end of period	$ 1,075,389	$ 1,096,458
Supplemental disclosure of cash flows:		
Cash paid for interest	$ 43,932	$ 17,703

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

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

1. NATURE OF BUSINESS

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

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

As of September 30, 2022, we have five products that have received marketing approval, including one partnered product, and multiple late-stage investigational programs advancing towards potential commercialization. As of September 30, 2022, we generated worldwide product revenues from four commercialized products, ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA, primarily in the U.S., Europe and Japan.

2. BASIS OF PRESENTATION AND PRINCIPLES OF CONSOLIDATION

The accompanying condensed consolidated financial statements of Alnylam are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America, or GAAP, applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to state fairly the results of operations for the reported periods. Our condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, our audited consolidated financial statements for the year ended December 31, 2021, which were included in our Annual Report on Form 10-K that was filed with the Securities and Exchange Commission on February 10, 2022. The year-end condensed consolidated balance sheet data was derived from our audited financial statements but does not include all disclosures required by GAAP. The results of our operations for any interim period are not necessarily indicative of the results of our operations for any other interim period or for a full fiscal year.

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

Our significant accounting policies are described in Note 2 of the Notes to Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2021. Updates to our significant accounting policies, including the convertible debt policy, are discussed below.

Use of Estimates

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

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

Liquidity

Based on our current operating plan, we believe that our cash, cash equivalents and marketable securities as of September 30, 2022, together with the cash we expect to generate from product sales and under our current alliances, including milestones and royalties on Leqvio sales, will be sufficient to enable us to advance our *Alnylam P^{5}x25* strategy for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q.

Recently Adopted Accounting Pronouncements

In August 2020, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2020-06, Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity, which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts in an entity's own equity. Specifically, ASU 2020-06 simplifies accounting for the issuance of convertible instruments by removing certain separation models required under existing guidance. In addition, the standard removes certain settlement conditions that are required for equity contracts to qualify for the derivative scope exception and requires use of the "if-converted" method when calculating the dilutive impact of convertible debt on earnings per share, or EPS. ASU 2020-06 is effective for financial statements issued for fiscal years beginning after December 15, 2021, and interim periods within those fiscal years, with early adoption permitted. We adopted the new standard on January 1, 2022 and there was no impact on the date of adoption. During the third quarter of 2022, we issued convertible notes as described in Note 10, Convertible Debt.

3. NET PRODUCT REVENUES

Net product revenues consist of the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
(In thousands)	2022	2021	2022	2021
ONPATTRO				
United States	$ 67,196	$ 51,247	$ 200,588	$ 153,109
Europe	57,217	51,019	167,185	136,576
Rest of World	20,537	18,051	67,614	46,422
Total	144,950	120,317	435,387	336,107
AMVUTTRA				
United States	25,060	—	25,060	—
Europe	169	—	169	—
Total	25,229	—	25,229	—
GIVLAARI				
United States	31,169	22,372	84,505	62,502
Europe	12,477	7,568	36,059	22,461
Rest of World	2,013	1,893	5,522	2,173
Total	45,659	31,833	126,086	87,136
OXLUMO				
United States	6,383	5,236	18,916	13,156
Europe	9,348	9,658	25,099	27,225
Rest of World	698	—	1,937	—
Total	16,429	14,894	45,952	40,381
Total net product revenues	$ 232,267	$ 167,044	$ 632,654	$ 463,624

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

(In thousands)	As of September 30, 2022	As of December 31, 2021
Receivables included in "Accounts receivable, net"	$ 160,162	$ 124,906

4. NET REVENUES FROM COLLABORATIONS

Net revenues from collaborations consist of the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
(In thousands)	2022	2021	2022	2021
Regeneron Pharmaceuticals	$ 21,979	$ 14,161	$ 34,405	$ 90,908
Novartis AG	5,803	4,160	27,472	21,179
Vir Biotechnology	441	1,233	1,137	8,033
Other	1,074	582	1,253	1,208
Total	$ 29,297	$ 20,136	$ 64,267	$ 121,328

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

(In thousands)	As of September 30, 2022	As of December 31, 2021
Receivables included in "Accounts receivable, net"	$ 21,933	$ 73,266
Contract liabilities included in "Deferred revenue"	$ 73,625	$ 88,627

We recognized revenue of $11.7 million and $17.0 million in the three and nine months ended September 30, 2022, respectively, and revenue of $12.7 million and $65.2 million in the three and nine months ended September 30, 2021, respectively, that was included in the contract liability balance at the beginning of the period.

In order to determine revenue recognized in the period from contract liabilities, we first allocate revenue to the individual contract liability balance outstanding at the beginning of the period until the revenue exceeds that balance. If additional consideration is received on those contracts in subsequent periods, we assume all revenue recognized in the reporting period first applies to the beginning contract liability as opposed to a portion applying to the new consideration for the period.

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

	Three Months Ended September 30,					
	2022			2021		
(In thousands)	Clinical Trial and Manufacturing	External Services	Other	Clinical Trial and Manufacturing	External Services	Other
Regeneron Pharmaceuticals	$ 9,812	$ 1,154	$ 8,982	$ 3,152	$ 285	$ 10,964
Other	—	357	—	572	37	728
Total	$ 9,812	$ 1,511	$ 8,982	$ 3,724	$ 322	$ 11,692

	Nine Months Ended September 30,					
	2022			2021		
(In thousands)	Clinical Trial and Manufacturing	External Services	Other	Clinical Trial and Manufacturing	External Services	Other
Regeneron Pharmaceuticals	$ 12,926	$ 2,141	$ 27,935	$ 17,343	$ 547	$ 34,082
Other	156	679	337	2,976	745	3,844
Total	$ 13,082	$ 2,820	$ 28,272	$ 20,319	$ 1,292	$ 37,926

The research and development expenses incurred for the agreements included in the table above consist of costs incurred for (i) clinical expenses, including manufacturing of clinical product, (ii) external services including consulting services and lab supplies and services, and (iii) other expenses, including professional services, facilities and overhead allocations, and a reasonable estimate of compensation and related costs as billed to our counterparties, for which we recognize net revenues from collaborations. For the three and nine months ended September 30, 2022 and 2021, we did not incur material selling, general and administrative expenses related to our collaboration agreements.

In addition, we recognized a reduction to our research and development expenses of $2.3 million and $9.7 million for the three and nine months ended September 30, 2022, respectively, and of $3.3 million and $12.7 million for the three and nine months ended September 30, 2021, respectively, from cost reimbursement due under certain of our collaboration agreements with Regeneron Pharmaceuticals, Inc., or Regeneron, accounted for under Accounting Standards Codification, or ASC, Topic 808, Collaborative Arrangements, or ASC 808.

Product Alliances

Regeneron Pharmaceuticals, Inc.

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 central nervous system, or CNS, in addition to a select number of targets expressed in the liver, which we refer to as the Regeneron Collaboration. The Regeneron Collaboration is governed by a Master Agreement, referred to as the Regeneron Master Agreement, which became effective on May 21, 2019. In connection with the Regeneron Master Agreement, we and Regeneron entered into (i) a binding co-co collaboration term sheet covering the continued development of cemdisiran, our C5 small interfering RNA, or siRNA, currently in Phase 2 development for C5 complement-mediated diseases, as a monotherapy and (ii) a binding license term sheet to evaluate anti-C5 antibody-siRNA combinations for C5 complement-mediated diseases including evaluating the combination of Regeneron's pozelimab (REGN3918), currently in Phase 3 development, and cemdisiran. The C5 co-co collaboration and license agreements were executed in August 2019.

Under the terms of the Regeneron Collaboration, we are working exclusively with Regeneron to discover RNAi therapeutics for eye and CNS diseases for an initial research period of approximately five 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 up to $400.0 million. The Regeneron Collaboration also covers a select number of RNAi therapeutic programs designed to target genes expressed in the liver, including our previously announced collaboration with Regeneron to identify RNAi therapeutics for the chronic liver disease nonalcoholic steatohepatitis. We retain broad global rights to all of our other unpartnered liver-directed clinical and pre-clinical pipeline programs. The Regeneron Collaboration is governed by a joint steering committee that is comprised of an equal number of representatives from each party.

Regeneron 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 covered by the Regeneron Collaboration, with the lead party retaining global development and commercial responsibility. For such CNS and liver programs, both we and Regeneron have the option at lead candidate selection to enter into a co-co collaboration agreement, the form of which has been agreed upon by the parties, whereby both companies will share equally all costs of, and profits from, all development and commercialization activities under the program. If the non-lead party elects to not enter into a co-co collaboration agreement with respect to a given CNS or liver program, we and Regeneron will enter into a license agreement with respect to such program and the lead party will be the "Licensee" for the purposes of the license agreement. If the lead party for a CNS or liver program elects to not enter into the co-co collaboration agreement, then we and Regeneron will enter into a license agreement with respect to such program and leadership of the program will transfer to the other party and the former non-lead party will be the "Licensee" for the purposes of the license agreement.

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

In connection with the Regeneron Master Agreement, Regeneron made an upfront payment of $400.0 million. We are also eligible to receive up to an additional $200.0 million in milestone payments upon achievement of certain criteria during early clinical development for eye and CNS programs. We and Regeneron plan to advance programs directed to up to 30 targets in

the first five years under the Regeneron Collaboration during the Initial Research Term. For each program, Regeneron will provide us with $2.5 million in funding at program initiation and an additional $2.5 million at lead candidate identification, with the potential for approximately $30.0 million in annual discovery funding to us as the Regeneron Collaboration reaches steady state.

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

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

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

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

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

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

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

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

targets, if any; however, these amounts are excluded from variable consideration under the Regeneron Collaboration as we are only eligible to receive such amounts if, after a drug candidate is identified, the form of license agreement is subsequently executed resulting in a license that is granted to Regeneron. Any such subsequently granted license would represent a separate transaction under ASC 606.

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

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

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

For the Research Services Obligation and the C5 License Obligation accounted for under ASC 606, we measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for each of the identified obligations, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the transaction price allocated to each obligation. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch up. We re-evaluate the transaction price as of the end of each reporting period and as of September 30, 2022, the total transaction price was determined to be $558.4 million, an increase of $20.0 million from December 31, 2021. As of September 30, 2022, the transaction price is comprised of the upfront payment and variable consideration related to development, manufacture and supply activities. For the C5 Co-Co Obligation accounted for under ASC 808, the transaction price allocated to this obligation is recognized using a proportional performance method. Revenue recognized under this agreement, inclusive of the amount allocated to the C5 Co-Co Obligation, is accounted for as collaboration revenue.

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

	Transaction Price Allocated	Deferred Revenue		
Performance Obligations	As of September 30, 2022	As of September 30, 2022	As of December 31, 2021	Accounting Guidance
Research Services Obligation	$ 215,680	$ 33,200	$ 42,300	ASC 606
C5 License Obligation	96,700	30,300	26,900	ASC 606
C5 Co-Co Obligation	246,000	203,100	212,500	ASC 808
	$ 558,380	$ 266,600	$ 281,700	

Performance Obligations	Revenue Recognized During				Accounting Guidance
	Three Months Ended September 30, 2022	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2022	Nine Months Ended September 30, 2021	
Research Services Obligation	$ 10,300	$ 8,900	$ 19,100	$ 28,900	ASC 606
C5 License Obligation	1,400	1,200	(2,100)	30,400	ASC 606
C5 Co-Co Obligation	5,400	2,500	9,400	16,400	ASC 808
	$ 17,100	$ 12,600	$ 26,400	$ 75,700	

As of September 30, 2022, the aggregate amount of the transaction price allocated to the remaining Research Services Obligation and C5 License Obligation that was unsatisfied was $140.3 million, which is expected to be recognized through the term of the Regeneron Collaboration as the services are performed. This amount excludes the transaction price allocated to the C5 Co-Co Obligation accounted for under ASC 808. Deferred revenue related to the Regeneron Collaboration is classified as either current or non-current in the condensed consolidated balance sheets based on the period the revenue is expected to be recognized.

Novartis AG

2013 Collaboration with The Medicines Company

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

As of September 30, 2022, we have earned $70.0 million of milestones and upon achievement of certain events, we will be entitled to receive additional milestones, up to an aggregate of $110.0 million, including $100.0 million in specified commercialization milestones and $10.0 million in other specified regulatory milestones. In addition, we are entitled to royalties ranging from 10% up to 20% based on annual worldwide net sales of licensed products by Novartis, its affiliates and sublicensees, subject to reduction under specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments under the MDCO License Agreement and future royalty payments may be less than anticipated.

Unless terminated earlier in accordance with the terms of the agreement, the MDCO License Agreement expires on a licensed product-by-licensed product and country-by-country basis upon expiration of the last royalty term for any licensed product in any country, where a royalty term is defined as the latest to occur of (1) the expiration of the last valid claim of patent rights covering a licensed product, (2) the expiration of the Regulatory Exclusivity, as defined in the MDCO License Agreement, and (3) the twelfth anniversary of the first commercial sale of the licensed product in such country. We estimate that our core technology patents covering licensed products under the MDCO License Agreement will expire in most countries by 2029. We also estimate that our Leqvio (inclisiran) product-specific patents covering licensed products under the MDCO License Agreement will expire in the U.S., Europe, China, Japan and elsewhere between 2027 and 2036. Certain of these patent rights are subject to potential patent term extensions and/or supplemental protection certificates extending such terms in countries where such extensions may become available due to regulatory delay. In addition, more patent filings relating to the collaboration may be made in the future.

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

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

We evaluated the MDCO License Agreement and concluded that Novartis meets the definition of a customer and that the MDCO License Agreement is a contract. We determined the transaction price, identified the performance obligations and allocated the transaction price to each performance obligation. We also determined that substantially all of our performance obligations are within the scope of the revenue standard as they relate to the delivery of goods and services to a customer for that customer's use in monetizing an asset. Specifically, we concluded that Novartis meets the definition of a customer as we are delivering intellectual property and know-how rights as well as research and development activities. In addition, we

determined that the MDCO License Agreement met the requirements to be accounted for as a contract, including that it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services that will be delivered to Novartis. We determined that, pursuant to ASC 606, the performance obligations were not separately identifiable and were not distinct (and did not have standalone value) due to the specialized nature of the services to be provided by us and the dependent relationship between the performance obligations. Given this fact pattern, we have concluded the MDCO License Agreement has a single identified or combined performance obligation.

None of the unearned milestones are included in the transaction price, as all unearned milestone amounts are not considered likely of achievement and therefore constrained. We considered several factors, including that achievement of the milestones is outside our control and contingent upon success in clinical trials and regulatory decisions and the licensee's efforts. Any consideration related to sales-based royalties (including milestones) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to MDCO and as a result have also been excluded from the transaction price. During 2018, we completed the performance obligations identified in the MDCO License Agreement, including the supply and technical transfer agreement, however, we continue to receive additional orders for supply of certain material. We consider such orders as promised goods to be distinct from the other performance obligations since Novartis now has the ability to manufacture on its own through its own vendors. Such orders will be treated as separate agreements and any associated revenue will be recognized upon transfer of control.

Novartis License Agreement

In December 2021, we and Novartis entered into a collaboration and license agreement, or the Novartis License Agreement, pursuant to which we granted to Novartis an exclusive, worldwide license to develop, manufacture and commercialize siRNAs targeting end-stage liver disease, or ESLD, potentially leading to the development of a treatment designed to promote the regrowth of functional liver cells and to provide an alternative to transplantation for patients with liver failure.

Pursuant to the Novartis License Agreement, we received an upfront fee of $12.5 million. We may also receive milestone payments upon the achievement of certain development, regulatory and commercial milestones, as well as royalties on the net sales of licensed products ranging from high-single-digit to sub-teen double-digit percentages. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments under the Novartis License Agreement.

Under the Novartis License Agreement, we are developing and testing potential siRNAs using target-specific assays developed by Novartis pursuant to an agreed upon research plan for a specified period referred to as the Collaboration Term. Novartis will reimburse us for the cost of our activities under the research plan, referred to as the DC Workplan, subject to an agreed upon cap. Once a lead candidate is identified, further development and clinical research will be conducted by Novartis. The collaboration is governed by a joint steering committee comprised of an equal number of representatives from each party.

Unless terminated earlier in accordance with the terms of the Novartis License Agreement, the Collaboration Term expires at the earlier of (1) 180 days after completion of the development activities assigned to us as agreed upon between the parties, or (2) December 17, 2024.

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

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

We identified one performance obligation under the Novartis License Agreement comprised of: i) the exclusive license to develop, manufacture and commercialize siRNAs targeting ESLD; and ii) the obligation to perform work under the DC Workplan. The license is not distinct from the services, including the obligation to deliver development candidates, as Novartis cannot benefit on its own from the value of the license without receipt of such services. We measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for the identified performance obligation, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the total transaction price. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch up. As of September 30, 2022, the total transaction price was determined to be approximately $16.0 million, comprised of the $12.5 million upfront payment and estimated variable consideration attributed to work to be performed under the DC Workplan. We utilized the expected value method to determine the amount of reimbursement for these activities. The total transaction price is allocated entirely to the single performance obligation. We determined any variable consideration related to

sales-based royalties and milestones related to the exclusive license to be constrained and therefore excluded such consideration from the transaction price.

As of September 30, 2022, the aggregate amount of the transaction price allocated to the performance obligation that was unsatisfied was $13.0 million, which is expected to be recognized through the term of the DC Workplan as the services are performed.

Vir Biotechnology, Inc.

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

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

Under the Vir Agreement, we have earned and received certain upfront and development milestone payments in the form of cash and Vir common stock, as well as sublicense revenue. We may receive additional milestone payments upon the achievement of certain development, regulatory and commercial milestones, as well as royalties on the net sales of licensed products ranging from high-single-digit to sub-teen double-digit percentages. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or any royalty payments under the Vir Agreement.

In March and April 2020, we entered into amendments to the Vir Agreement to expand our collaboration to include the development and commercialization of RNAi therapeutics targeting SARS-CoV-2, the virus that causes the disease COVID-19, along with three additional targets focused on human host factors for SARS-CoV-2, including angiotensin converting enzyme-2 and transmembrane protease, serine 2 and potentially a third mutually selected host factor target. Under the Vir amendments, we and Vir were each responsible for our own pre-clinical development costs incurred in performing our allocated responsibilities under an agreed-upon initial pre-clinical development plan. Under the original agreements, we and Vir agreed to equally share certain costs incurred in connection with the manufacture of non-GMP drug product required for pre-clinical development prior to filing an IND for the first product in the coronavirus program. We also agreed that Vir would lead all development and commercialization of any selected development candidates.

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

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

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

We identified one performance obligation under the Vir Agreement, as amended, comprised of: i) the exclusive license to develop, manufacture and commercialize RNAi therapeutics (including ALN-HBV02); ii) the obligation to deliver four additional development candidates and supply product for each such RNAi therapeutic program; and iii) the obligation to deliver up to four development candidates and supply product for RNAi therapeutic programs targeting SARS-CoV-2 (through

July 2021). The license is not distinct from the services, including the obligation to deliver development candidates and supply product, as Vir cannot benefit on its own from the value of the license without receipt of such services and supply.

We measure proportional performance over time using an input method based on cost incurred relative to the total estimated costs for the identified performance obligation, on a quarterly basis, by determining the proportion of effort incurred as a percentage of total effort we expect to expend. This ratio is applied to the total transaction price. Management has applied significant judgment in the process of developing our estimates. Any changes to these estimates will be recognized in the period in which they change as a cumulative catch up. As of September 30, 2022, the total transaction price was determined to be $111.1 million, comprised of the upfront payment, fair value of non-cash equity consideration at contract inception, milestones achieved, and variable consideration related to development, manufacture and supply activities.

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

As of September 30, 2022, the aggregate amount of the transaction price allocated to the performance obligation that was unsatisfied was $36.3 million, which is expected to be recognized through the term of the Vir Agreement as the services are performed.

Other Strategic License Agreements

PeptiDream, Inc.

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

5. LIABILITY RELATED TO THE SALE OF FUTURE ROYALTIES

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

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

In order to determine the amortization of the liability related to the sale of future royalties, we are required to estimate the total amount of future payments to Blackstone Royalties over the life of the Purchase Agreement. The $1.00 billion liability, recorded at execution of the agreement, will be accreted to the total of these royalty and commercial milestone payments as interest expense over the life of the Purchase Agreement. At execution and as of September 30, 2022, our estimate of this total interest expense resulted in an effective annual interest rate of 11% and 8%, respectively. These estimates contain assumptions that impact both the amount recorded at execution and the interest expense that will be recognized in future periods.

As payments are made to Blackstone Royalties, the balance of the liability will be effectively repaid over the life of the Purchase Agreement. The exact timing and amount of repayment is likely to change each reporting period. A significant increase or decrease in Leqvio global net revenue will materially impact the liability related to the sale of future royalties, interest expense and the time period for repayment. We will periodically assess the expected payments to Blackstone Royalties

and to the extent the amount or timing of such payments is materially different than our initial estimates, we will prospectively adjust the amortization of the liability related to the sale of future royalties and the related interest expense.

As of September 30, 2022, the carrying value of the liability related to the sale of future royalties was $1.27 billion, net of closing costs of $11.0 million. The carrying value of the liability related to the sale of future royalties approximates fair value as of September 30, 2022 and is based on our current estimates of future royalties and commercial milestones expected to be paid to Blackstone Royalties over the life of the arrangement, which are considered Level 3 inputs.

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, 2021	$ 1,188,103
Interest expense recognized	81,343
Payments	(1,722)
Carrying value as of September 30, 2022	$ 1,267,724

6. FAIR VALUE MEASUREMENTS

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

(In thousands)	As of September 30, 2022	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	$ 430,470	$ 430,470	$ —	$ —
U.S. treasury securities	62,863	—	62,863	—
Commercial paper	6,215	—	6,215	—
Marketable debt securities:				
U.S. treasury securities	817,631	—	817,631	—
Corporate notes	166,384	—	166,384	—
U.S. government-sponsored enterprise securities	175,205	—	175,205	—
Commercial paper	9,830	—	9,830	—
Marketable equity securities	23,051	23,051	—	—
Restricted cash (money market funds)	1,196	1,196	—	—
Total financial assets	$ 1,692,845	$ 454,717	$ 1,238,128	$ —
Financial liabilities				
Development derivative liability	$ 177,894	$ —	$ —	$ 177,894

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

(In thousands)	As of December 31, 2021	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets				
Cash equivalents:				
Money market funds	$ 255,869	$ 255,869	$ —	$ —
U.S. treasury securities	54,998	—	54,998	—
Marketable debt securities:				
U.S. treasury securities	1,030,578	—	1,030,578	—
Corporate notes	253,239	—	253,239	—
U.S. government-sponsored enterprise securities	177,741	—	177,741	—
Commercial paper	78,543	—	78,543	—
Certificates of deposit	7,501	—	7,501	—
Municipal securities	1,015	—	1,015	—
Marketable equity securities	66,972	66,972	—	—
Restricted cash (money market funds)	1,195	1,195	—	—
Total financial assets	$ 1,927,651	$ 324,036	$ 1,603,615	$ —
Financial liabilities				
Development derivative liability	$ 83,618	$ —	$ —	$ 83,618

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.

7. MARKETABLE DEBT SECURITIES

We invest our excess cash balances in marketable debt securities and at each balance sheet date presented, we classify all of our investments in debt securities as available-for-sale and as current assets as they represent the investment of funds available for current operations. We did not record any impairment charges related to our marketable debt securities during the three or nine months ended September 30, 2022 or 2021.

The following tables summarize our marketable debt securities:

	As of September 30, 2022			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 886,783	$ 27	$ (6,316)	$ 880,494
Corporate notes	169,358	—	(2,974)	166,384
U.S. government-sponsored enterprise securities	178,576	11	(3,382)	175,205
Commercial paper	16,045	—	—	16,045
Total	$ 1,250,762	$ 38	$ (12,672)	$ 1,238,128

	As of December 31, 2021			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. treasury securities	$ 1,086,232	$ 6	$ (662)	$ 1,085,576
Corporate notes	253,926	1	(688)	253,239
U.S. government-sponsored enterprise securities	178,027	2	(288)	177,741
Commercial paper	78,543	—	—	78,543
Certificates of deposit	7,501	—	—	7,501
Municipal securities	1,016	—	(1)	1,015
Total	$ 1,605,245	$ 9	$ (1,639)	$ 1,603,615

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

(In thousands)	As of September 30, 2022	As of December 31, 2021
Marketable debt securities	$ 1,169,050	$ 1,548,617
Cash and cash equivalents	69,078	54,998
Total	$ 1,238,128	$ 1,603,615

8. OTHER BALANCE SHEET DETAILS

Inventory

The components of inventory are summarized as follows:

(In thousands)	As of September 30, 2022	As of December 31, 2021
Raw materials	$ 17,718	$ 14,754
Work in progress	102,447	100,942
Finished goods	21,483	7,005
Total	$ 141,648	$ 122,701

As of September 30, 2022 and December 31, 2021, we had $26.2 million and $36.3 million of long-term inventory, respectively, included within other assets in our condensed consolidated balance sheet as we anticipate it being consumed beyond our normal operating cycle.

Cash, Cash Equivalents and Restricted Cash

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

	As of September 30,	
(In thousands)	2022	2021
Cash and cash equivalents	$ 1,073,228	$ 1,093,991
Total restricted cash included in other assets	2,161	2,467
Total cash, cash equivalents, and restricted cash shown in the condensed consolidated statements of cash flows	$ 1,075,389	$ 1,096,458

Accumulated Other Comprehensive (Loss) Income

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

(In thousands)	Loss on Investment in Joint Venture	Defined Benefit Pension Plans	Unrealized (Losses) Gains from Debt Securities	Foreign Currency Translation Adjustment	Total Accumulated Other Comprehensive (Loss) Income
Balance as of December 31, 2021	$ (32,792)	$ (2,811)	$ (1,630)	$ 3,974	$ (33,259)
Other comprehensive income before reclassifications	—	—	6	377	383
Amounts reclassified from other comprehensive income (loss)	—	103	(11,010)	—	(10,907)
Net other comprehensive income (loss)	—	103	(11,004)	377	(10,524)
Balance as of September 30, 2022	$ (32,792)	$ (2,708)	$ (12,634)	$ 4,351	$ (43,783)

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

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

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

9. CREDIT AGREEMENT

In April 2020, we entered into a credit agreement, or Credit Agreement, among us, certain of our subsidiaries (such subsidiaries, together with us, the Loan Parties), funds or accounts managed or advised by GSO Capital Partners LP (now Blackstone Alternative Credit Advisors LP) and certain other affiliates of The Blackstone Group Inc., and the other lenders from time to time parties thereto, collectively, the Lenders, and Wilmington Trust, National Association, as the administrative agent for the Lenders. The Credit Agreement provided for a senior secured delayed draw term loan facility, referred to as the Term Loans, which consisted of three tranches providing funding of $700.0 million. The Tranche 1 Loan of $200.0 million, the Tranche 2 Loan of $250.0 million and the Tranche 3 Loan of $250.0 million were drawn as of December 31, 2020, June 30, 2021, and December 31, 2021 respectively, and are included in long-term debt in the condensed consolidated balance sheets. As of September 30, 2022, we extinguished the Term Loans and paid all outstanding balances, including principal of $700.0 million and prepayment premiums of $62.1 million and terminated the Credit Agreement.

The Term Loans were initially set to mature in December 2027. During the period the Term Loans were outstanding, we had elected a LIBOR Rate plus 7%, and paid $17.5 million in total funding fees in connection with such Term Loans. Our interest rate was 9% and 8% as of June 30, 2022 and December 31, 2021, respectively.

We were obligated to pay interest due on the Term Loans calculated through December 31, 2022 notwithstanding prepayment. Prepayment of Term Loans was subject to a fee of 5% of the loan principal.

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

The Credit Agreement contained negative covenants that, among other things and subject to certain exceptions, could have restricted our ability to, incur additional liens, incur additional indebtedness, make investments, including acquisitions, engage in fundamental changes, sell or dispose of assets that constitute collateral, including certain intellectual property, pay dividends or make any distribution or payment on or redeem, retire or purchase any equity interests, amend, modify or waive certain material agreements or organizational documents and make payments of certain subordinated indebtedness. Additionally, the Credit Agreement contained certain customary representations and warranties, affirmative covenants and provisions relating to events of default, including nonpayment of principal, interest and other amounts; failure to comply with covenants; the rendering of judgments or orders or default by us in respect of other material indebtedness; and certain insolvency and ERISA events. The Credit Agreement also required us to have consolidated liquidity of at least $100.0 million as of the last day of each fiscal quarter.

10. CONVERTIBLE DEBT

Convertible Senior Notes Due 2027

On September 12, 2022, we commenced a private offering of $900.0 million in aggregate principal amount of 1% Convertible Senior Notes due 2027, or the Initial Notes. On September 13, 2022, the initial purchasers in such offering exercised their option to purchase an additional $135.0 million in aggregate principal amount of our 1% Convertible Senior

Notes due 2027, or the Additional Notes, and together with the Initial Notes collectively referred to as the Notes, bringing the total aggregate principal amount of the Notes to $1.04 billion. The Notes were issued pursuant to an indenture, dated September 15, 2022, or the Indenture. The Indenture includes customary covenants and sets forth certain events of default after which the Notes may be declared immediately due and payable and sets forth certain types of bankruptcy or insolvency events of default involving the Company after which the Notes become automatically due and payable.

The Notes will mature on September 15, 2027, unless earlier converted, redeemed or repurchased. The Notes will bear interest from September 15, 2022 at a rate of 1% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2023. The Notes are convertible at the option of the noteholder on or after June 15, 2027. Prior to June 15, 2027, the Notes are convertible only under the following circumstances: (1) During any calendar quarter commencing after the calendar quarter ending on December 31, 2022 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (2) During the five business day period after any ten consecutive trading day period in which the trading price per $1,000 principal amount of the Notes for each trading day of that ten consecutive trading day period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate of the Notes on such trading day; (3) If we call any or all of the Notes for redemption; or (4) Upon the occurrence of specific corporate events as set forth in the Indenture governing the Notes. We will settle any conversions of Notes by paying or delivering, as applicable, cash, shares of our common stock, or a combination of cash and shares of common stock, at our election.

The conversion rate for the Notes will initially be 3.4941 shares of common stock per $1,000 principal amount of Notes, which is equivalent to an initial conversion price of approximately $286.20 per share of common stock. The initial conversion price of the Notes represents a premium of approximately 35% over the $212.00 per share last reported sale price of common stock on September 12, 2022. The conversion rate is subject to adjustment under certain circumstances in accordance with the terms of the Indenture.

We may not redeem the Notes prior to September 20, 2025. We may redeem for cash equal to 100% of the principal amount of the Notes being redeemed plus accrued and unpaid interest all or any portion of the Notes, at our option, on or after September 20, 2025, if the last reported sales price of our common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period. No sinking fund is provided for the Notes and therefore we are not required to redeem or retire the Notes periodically.

If we undergo a fundamental change, as defined in the indenture agreement, then subject to certain conditions, holders may require us to repurchase for cash all or any portion of their Notes at a fundamental change repurchase price equal to 100% of the principal amount of the Notes to be repurchased plus accrued and unpaid interest. In addition, if specific corporate events occur prior to the maturity date or if we issue a notice of redemption, we will increase the conversion rate by pre-defined amounts for holders who elect to convert their notes in connection with such a corporate event. The conditions allowing holders of the Notes to convert were not met this quarter.

As of September 30, 2022, the Notes are classified as a long-term liability, net of issuance costs of $19.2 million, on the condensed consolidated balance sheets. As of September 30, 2022, the net carrying amount of the Notes approximates fair value as the Notes were issued on September 15, 2022. Interest expense recognized related to the Notes for the three months ended September 30, 2022 was immaterial. The Notes were issued at par and costs associated with the issuance of the Notes are amortized to interest expense over the contractual term of the Notes. As of September 30, 2022, the effective interest rate of the Notes is 1%.

Capped Call Transactions

In September 2022, in connection with the pricing of the Initial Notes and the initial purchasers' exercise of their option to purchase the Additional Notes, we entered into privately negotiated capped call transactions, or Capped Call Transactions. The Capped Call Transactions initially cover, subject to customary anti-dilution adjustments, the number of shares of common stock that underlie the Notes. The cap price of the Capped Call Transactions is initially $424.00 per share, which represents a premium of 100% over the last reported sale price of common stock of $212.00 per share on September 12, 2022, and is subject to certain adjustments under the terms of the capped call transactions. We used approximately $118.6 million of the proceeds from the offering of Notes to pay the cost of the Capped Call Transactions.

We evaluated the Capped Call Transactions and determined that they should be accounted for separately from the Notes. The cost of $118.6 million to purchase the Capped Call Transactions was recorded as a reduction to additional paid-in capital in the condensed consolidated balance sheet as of September 30, 2022 as the Capped Call Transactions are indexed to our own stock and met the criteria to be classified in stockholders' equity.

11. DEVELOPMENT DERIVATIVE LIABILITY

In August 2020, we entered into a co-development agreement, referred to as the Funding Agreement, with BXLS V Bodyguard – PCP L.P. and BXLS Family Investment Partnership V – ESC L.P., collectively referred to as Blackstone Life Sciences, pursuant to which Blackstone Life Sciences will provide up to $150.0 million in funding for the clinical development of vutrisiran and zilebesiran (formerly ALN-AGT), two of our cardiometabolic programs. With respect to vutrisiran, Blackstone Life Sciences has committed to provide up to $70.0 million to fund development costs related to the HELIOS-B Phase 3 clinical trial. In November 2021, Blackstone Life Sciences opted in to Phase 2 clinical trial funding of zilebesiran, committing to fund, upon meeting certain patient enrollment thresholds, up to $26.0 million. Furthermore, Blackstone Life Sciences has the right, but is not obligated, to fund up to $54.0 million for development costs related to a Phase 3 clinical trial of zilebesiran. The amount of funding ultimately provided by Blackstone Life Sciences is dependent on us achieving specified development milestones with respect to each clinical trial. We retain sole responsibility for the development and commercialization of both vutrisiran and zilebesiran.

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

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

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

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

As of September 30, 2022, 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, assuming regulatory approval for ATTR-cardiomyopathy, (iv) our cost of borrowing (13%), and (v) Blackstone Life Sciences' cost of borrowing (4%).

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

Carrying value as of December 31, 2021	$	83,618
Amount received under the Funding Agreement		23,500
Loss recorded from remeasurement		70,776
Carrying value as of September 30, 2022	$	177,894

12. STOCK-BASED COMPENSATION

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
(In thousands)	2022	2021	2022	2021
Research and development	$ 52,962	$ 12,417	$ 75,217	$ 49,878
Selling, general and administrative	75,156	20,950	112,665	71,257
Total	$ 128,118	$ 33,367	$ 187,882	$ 121,135

13. NET LOSS PER COMMON SHARE

We compute basic net loss per common share by dividing net loss by the weighted-average number of common shares outstanding during the period. We compute diluted net loss per common share by dividing net loss by the weighted-average number of common shares and dilutive potential common share equivalents outstanding during the period. In the diluted net loss per share calculation, net loss would be adjusted for the elimination of interest expense on the Convertible debt. Potential common shares consist of shares issuable upon the exercise of stock options (the proceeds of which are then assumed to have been used to repurchase outstanding shares using the treasury stock method) or upon conversion of the convertible debt outstanding during the period (calculated using the if-converted method assuming the conversion of the convertible debt as of the earliest period reported or at the date of issuance, if later). Because the inclusion of potential common shares would be anti-dilutive for all periods presented, diluted net loss per common share is the same as basic net loss per common share.

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

	As of September 30,	
(In thousands)	2022	2021
Options to purchase common stock	10,741	11,715
Unvested restricted common stock	1,617	1,246
Convertible debt	3,616	—
Total	15,974	12,961

14. 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 December 31, 2021, 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.

Government Investigation

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

Patent Infringement Lawsuits

In March 2022, we filed separate lawsuits in the U.S. District Court for the District of Delaware against (1) Pfizer, Inc. and its subsidiary Pharmacia & Upjohn Co. LLC, collectively referred to as Pfizer, and (2) Moderna, Inc., and its subsidiaries ModernaTX, Inc., and Moderna US, Inc., collectively referred to as Moderna. The lawsuits seek damages for infringement of U.S. Patent No. 11,246,933, or '933 Patent, in Pfizer's and Moderna's manufacture and sale of their messenger RNA, or mRNA, COVID-19 vaccines. The patent relates to the Company's biodegradable cationic lipids that are foundational to the success of the mRNA COVID-19 vaccines.

We are seeking judgment that each of Pfizer and Moderna is infringing the '933 Patent, as well as damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the unlicensed uses made of our patented lipids by Pfizer and Moderna, together with interest and costs as may be awarded by the court. As stated in the filed complaints, we are not seeking injunctive relief in these lawsuits.

On May 23, 2022, Moderna filed a partial motion to dismiss, asserting an affirmative defense under Section 1498(a). We responded on May 27, 2022, opposing their motion arguing Moderna had significant non-government sales and the government contract ended in April 2022. Moderna responded on June 13, 2022, requesting a partial motion to dismiss those claims for sales under 1498(a). This motion is fully briefed and pending before the court.

On May 27, 2022, Pfizer filed an answer to our complaint, denying the allegations, and asserting invalidity and non-infringement defenses. In addition, Pfizer added BioNTech SE to the suit and added counter-claims seeking a declaratory judgment that our patent is invalid and a second claim alleging that our patent is invalid due to patent misuse. We believe their defenses and counter-claims have no merit and responded on June 10, 2022, with substantive arguments as to the validity of our claims and the lack of merit of their patent misuse claim.

On July 12, 2022, we filed a new lawsuit against each of Pfizer and Moderna seeking damages for infringing our newly granted U.S. Patent No. 11,382,979 in Pfizer's and Moderna's manufacture and sale of their mRNA COVID-19 vaccines. The parties agreed to combine the two patents in one lawsuit, separately against each of Moderna and Pfizer/BioNTech.

The court has set a trial date of November 12, 2024 for Alnylam v. Moderna and November 18, 2024 for Alnylam v. Pfizer/BioNTech.

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, including, for example, the current government investigation, 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 determined that the estimated aggregate fair value of our potential liabilities under all such indemnification provisions is minimal and had not recorded any liability related to such indemnification obligations as of September 30, 2022.

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

Overview

We are a global commercial-stage biopharmaceutical company developing novel therapeutics based on ribonucleic acid interference, or RNAi. RNAi is a naturally occurring biological pathway within cells for sequence-specific silencing and regulation of gene expression. By harnessing the RNAi pathway, we have developed a new class of innovative medicines, known as RNAi therapeutics. RNAi therapeutics are comprised of small interfering RNA, or siRNA, and function upstream of conventional medicines by potently silencing messenger RNA, or mRNA, that encode for 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 with rare and prevalent diseases. To date, our efforts to advance this revolutionary approach have yielded the approval of five first-in-class RNAi-based medicines, ONPATTRO® (patisiran), GIVLAARI® (givosiran), OXLUMO® (lumasiran), AMVUTTRA® (vutrisiran) and Leqvio® (inclisiran).

Our research and development strategy is to target genetically validated genes that have been implicated in the cause or pathway of human disease. We utilize a N-acetylgalactosamine (GalNAc) conjugate 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 lung, 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 studies, 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 five biotech company, as measured by market capitalization, by the end of 2025. With *Alnylam P^{5}x25*, we aim to deliver transformative rare and prevalent disease medicines for patients around the world through sustainable innovation, while delivering exceptional financial performance.

We currently have five marketed products and over a dozen clinical programs, including multiple programs in late-stage development, across four Strategic Therapeutic Areas, or "STArs:" Genetic Medicines; Cardio-Metabolic Diseases; Hepatic Infectious Diseases; and CNS/Ocular Diseases. Four of our marketed products are within the Genetic Medicines STAr, ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA. ONPATTRO is approved by the United States Food and Drug Administration, or the FDA, for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis, or hATTR amyloidosis, in adults and has also been approved in the European Union, or EU, for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, in Japan for the treatment of transthyretin, or TTR, type familial amyloidosis with polyneuropathy, and in multiple additional countries, including Brazil. In August 2022, we reported positive results from the APOLLO-B Phase 3 study of patisiran (the non-branded name of ONPATTRO) in patients with ATTR amyloidosis with cardiomyopathy and announced that we plan to submit a supplemental New Drug Application, or sNDA, for ONPATTRO as a potential treatment for ATTR amyloidosis with cardiomyopathy for review by the FDA in late 2022. 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 additional countries, including Brazil, Canada, Switzerland and Japan. Regulatory filings for givosiran (the non-branded drug name for GIVLAARI) are pending or planned during the remainder of 2022 and beyond. In November 2020, we received regulatory approval for OXLUMO in the U.S. and EU for the treatment of primary hyperoxaluria type 1, or PH1, in all age groups. In June 2021, we received marketing authorization approval for OXLUMO in Brazil for the treatment of PH1 in both children and adult patients. In October 2022, we announced that the FDA approved our sNDA for lumasiran (the non-branded drug name for OXLUMO), for the treatment of PH1 to lower urinary oxalate and plasma oxalate levels in pediatric and adult patients. Regulatory filings in other territories are pending and additional filings are planned during the remainder of 2022 and beyond. In June 2022, we received regulatory approval for AMVUTTRA in the U.S. for the treatment of the polyneuropathy of hATTR amyloidosis in adults. In September 2022, the European Commission, or EC, granted marketing authorization for AMVUTTRA for the treatment of hATTR amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy. We have also filed for regulatory approval for vutrisiran (the non-branded name of AMVUTTRA) with the Brazilian Health Regulatory Agency and the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA. Additional regulatory filings are planned during the remainder of 2022 and beyond.

Our fifth product, Leqvio (inclisiran), is in the Cardio-Metabolic Diseases STAr. Leqvio is being developed and commercialized by our partner 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 LDL-C. As of the end of September 2022, Leqvio has been approved in more than 60 countries.

In addition to our marketed products, we have multiple late-stage investigational programs advancing toward potential commercialization. These programs include our wholly owned programs: lumasiran for the treatment of recurrent renal stones; patisiran for the treatment of transthyretin amyloidosis, or ATTR amyloidosis, with cardiomyopathy; vutrisiran for the

treatment of ATTR amyloidosis with cardiomyopathy; as well as fitusiran for the treatment of hemophilia, which is being advanced by our partner Genzyme Corporation, a Sanofi Company, or Sanofi; and cemdisiran for the treatment of complement-mediated diseases, which we are advancing as a monotherapy in a Phase 2 study, and our partner Regeneron Pharmaceuticals, Inc., or Regeneron, is advancing cemdisiran in combination with pozelimab in Phase 3 studies in myasthenia gravis and paroxysmal nocturnal hemoglobinuria.

As part of our *Alnylam P5x25* strategy, we are focused on developing transformative prevalent disease medicines. In addition to Leqvio, we are advancing zilebesiran, an investigational, subcutaneously administered RNAi therapeutic targeting angiotensinogen, or AGT, in development for the treatment of hypertension. In November 2021, we reported positive interim data from the ongoing Phase 1 study of zilebesiran, and initiated the KARDIA Phase 2 clinical studies for zilebesiran. KARDIA-1 is designed to evaluate zilebesiran as a monotherapy across different doses administered quarterly and biannually. KARDIA-2 will evaluate the safety and efficacy of zilebesiran administered biannually as a concomitant therapy in patients whose blood pressure is not adequately controlled by standard of care antihypertensive medications.

In further support of our *Alnylam P5x25* strategy and in view of our evolving risk profile, we remain focused on 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 maintain focus on our global compliance program to drive its evolution and enhancement in view of the *Alnylam P5x25* strategy. 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. 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 relationships and investigations and remediation; our program and related controls are built to enhance our business processes, structures, and controls across our global operations.

Based on our expertise in RNAi therapeutics and broad intellectual property estate, we have formed alliances with leading pharmaceutical and life sciences companies to support our development and commercialization efforts, including Regeneron, Novartis (which acquired our partner The Medicines Company, or MDCO, in 2020), Sanofi, Vir Biotechnology, Inc., or Vir, Dicerna Pharmaceuticals, Inc. (acquired by Novo Nordisk A/S, or Novo Nordisk, in December 2021), or Dicerna, and PeptiDream, Inc., or PeptiDream.

We have incurred significant losses since we commenced operations in 2002 and as of September 30, 2022, we had an accumulated deficit of $6.36 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 establishment 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 expect to incur additional operating losses, however we expect 2019 represents our peak operating loss year as we transition towards a self-sustainable financial profile. We anticipate that our operating results will continue to fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods.

We currently have programs focused on a number of therapeutic areas and, as of September 30, 2022, we generate worldwide product revenues from four commercialized products, ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA, primarily in the U.S., Europe and Japan. However, our ongoing development efforts may not be successful and we may not be able to commence sales of any other products and/or successfully market and sell our approved products or any other products approved in the future. A portion of our total revenues in recent years has been derived from collaboration revenues from strategic alliances with Regeneron, Vir 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 alliances. Such alliances include, or may include in the future, license and other fees, funded research and development, milestone payments and royalties on product sales by our licensors, including royalties on sales of Leqvio made by our partner Novartis, as well as proceeds from the sale of equity or debt.

Convertible Senior Notes

In September 2022, we issued $1.04 billion aggregate principal amount of 1.00% Convertible Senior Notes due 2027, or Notes. The Notes will mature on September 15, 2027, unless earlier converted, redeemed or repurchased. The Notes will bear interest from September 15, 2022 at a rate of 1.00% per year payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2023. Before June 15, 2027, noteholders will have the right to convert their Notes in certain circumstances and during specified periods. From and after June 15, 2027, the Notes will be convertible at the option of the noteholders at any time prior to the close of business on the second scheduled trading day immediately preceding the maturity date. We will settle any conversions of Notes by paying or delivering, as applicable, cash shares of our common stock, par value $0.01 per share, or Common Stock, or a combination of cash and shares of Common Stock, at our election.

In connection with the issuance of the Notes, we paid $118.6 million, including expenses, to enter into privately negotiated capped call transactions with certain initial purchasers of the Notes or their respective affiliates and certain other financial institutions, or capped call transactions. The capped call transactions are expected generally to reduce the potential dilution upon conversion of the Notes in the event that the market price per share of our common stock, as measured under the terms of the capped call transactions, is greater than the strike price of the capped call transactions, which initially corresponds to the conversion price of the Notes, and is subject to anti-dilution adjustments generally similar to those applicable to the conversion rate of the Notes. The cap price of the capped call transactions will initially be $424.00 per share, which represents a premium of approximately 100% based on the last reported sale price of our common stock of $212.00 per share on September 12, 2022, and is subject to certain adjustments under the terms of the capped call transactions. If, however, the market price per share of our common stock, as measured under the terms of the capped call transactions, exceeds the cap price of the capped call transactions, there would nevertheless be dilution upon conversion of the Notes to the extent that such market price exceeds the cap price of the capped call transactions.

We used approximately $762.0 million of the net proceeds from the offering to repay borrowings, inclusive of prepayment premiums, under our credit agreement with Blackstone, and intend to use the remainder of the net proceeds for general corporate purposes.

The COVID-19 Pandemic

The ongoing COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions, and other public health safety measures. We have and will continue to closely monitor the spread of COVID-19 and its variants, and plan to continue taking steps to identify and mitigate the adverse impacts on, and risks to, our business posed by its spread and actions taken by governmental and health authorities to address the ongoing COVID-19 pandemic. We expect to continue to take actions as may be required or recommended by government authorities or as we determine are in the best interests of our employees, the patients we serve and other business partners in light of COVID-19 and variants thereof. The extent to which COVID-19 ultimately impacts our business, results of operations or financial condition will depend on future developments, which, despite progress in vaccination efforts, remain highly uncertain and cannot be predicted with confidence, such as the duration of the COVID-19 pandemic, new strains of the virus, including any future variants that may emerge, which may impact rates of infection and vaccination efforts, developments or perceptions regarding the safety of vaccines, new information that may emerge concerning the severity of COVID-19, and any additional preventative and protective actions taken to contain the pandemic or treat its impact, among others. The estimates of the impact on the Company's business may change based on new information that may emerge concerning COVID-19 and the actions to contain it or treat its impact and the economic impact on local, regional, national and international markets. For additional information related to the actual or potential impacts of COVID-19 on our business, please read Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q.

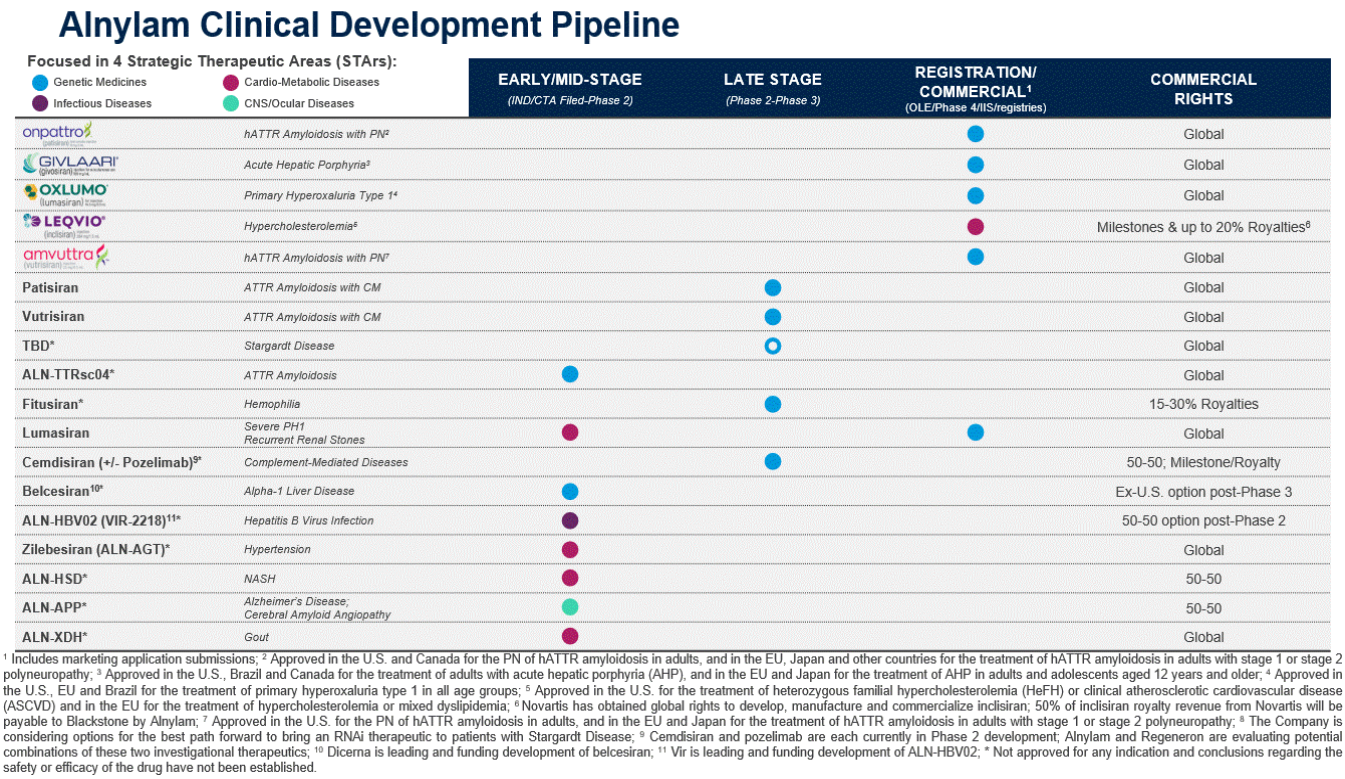
Research and Development

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

Our Product Pipeline

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

The chart below is a summary of our commercial products and late- and early-stage development programs as of October 2022. It identifies those programs for which we have received marketing approval, the stage of our programs and our commercial rights to such programs:



[1] Includes marketing application submissions; [2] Approved in the U.S. and Canada for the PN of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; [3] Approved in the U.S., Brazil and Canada for the treatment of adults with acute hepatic porphyria (AHP), and in the EU and Japan for the treatment of AHP in adults and adolescents aged 12 years and older; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Approved in the U.S. for the treatment of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) and in the EU for the treatment of hypercholesterolemia or mixed dyslipidemia; [6] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [7] Approved in the U.S. for the PN of hATTR amyloidosis in adults, and in the EU and Japan for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; [8] The Company is considering options for the best path forward to bring an RNAi therapeutic to patients with Stargardt Disease; [9] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [10] Dicerna is leading and funding development of belcesiran; [11] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

During the third quarter of 2022 and recent period, we reported the following updates from our commercially approved products and our late-stage clinical programs:

Commercial

TTR Franchise: ONPATTRO & AMVUTTRA

- We achieved global net product revenues for ONPATTRO and AMVUTTRA for the third quarter of 2022 of $145.0 million and $25.2 million, respectively.

GIVLAARI

- We achieved GIVLAARI global net product revenues for the third quarter of 2022 of $45.7 million.

OXLUMO

- We achieved OXLUMO global net product revenues for the third quarter of 2022 of $16.4 million.

Leqvio

- Our partner, Novartis, continued the launch of Leqvio in the U.S. and in other markets, with focus on patient on-boarding, removing access hurdles and enhancing medical education.

Late-Stage Clinical Development

- We continued to advance patisiran, in development for the treatment of ATTR amyloidosis:
  - Reported positive results from the APOLLO-B Phase 3 study in patients with ATTR amyloidosis with cardiomyopathy, and announced that we remain on track to submit an sNDA for review by the FDA by year-end.
- We continued to advance vutrisiran, in development for the treatment of ATTR amyloidosis:
  - Received marketing authorization for AMVUTTRA for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy in Europe and the UK, as well as approval for TTR type familial amyloidosis with polyneuropathy in Japan; and
  - Announced that we do not plan to conduct the optional interim analysis for the HELIOS-B Phase 3 study in patients with ATTR amyloidosis with cardiomyopathy, and that the study remains on track for topline results in early 2024.
- We continued to advance lumasiran for the treatment of PH1 and in development for the treatment of recurrent kidney stone disease:
  - Based on the successful outcome of the ILLUMINATE-C study in children and adults with advanced PH1, received approval from the FDA of an sNDA for OXLUMO, expanding the indication for the treatment of PH1 to lower urinary oxalate and plasma oxalate levels in pediatric and adult patients, and received approval from the EMA of a Type II variation to include the ILLUMINATE-C data in the label.
- We continued to advance cemdisiran for the treatment of complement-mediated diseases, in collaboration with our partner, Regeneron:
  - Reported positive results from the Phase 2 study in patients with immunoglobulin A nephropathy, or IgAN; and
  - Announced that we are working with Regeneron to finalize plans for the Phase 3 clinical development of cemdisiran in IgAN.

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

Strategic Alliances

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

Our collaboration strategy is to form alliances that create significant value for ourselves and our collaborators in the advancement of RNAi therapeutics as a new class of innovative medicines. Specifically, with respect to our CNS/Ocular Disease pipeline, in April 2019, we entered into a global, strategic collaboration with Regeneron to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing disease targets expressed in the eye and CNS, in addition to a select number of targets expressed in the liver. In July 2020, Regeneron exercised its co-development/co-commercialization option on our first CNS-targeted development candidate, ALN-APP, an investigational RNAi therapeutic in development for the treatment of hereditary cerebral amyloid angiopathy and autosomal dominant Alzheimer’s Disease, which we are leading. We are also advancing multiple other programs with Regeneron.

With respect to our Cardio-Metabolic pipeline, in March 2013, we entered into an exclusive, worldwide license with MDCO (acquired by Novartis AG in January 2020) pursuant to which MDCO was granted the right to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9 for the treatment of

hypercholesterolemia and other human diseases, including inclisiran. In March 2018, we entered into a discovery collaboration with Regeneron to identify RNAi therapeutics for nonalcoholic steatohepatitis, or NASH, and potentially other related diseases, and in November 2018, we and Regeneron entered into a separate, fifty-fifty collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts. In April 2020, we entered into a development and commercialization collaboration with Dicerna to advance investigational RNAi therapeutics for the treatment of alpha-1 antitrypsin deficiency-associated liver disease, or alpha-1 liver disease.

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

With respect to our Genetic Medicine pipeline, we formed a broad strategic alliance with Sanofi 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 have the exclusive right to pursue the further global development and commercialization of all TTR products, including ONPATTRO, AMVUTTRA 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 fitusiran and any back-up products. In April 2019, we and Sanofi agreed to further amend the 2014 Sanofi collaboration to conclude the research and option phase and to amend and restate the AT3 License Terms to modify certain of the business terms.

We intend to continue to evaluate and explore partnership opportunities through collaboration and licensing arrangements, and may enter into new collaborations to advance certain products or disease areas. For example, in January 2022, we announced that we and Novartis agreed to collaborate on the discovery and development of an siRNA-based targeted therapy to restore functional liver cells in patients with end-stage liver diseases.

We also have entered into license agreements to obtain rights to intellectual property in the field of RNAi. In addition, because delivery of RNAi therapeutics has historically been an important objective of our research activities, we have entered into various collaboration and licensing arrangements with other companies and academic institutions to gain access to delivery technologies, including various LNP delivery technologies, and we may enter into such agreements in the future to gain access to products or technologies. For example, in 2021, we entered into a license and collaboration agreement with PeptiDream to discover and develop peptide-siRNA conjugates leveraging PeptiDream's proprietary Peptide Discovery Platform System technology.

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, 2021, which we filed with the SEC on February 10, 2022. 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 September 30,				Nine Months Ended September 30,			
(In thousands, except percentages)	2022	2021	$ Change	% Change	2022	2021	$ Change	% Change
Total revenues	$ 264,306	$ 187,633	$ 76,673	41 %	$ 702,383	$ 585,752	$ 116,631	20 %
Operating costs and expenses	$ 522,346	$ 369,310	$ 153,036	41 %	$ 1,298,841	$ 1,099,843	$ 198,998	18 %
Loss from operations	$ (258,040)	$ (181,677)	$ (76,363)	42 %	$ (596,458)	$ (514,091)	$ (82,367)	16 %
Total other expense, net	$ (147,903)	$ (22,559)	$ (125,344)	556 %	$ (323,514)	$ (77,751)	$ (245,763)	316 %
Net loss	$ (405,920)	$ (204,514)	$ (201,406)	98 %	$ (923,663)	$ (594,364)	$ (329,299)	55 %

Discussion of Results of Operations

Revenues

Total revenues consist of the following:

(In thousands, except percentages)	Three Months Ended September 30, 2022	2021	$ Change	% Change	Nine Months Ended September 30, 2022	2021	$ Change	% Change
Net product revenues	$ 232,267	$ 167,044	$ 65,223	39 %	$ 632,654	$ 463,624	$ 169,030	36 %
Net revenues from collaborations	29,297	20,136	9,161	45 %	64,267	121,328	(57,061)	(47)%
Royalty revenue	2,742	453	2,289	505 %	5,462	800	4,662	583 %
Total	$ 264,306	$ 187,633	$ 76,673	41 %	$ 702,383	$ 585,752	$ 116,631	20 %

Net Product Revenues

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

(In thousands, except percentages)	Three Months Ended September 30, 2022	2021	$ Change	% Change	Nine Months Ended September 30, 2022	2021	$ Change	% Change
ONPATTRO								
United States	$ 67,196	$ 51,247	$ 15,949	31 %	$ 200,588	$ 153,109	$ 47,479	31 %
Europe	57,217	51,019	6,198	12 %	167,185	136,576	30,609	22 %
Rest of World	20,537	18,051	2,486	14 %	67,614	46,422	21,192	46 %
Total	144,950	120,317	24,633	20 %	435,387	336,107	99,280	30 %
AMVUTTRA								
United States	25,060	—	25,060	N/A	25,060	—	25,060	N/A
Europe	169	—	169	N/A	169	—	169	N/A
Total	25,229	—	25,229	N/A	25,229	—	25,229	N/A
GIVLAARI								
United States	31,169	22,372	8,797	39 %	84,505	62,502	22,003	35 %
Europe	12,477	7,568	4,909	65 %	36,059	22,461	13,598	61 %
Rest of World	2,013	1,893	120	6 %	5,522	2,173	3,349	154 %
Total	45,659	31,833	13,826	43 %	126,086	87,136	38,950	45 %
OXLUMO								
United States	6,383	5,236	1,147	22 %	18,916	13,156	5,760	44 %
Europe	9,348	9,658	(310)	(3)%	25,099	27,225	(2,126)	(8)%
Rest of World	698	—	698	N/A	1,937	—	1,937	N/A
Total	16,429	14,894	1,535	10 %	45,952	40,381	5,571	14 %
Total net product revenues	$ 232,267	$ 167,044	$ 65,223	39 %	$ 632,654	$ 463,624	$ 169,030	36 %

Net product revenues increased during the three and nine months ended September 30, 2022, compared to the same periods in 2021, as a result of increased patients on ONPATTRO, AMVUTTRA, GIVLAARI, and OXLUMO therapies, offset by an unfavorable impact from foreign exchange rates on our international revenues.

We expect net product revenues to increase during 2022, as compared to 2021, as we continue to add new patients onto our commercial products, as well as launch these products into additional markets, assuming regulatory approvals.

Net Revenues from Collaborations and Royalty Revenue

Net revenues from collaborations consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2022	2021	$ Change	% Change	2022	2021	$ Change	% Change
Regeneron Pharmaceuticals	$ 21,979	$ 14,161	$ 7,818	55 %	$ 34,405	$ 90,908	$ (56,503)	(62)%
Novartis AG	5,803	4,160	1,643	39 %	27,472	21,179	6,293	30 %
Vir Biotechnology	441	1,233	(792)	(64)%	1,137	8,033	(6,896)	(86)%
Other	1,074	582	492	85 %	1,253	1,208	45	4 %
Total	$ 29,297	$ 20,136	$ 9,161	45 %	$ 64,267	$ 121,328	$ (57,061)	(47)%

Net revenues from collaborations increased during the three months ended September 30, 2022, as compared to the same period in 2021, primarily due to an increase in revenue recognized in connection with our collaboration agreement with Regeneron, attributed to an increase in reimbursable activities under our research services arrangement in addition to an increase in revenue recognized associated with our clinical trial activities.

Net revenues from collaborations decreased during the nine months ended September 30, 2022, as compared to the same periods in 2021, primarily due to a decrease in revenue recognized in connection with our collaboration agreement with Regeneron, attributed to reduced research and manufacturing activities and timing of reimbursable activities.

We earn royalty revenue from global net sales of Leqvio by our partner, Novartis. In December 2020, Leqvio received marketing authorization from the EC for the treatment of adults with hypercholesterolemia or mixed dyslipidemia, and in December 2021, Leqvio was approved by the FDA for the treatment of adults with HeFH or ASCVD. During the quarter ended September 30, 2022, we recorded $2.7 million in royalty revenue.

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 partners, achievement of milestones under our collaboration agreements, and royalties associated with sales of Leqvio. We expect net revenues from collaboration and royalty revenue to decrease in 2022, as compared to 2021, primarily due to the timing of reimbursable activities in our collaboration with Regeneron.

Operating Costs and Expenses

Operating costs and expenses consist of the following:

(In thousands, except percentages)	Three Months Ended September 30,				Nine Months Ended September 30,			
	2022	2021	$ Change	% Change	2022	2021	$ Change	% Change
Cost of goods sold	$ 36,507	$ 28,091	$ 8,416	30 %	$ 94,002	$ 81,370	$ 12,632	16 %
Cost of collaborations and royalties	4,609	4,572	37	1 %	23,549	21,110	2,439	12 %
Research and development	245,371	194,572	50,799	26 %	620,976	563,106	57,870	10 %
Selling, general and administrative	235,859	142,075	93,784	66 %	560,314	434,257	126,057	29 %
Total	$ 522,346	$ 369,310	$ 153,036	41 %	$ 1,298,841	$ 1,099,843	$ 198,998	18 %

Cost of goods sold.

Cost of goods sold as a percentage of net product revenues decreased to 15.7% and 14.9% for the three and nine months ended September 30, 2022, respectively, as compared to 16.8% and 17.6% for the three and nine months ended September 30, 2021, respectively, primarily due to fully amortized intangible assets and reduced royalties as a result of the expiry of third-party intellectual property.

We anticipate variability in our cost of goods sold as a percentage of net product revenues due to the timing of manufacturing runs and utilization and the depletion of zero-cost inventories, as well as launch our approved products into additional markets, assuming regulatory approvals. We expect cost of goods sold will increase during 2022, as compared to 2021, primarily as a result of an expected increase in net product sales as well as the sale of capitalized inventory.

Cost of collaborations and royalties.

Cost of collaborations and royalties increased during the three and nine months ended September 30, 2022, as compared to the same periods in 2021, primarily due to timing and demand of GalNAc material supply to our collaboration partners to support certain product manufacturing and ongoing clinical trials.

We expect cost of collaborations and royalties to remain relatively consistent during 2022, as compared to 2021, due to consistency in planned GalNAc material to be supplied to our collaboration partners.

Research and development.

Research and development expenses consist of the following:

	Three Months Ended September 30,				Nine Months Ended September 30,			
(In thousands, except percentages)	2022	2021	$ Change	% Change	2022	2021	$ Change	% Change
Clinical research and outside services	$ 104,762	$ 108,851	$ (4,089)	(4)%	$ 288,833	$ 290,627	$ (1,794)	(1)%
Compensation and related	58,377	47,168	11,209	24 %	163,416	142,547	20,869	15 %
Stock-based compensation	52,962	12,417	40,545	327 %	75,217	49,878	25,339	51 %
Occupancy and all other costs	29,270	26,136	3,134	12 %	93,510	80,054	13,456	17 %
Total	$ 245,371	$ 194,572	$ 50,799	26 %	$ 620,976	$ 563,106	$ 57,870	10 %

For the three and nine months ended September 30, 2022, the increases in research and development expenses, as compared to the same periods in the prior year, were primarily due to the following:

- Increased stock-based compensation expense primarily due to the accounting for certain performance-based awards; and
- Increased compensation and related expenses as a result of increased headcount to support our R&D pipeline and development expenses associated with the KARDIA-1 and KARDIA-2 zilebesiran phase 2 studies.

Offset by:

- Decreased clinical research and outside services due to a decrease in clinical batches manufactured.

During the three and nine months ended September 30, 2022 and 2021, in connection with advancing activities under our collaboration agreements, we incurred research and development expenses, primarily related to external development and clinical expenses, including the manufacture of clinical product.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
(In thousands)	2022	2021	2022	2021
Regeneron Pharmaceuticals	$ 19,948	$ 14,401	$ 43,002	$ 51,972
Other	357	1,337	1,172	7,565
Total	$ 20,305	$ 15,738	$ 44,174	$ 59,537

Selling, general and administrative.

Selling, general and administrative expenses consist of the following:

(In thousands, except percentages)	Three Months Ended September 30, 2022	2021	$ Change	% Change	Nine Months Ended September 30, 2022	2021	$ Change	% Change
Compensation and related	$ 70,361	$ 52,075	$ 18,286	35 %	$ 197,346	$ 162,516	$ 34,830	21 %
Consulting and professional services	59,557	45,622	13,935	31 %	155,138	129,887	25,251	19 %
Stock-based compensation	75,156	20,950	54,206	259 %	112,665	71,257	41,408	58 %
Occupancy and all other costs	30,785	23,428	7,357	31 %	95,165	70,597	24,568	35 %
Total	$ 235,859	$ 142,075	$ 93,784	66 %	$ 560,314	$ 434,257	$ 126,057	29 %

For the three and nine months ended September 30, 2022, the increases in selling, general and administrative expenses, as compared to the same periods in the prior year, were primarily due to the following:

- Increased stock-based compensation expense primarily due to the accounting for certain performance-based awards;
- Increased compensation and related expenses as a result of increased headcount; and
- Increased consulting and professional services expenses to support our commercial portfolio.

We expect that research and development expenses combined with selling, general and administrative expenses will increase during 2022, as compared to 2021, as we continue to advance and develop our platform and pipeline, advance our product candidates, including partnered programs, into later-stage development, prepare regulatory submissions and continue to build-out our global commercial and compliance infrastructure and field team to support ONPATTRO, GIVLAARI, OXLUMO, and the launch of AMVUTTRA in the U.S. and EU, as well as launch these products into additional markets, assuming regulatory approvals. However, we expect that certain expenses will be variable depending on the timing of manufacturing batches, clinical trial enrollment and results, regulatory review of our product candidates and programs, and stock-based compensation expenses due to our determination regarding the probability of vesting for performance-based awards.

Other (Expense) Income.

Other (expense) income consists of the following:

(In thousands, except percentages)	Three Months Ended September 30, 2022	2021	$ Change	% Change	Nine Months Ended September 30, 2022	2021	$ Change	% Change
Interest expense	$ (41,084)	$ (40,274)	$ (810)	2 %	$ (126,055)	$ (106,205)	$ (19,850)	19 %
Other (expense) income, net								
Interest income	7,820	225	7,595	3,376 %	10,731	1,084	9,647	890 %
Realized and unrealized (losses) gains on marketable equity securities	(7,850)	18,691	(26,541)	(142)%	(40,108)	61,273	(101,381)	(165)%
Change in fair value of development derivative liability	(25,084)	3,188	(28,272)	(887)%	(70,776)	(19,655)	(51,121)	260 %
Other	(5,119)	(4,389)	(730)	17 %	(20,720)	(14,248)	(6,472)	45 %
Loss on the extinguishment of debt	(76,586)	—	(76,586)	N/A	(76,586)	—	(76,586)	N/A
Total	$ (147,903)	$ (22,559)	$ (125,344)	556 %	$ (323,514)	$ (77,751)	$ (245,763)	316 %

Total other expense increased during the three and nine months ended September 30, 2022, as compared to the same periods in 2021, primarily due to a $76.6 million loss on the extinguishment of the Blackstone credit agreement, increased loss as a result of a mark-to-market adjustment related to the development derivative liability and increased realized and unrealized losses on our marketable equity securities holdings.

Liquidity and Capital Resources

The following table summarizes our cash flow activities:

(In thousands)	Nine Months Ended September 30, 2022	2021
Net loss	$ (923,663)	$ (594,364)
Non-cash adjustments to reconcile net loss to net cash used in operating activities:	536,245	250,524
Changes in operating assets and liabilities	(21,878)	(147,712)
Net cash used in operating activities	(409,296)	(491,552)
Net cash provided by investing activities	309,265	140,105
Net cash provided by financing activities	362,316	954,827
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(9,049)	(5,968)
Net increase in cash, cash equivalents and restricted cash	253,236	597,412
Cash, cash equivalents and restricted cash, beginning of period	822,153	499,046
Cash, cash equivalents and restricted cash, end of period	$ 1,075,389	$ 1,096,458

Operating activities

Net cash used in operating activities decreased during the nine months ended September 30, 2022, compared to the same periods ended September 30, 2021, primarily due to decreased cash disbursements related to working capital payments and stronger cash receipts from increased product sales.

Investing activities

Net cash used in investing activities increased during the nine months ended September 30, 2022, compared to the nine months ended September 30, 2021, primarily due to net activities related to our marketable debt securities.

Financing activities

Net cash provided by financing activities decreased during the nine months ended September 30, 2022, compared to the nine months ended September 30, 2021, primarily due to greater cash received in 2021, including $500.0 million received from our sale of one-half of our royalty interest under the Novartis agreement in September 2021 and $250.0 million received in connection with the second drawdown on our credit agreement in June 2021, offset by $136.2 million received from the issuance of convertible debt, net of repayment of credit facility and purchase of capped call transactions in September 2022.

Additional Capital Requirements

We currently have programs focused on a number of therapeutic areas and, as of September 30, 2022, have received regulatory approval and commercially launched four products. However, our ongoing development efforts may not be successful and we may not be able to commence sales of any other products or successfully expand the indications for our approved products, including ONPATTRO, AMVUTTRA and OXLUMO in the future. In addition, we anticipate that we will continue to generate losses as a result of planned expenditures for research and development activities relating to our research platform, our drug development programs, including clinical trial and manufacturing costs, the establishment of late-stage clinical, manufacturing, 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 2021 Annual Report on Form 10-K in “Part II, Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.” As of September 30, 2022, 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 2021 Annual Report on Form 10-K.

Based on our current operating plan, we believe that our cash, cash equivalents and marketable equity and debt securities as of September 30, 2022, together with the cash we expect to generate from product sales and under our current alliances, including milestones and royalties on Leqvio sales, will be sufficient to enable us to advance our long-term strategic goals for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q. However, due to numerous factors described in more detail under the caption Part II, Item 1A, "Risk Factors" of this Quarterly Report on Form 10-Q, we may require significant additional funds earlier than we currently expect in order to continue to commercialize 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, 2021. As of September 30, 2022, there have been no significant changes to the financial market risks described as of December 31, 2021. We do not currently anticipate any other near-term changes in the nature of our financial market risk exposures or in management's objectives and strategies with respect to managing such exposures.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer (principal executive officer) and executive vice president, Chief Financial Officer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2022, our Chief Executive Officer and executive vice president, Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control

There were no changes in our internal control over financial reporting during the quarter ended September 30, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

For a discussion of material pending legal proceedings, please read Note 14, Commitments and Contingencies, 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

We operate in an environment that involves a number of significant risks and uncertainties. We caution you to read the following risk factors, which have affected, and/or in the future could affect, our business, prospects, operating results, and financial condition. The risks described below include forward-looking statements, and actual events and our actual results may differ materially from these forward-looking statements. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also impair our business, prospects, operating results, and financial condition. Furthermore, additional risks and uncertainties are described under other captions in this report and should also be considered by our investors.

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

Risks Related to Our Dependence on Third Parties

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

Risks Related to Managing Our Operations

- If we are unable to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors, our ability to implement our business plan may be adversely affected.
- At the start of 2022 we underwent our first CEO succession. Any leadership transition carries with it disruption risks that could have a negative impact on the execution of our *Alnylam P^{5}x25* strategy. These risks include our ability to attract and retain qualified employees.
- We may have difficulty expanding our operations successfully as we continue our evolution from a U.S.- and Europe-based company primarily involved in discovery, pre-clinical testing and clinical development into a global company

that develops and commercializes multiple drugs in multiple geographies including Asia, Latin America and the Middle East.

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

- Any product candidates we or our partners develop may fail in development or be delayed to a point where they do not become commercially viable.
- We or our partners may be unable to obtain U.S. or foreign regulatory approval for our or our partnered product candidates, or if approved, may fail to obtain desired labeling for such products.
- Even if we or our partners obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory oversight.
- Even if we receive regulatory approval to market our product candidates, and our collaborators receive regulatory approval to market product candidates discovered by us or developed with our technology, the market may not be receptive to such product candidates upon their commercial introduction, which could prevent us from becoming profitable.
- We are a multi-product commercial company and expect to continue to invest significant financial and management resources to continue to scale our marketing, sales, market access and distribution capabilities and further establish our global commercial and compliance infrastructure, and our commercial efforts may not be successful.
- The patient populations suffering from hATTR amyloidosis with polyneuropathy, AHP, and PH1 are small and have not been established with precision.
- We may incur significant liability if enforcement authorities allege or determine that we are engaging in commercial activities or promoting our commercially approved products in a way that violates applicable regulations, including in connection with the ongoing DOJ investigation.
- Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

Risks Related to Patents, Licenses and Trade Secrets

- If we are not able to obtain and enforce patent protection for our discoveries, our ability to develop and commercialize our product candidates will be harmed.
- We license patent rights from third-party owners. If such owners do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, our competitive position and business prospects may be harmed.
- Other companies or organizations may challenge our patent rights or may assert patent rights that prevent us from developing and commercializing our products.
- If we become involved in 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., 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 RNAi technology.

Risks Related to Competition

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

Risks Related to Our Common Stock

- If our stock price fluctuates, purchasers of our common stock could incur substantial losses.
- We may incur significant costs from class action litigation.

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

Risks Related to Our Convertible Notes

- Servicing our debt may require a significant amount of cash. 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 the Notes or to repurchase the Notes for cash upon a fundamental change, and our future debt may contain limitations on our ability to pay cash upon conversion of the Notes or to repurchase the Notes.
- The conditional conversion feature of the Notes, if triggered, may adversely affect our financial condition and operating results.

Risks Related to Our Business

Risks Related to Our Financial Results

The marketing and sale of our approved products or any future products may be less successful than anticipated, and we may be unable to expand the indications for ONPATTRO, AMVUTTRA or OXLUMO.

In 2018, our first commercial product, ONPATTRO, was approved by the FDA and EMA, and we have since received approval and launched ONPATTRO in several additional territories. In 2019, the FDA approved our second product, GIVLAARI, which was also approved by the EMA and has since received approval in several additional territories, and in 2020, the FDA and EMA approved our third product, OXLUMO, which received additional regulatory approvals in 2021 and 2022. In June 2022, the FDA approved AMVUTTRA, which was granted marketing authorization in Europe and the United Kingdom, or UK, by the EC in September 2022 and has since received regulatory approval in Japan. We also have multiple product candidates in late-stage clinical development. While we have commercially launched four products, we cannot predict whether we will successfully market and sell our approved products, or successfully expand the indications of certain of our approved products. For example, in August and September 2022, we reported positive safety and efficacy results from the APOLLO-B Phase 3 clinical trial of patisiran, which was designed and powered to evaluate the effects of patisiran on functional capacity and quality of life in patients with ATTR amyloidosis with cardiomyopathy. While we believe that the APOLLO-B results after 12 months validate the therapeutic hypothesis of RNAi therapeutics targeting TTR as potential treatment for patients with ATTR amyloidosis with cardiomyopathy and intend to submit an sNDA to the FDA for review in late 2022, we cannot be certain that the results from the APOLLO-B clinical trial will support regulatory approval of patisiran for the treatment of patients with ATTR amyloidosis with cardiomyopathy.

To execute our business plan of building a profitable, top five biotech company over the next 5 years and achieving our *Alnylam P^{5}x25* strategy and the metrics associated with such strategy, in addition to successfully marketing, selling and expanding the indications of 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 and muscle;
- build and maintain a strong intellectual property portfolio;
- gain regulatory acceptance for the development and commercialization of our product candidates and market success for our approved products, as well as any other products we commercialize;
- attract and retain customers for our products;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

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

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

We have experienced significant operating losses since our inception. As of September 30, 2022, we had an accumulated deficit of $6.36 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 in additional countries during the remainder of 2022 and beyond, we may never attain profitability or positive cash flow from operations. For the three months ended September 30, 2022, we recognized $232.3 million in net product revenues from sales of ONPATTRO, AMVUTTRA, GIVLAARI and OXLUMO. While our full year operating loss for 2021 and 2020 each improved relative to the prior year, marking 2019 as our peak operating loss year, we expect to 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 self-

sustainability by the end of 2025. While we believe our current cash, cash equivalents and marketable equity and debt securities, as well as the revenue we expect to generate from product sales and under our current alliances, including milestones and royalties on Leqvio sales, should enable us to achieve a self-sustainable profile without the need for future equity financing, we will depend on our ability to generate revenues to achieve this goal. In addition to revenues derived from sales of our current and future, if any, commercially approved products, we anticipate that a portion of any revenues we generate over the next several years will continue to be from alliances with pharmaceutical and biotechnology companies, including Novartis and Regeneron. We cannot be certain that we will be able to maintain our existing alliances, secure and maintain new alliances, meet the obligations, or achieve any milestones that we may be required to meet or achieve to receive payments under our existing or new alliances. Moreover, we cannot be certain that our partners, including Novartis, will continue to successfully execute their obligations under our alliance agreements and generate additional revenues for us.

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

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

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

We believe 2019 was our peak operating loss year, and believe that our current cash, cash equivalents and marketable equity and debt securities, as well as revenue we expect to generate from product sales and under our current alliances, including milestones and royalties on Leqvio sales, will enable us to achieve a self-sustainable financial profile without need for future equity financing. However, our future capital requirements and the period for which we expect our existing resources to support our operations may vary from what we expect. We have based our expectations on a number of factors, many of which are difficult to predict or are outside of our control, including:

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

- the timing, receipt and amount of sales and royalties, if any, from our approved products and our potential products, if and when approved; and
- the outcome of the regulatory review process and commercial success of drug products for which we are entitled to receive royalties, including Leqvio.

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

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, further dilution to our existing stockholders will result. In addition, as a condition to providing additional funding to us, future investors may demand, and may be granted, rights superior to those of existing stockholders.

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

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

The ongoing COVID-19 pandemic continues to rapidly evolve and the ultimate impact of this pandemic remains uncertain. COVID-19 has and may continue to impact our operations and those of our third-party partners and the ultimate impact on our business and financial results remains uncertain and cannot be predicted with confidence, and will depend on many factors, including the scope, severity, duration and any recurrence of the COVID-19 pandemic, including through any new variant strains of the underlying virus, the actions taken to contain the pandemic or mitigate its impact, the direct and indirect economic effects of the pandemic and containment measures, the effectiveness of vaccination and booster vaccination campaigns, among others. The continued development and fluidity of the COVID-19 pandemic precludes any prediction as to its full impact on our business.

In response to the spread of COVID-19, we took, and have continued to take, both temporary and ongoing precautionary measures, intended to help minimize the risk of the virus to our employees and their families, including implementing a global work from home policy in early March 2020 for nearly all employees who were able to perform their duties remotely. Our office sites are currently operational with appropriate safety precautions based on COVID-19 vaccination rates and local guidance, and in October 2021, we formally re-opened our U.S. offices, and implemented a mandatory vaccination policy requiring all U.S. employees and contractors to be fully vaccinated, subject to certain medical and religious accommodations. Working arrangements for many of our employees differ from the arrangements before the COVID-19 pandemic, and we expect a number of employees will continue to work in a remote capacity or a hybrid of in-person and remote work. We may face several challenges or disruptions as result of these working arrangements, and our hybrid of in-person and remote work option may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. To the extent that we have less remote work opportunities and less flexibility than our competitors, our ability to attract and retain talent may be materially affected, which could adversely impact our employee recruitment and retention efforts. In addition, the increase in certain of our employees working remotely has amplified certain risks to our business, including increased demand on our information technology resources and systems, increased phishing and other cybersecurity attacks, and any failure to effectively manage these risks, including to timely identify and appropriately respond to any cyberattacks, could adversely impact our business operations.

If conditions worsen or if the duration of the pandemic extends significantly, we may experience disruptions that could impact our business and operations, including our ability to successfully commercialize our approved products, and we may not be able to meet expectations with respect to commercial sales. In addition, we may also experience decreased patient demand for our approved products if current or potential patients decide to delay treatment as a result of the COVID-19 or a future pandemic. Business interruptions from the current or future pandemics, including staffing shortages, raw material or other supply chain shortages, production slowdowns and disruptions in delivery systems, may also adversely impact the third parties we or our partners rely on in the U.S. and abroad to sufficiently manufacture our approved products and to produce product candidates in quantities we require, which may impair our commercialization efforts, our research and development activities and the potential commercialization of our product candidates.

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

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

Health regulatory agencies globally may also experience disruptions in their operations as a result of the ongoing COVID-19 pandemic, which may impact review, inspection and approval timelines. Since March 2020, when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, and the agency does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. For example, in December 2020, the FDA issued a complete response letter regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the Prescription Drug User Free Act, or the PDUFA, action date due to unresolved facility inspection-related conditions. The FDA ultimately approved Novartis' NDA in December 2021. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

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

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

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

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

Geopolitical risks associated with the ongoing military conflict between Russia and Ukraine could have an adverse impact on our business, financial condition and results of operations, including our clinical trials.

Russia's invasion of Ukraine, which has persisted for months, and the global response, including the imposition of sanctions by the U.S., EU and other countries, may have an adverse impact on our business, including our clinical trials, the financial markets and the global economy. The uncertain nature, magnitude, and duration of hostilities stemming from the

conflict in Ukraine, including the potential effects of sanctions limitations, retaliatory cyber-attacks on the world economy and markets, have also contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business and operations.

Additionally, the ongoing conflict in Ukraine may disrupt the ability of our commercial research organizations, or CROs, to conduct clinical trials at certain sites in Ukraine. Moreover, enrollment and retention of clinical trial participants may be adversely affected. We cannot be certain what the overall impact of this conflict will be on our ability to conduct and complete our clinical trials on schedule. However, interruptions of our clinical trials could significantly delay our clinical development plans and potential authorization or approval of our product candidates, which could increase our costs and jeopardize our ability to successfully commercialize our product candidates.

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

Our quarterly operating results have fluctuated in the past, and may continue to do so in the future. Our operating results may fluctuate due to the impact of the COVID-19 and related variants or a future pandemic, the level of success of our commercial efforts and resulting revenues, as well as the variable nature of our operating expenses as a result of the timing and magnitude of expenditures. For example, due to the impact of the COVID-19 pandemic, combined net product revenues in the first quarter of 2022 for our commercially approved products were negatively impacted. In addition, in one or more future periods, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could substantially decline.

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

Our condensed consolidated financial statements have been prepared in accordance with 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 management. If, for any reason, our revenues and/or expenses differ materially from our guidance, we may have to adjust our publicly announced financial guidance. For example, in April 2022, we decreased our 2022 guidance range for combined net product revenues, and in October 2022, we decreased our guidance range for our collaboration and royalty revenue. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline.

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

As of September 30, 2022, we had $2.27 billion in cash, cash equivalents and marketable securities. We historically have invested these amounts in high–grade corporate notes, commercial paper, securities issued or sponsored by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. Corporate notes may also include foreign bonds denominated in U.S. dollars. These investments are subject to general credit, liquidity, market and interest rate risks. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

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

Our revenue from outside of the U.S. will increase as our products, whether commercialized by us or our collaborators, gain marketing approval in such jurisdictions. 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. For example, during the first three quarters of 2022, we experienced an unfavorable impact from foreign exchange rates on our international revenues. Continued volatility in foreign exchange rates is likely to impact our operating results and financial condition.

Changes in tax law could adversely affect our business and financial condition.

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

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

Risks Related to Our Dependence on Third Parties

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

We are continuing to advance our commercial capabilities, including in marketing, sales, market access and distribution, to support our wholly-owned products. We also continue to advance our growing pipeline of RNAi therapeutic opportunities. However, we may not have adequate capacity or capabilities to advance all of our therapeutic opportunities. Accordingly, we have entered into alliances with other companies and collaborators that we believe can provide such capabilities in certain territories and/or for certain product candidates, and we intend to enter into additional such alliances in the future. Our collaboration strategy is to form alliances that create significant value for us and our collaborators in the advancement of RNAi therapeutics as a new class of innovative medicines. Specifically, with respect to our Genetic Medicine pipeline, as a result of our broad strategic alliance with Sanofi formed in 2014, Sanofi has the right to develop and commercialize fitusiran globally. In addition, we formed a collaboration with MDCO (which was acquired by Novartis in January 2020) to advance inclisiran. In March 2018, we entered into a discovery collaboration with Regeneron to identify RNAi therapeutics for NASH and potentially other related diseases, and in November 2018, we and Regeneron entered into a separate, fifty-fifty collaboration to further research, co-develop and commercialize any therapeutic product candidates that emerge from these discovery efforts. In October 2017, we announced an exclusive licensing agreement with Vir for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic HBV infection. In April 2020, we entered into a development and commercialization collaboration with Dicerna (which was acquired by Novo Nordisk in December 2021) to advance investigational RNAi therapeutics for the treatment of alpha-1 liver disease. With respect to our CNS/Ocular Disease pipeline, in April 2019, we announced a global, strategic collaboration with Regeneron to discover, develop and commercialize RNAi therapeutics for a broad range of diseases by addressing therapeutic targets expressed in the eye and CNS, in addition to a select number of targets expressed in the liver.

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

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

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

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

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

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

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

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

- pursue alternative technologies or develop alternative products, either on its own or jointly with others, that may be competitive with the products on which it is collaborating with us or which could affect its commitment to the collaboration with us;
- pursue higher-priority programs or change the focus of its development programs, which could affect the collaborator's commitment to us; or

- if it has marketing rights, choose to devote fewer resources to the marketing of our product candidates, if any are approved for marketing, than it does for product candidates developed without us.

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

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

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

At the present time, we may manufacture limited quantities of clinical trial materials ourselves, but otherwise we continue to rely on third parties to manufacture the drug substance and finished product we will require for clinical trials that we initiate and to support the commercial supply of our approved products and any of our other product candidates. There are a limited number of manufacturers that supply synthetic siRNAs. We currently rely on a limited number of CMOs for our supply of synthetic siRNAs. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our CMOs to meet our delivery time requirements or provide adequate amounts of material to meet our needs, and ultimately delay our clinical trials and potentially put at risk commercial supply, as well as result in additional expense to us. To fulfill our siRNA requirements, we will likely need to secure alternative suppliers of synthetic siRNAs and such alternative suppliers are limited and may not be readily available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. As noted above, in order to ensure long-term supply capabilities for our RNAi therapeutics, we are developing our own capabilities to manufacture drug substance for clinical and commercial use.

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

In developing manufacturing capabilities by building our own manufacturing facilities, we have incurred substantial expenditures, and expect to incur significant additional expenditures in the future. Also, we have had to, and will likely need to continue to, hire and train qualified employees to staff our facilities. If we are unable to manufacture sufficient quantities of material or if we encounter problems with our facilities in the future, we may also need to secure alternative suppliers, and such alternative suppliers may not be available, or we may be unable to enter into agreements with them on reasonable terms and in a timely manner. Given our dependence on a limited number of CMOs to supply our commercial products and clinical candidates, and our dependence on our own facility, any delay in supply caused by the COVID-19 pandemic could impact our ability to procure sufficient supplies for our approved products, and the development of our product candidates could also be

delayed. Any delay or setback in the manufacture of our approved products could impede ongoing commercial supply, which could significantly impact our revenues and operating results. In addition, to the extent we or our partners rely on CMOs outside of the U.S. to supply drug substance for our product candidates, any delays or disruptions in supply caused by the COVID-19 pandemic could have a material adverse impact on the research and development activities and potential commercialization of our or our partners' product candidates.

The manufacturing process for our approved products and any other products that we may develop, is subject to the FDA and foreign regulatory authority approval process and we will need to meet, and will need to contract with CMOs who can meet, all applicable FDA and foreign regulatory authority requirements on an ongoing basis. 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 existing regulatory 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 for vutrisiran. 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.

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

- we or our current or future collaborators may not be able to initiate or continue clinical trials of product candidates that are under development;
- we or our current or future collaborators may be delayed in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;
- we may lose the cooperation of our collaborators;
- our facilities and those of our CMOs, and our products could be the subject of inspections by regulatory authorities that could have a negative outcome and result in delays in supply;
- we may be required to cease distribution or recall some or all batches of our products or take action to recover clinical trial material from clinical trial sites; and
- ultimately, we may not be able to meet commercial demands for our products.

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

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

If our third-party service providers cannot adequately and timely fulfill their obligations to us for any reason, including due to disruptions caused by the COVID-19 pandemic or the ongoing conflict in Ukraine on their operations or at the sites they are overseeing, or if the quality and accuracy of our clinical trial data is compromised due to failure by such third party to adhere to our protocols or regulatory requirements or if such third parties otherwise fail to meet deadlines, our development plans and/or

regulatory reviews for marketing approvals may be delayed or terminated. As a result, our stock price would likely be negatively impacted, and our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate additional revenues could be delayed.

Risks Related to Managing Our Operations

If we are unable to attract and retain qualified key management and scientists, development, medical and commercial staff, consultants and advisors, in particular following our January 2022 leadership transition, our ability to implement our business plan may be adversely affected.

We are highly dependent upon our senior management and our scientific, clinical, sales and medical staff. At the start of 2022, we underwent our first leadership transition as a publicly traded company with commercial operations, and we believe our current management team is well-positioned to execute our strategy. Nonetheless, this leadership transition may be viewed negatively by employees, investors and/or our strategic partners. Moreover, attrition associated with this transition could significantly delay or prevent the achievement of product development and commercialization, and other business objectives, and adversely impact our stock price. Our employment arrangements with our key personnel are terminable without notice. We do not carry key person life insurance on any of our employees.

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

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

As we continue the commercial launches of our approved products, and increase the number of product candidates we are developing, we will need to continue to expand our operations in the U.S. and further develop operations in the EU and other geographies, including Asia and Latin America. To date, we have received regulatory approval for 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 five years and anticipate continuing to hire additional employees globally in the future as we focus on the commercialization of our approved products, and achieving our *Alnylam P^{5}x25* strategy. This growth has placed a strain on our administrative and operational infrastructure and, as a result, we will need to continue to develop additional and/or new infrastructure and capabilities to support our growth and obtain additional space to conduct our global operations in the U.S., the EU, Japan, Latin America and other geographies. If we are unable to develop such additional infrastructure or obtain sufficient space to accommodate our growth in a timely manner and on commercially reasonable terms, our business could be negatively impacted. As we continue the commercialization of our approved products, and as the product candidates we develop enter and advance through clinical trials, we will need to continue to expand our global development, regulatory, manufacturing, quality, compliance, and marketing and sales capabilities, or contract with other organizations to provide these capabilities for us. In addition, as our operations continue to expand, we will need to successfully manage additional relationships with various collaborators, suppliers, distributors and other organizations. Our ability to manage our operations and future growth will require us to continue to enhance our operational, financial and management controls and systems, reporting systems and infrastructure, 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.

Social media is being used to communicate about our clinical development programs and the diseases our investigational RNAi therapeutics are being developed to treat, and we are utilizing what we believe is appropriate social media in connection with our commercialization efforts for our approved products, and we intend to do the same for our future products, if approved. Social media practices in the biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities. For example, for our clinical-stage candidates, patients may use social media channels to comment on their experience in an ongoing blinded clinical study or to report an alleged AE. When

such disclosures occur, there is a risk that study enrollment may be adversely impacted, we fail to monitor and comply with applicable adverse event, or AE, reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our investigational products. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any online platform, including a blog on the internet, or a post on a website, that can be distributed rapidly and could negatively harm our reputation. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

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

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

The pervasiveness of cybersecurity incidents in general and the risks of cyber-crime are complex and continue to evolve. Although we are making significant efforts to maintain the security and integrity of our information systems and are exploring various measures to manage the risk of a security breach or disruption, there can be no assurance that our security efforts and measures will be effective or that attempted security breaches or disruptions would not be successful or damaging. Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage or interruption from computer viruses, unauthorized or inappropriate access or use, natural disasters, pandemics (including COVID-19), terrorism, war (including the ongoing conflict in Ukraine), and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss of pre-clinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts, as well as delays in the commercialization of our products, and significantly increase our costs. To the extent that any disruption, security breach or unauthorized or inappropriate use or access to our systems were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, including but not limited to patient, employee or vendor information, we could incur notification obligations to affected individuals and government agencies, liability, including potential lawsuits from patients, collaborators, employees, stockholders or other third parties and liability under foreign, federal and state laws that protect the privacy and security of personal information, and the development and potential commercialization of our product candidates could be delayed.

Risks Related to Our Industry

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

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

Before obtaining regulatory approval for the commercial distribution of our product candidates, we must conduct, at our own expense, extensive nonclinical tests and clinical trials to demonstrate the safety and/or efficacy in humans of our product candidates. Nonclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome, and the historical failure rate for product candidates is high. We currently have multiple programs in clinical development, including internal and partnered programs in Phase 3 development, as well as several earlier-stage clinical programs. However, we may not be able to further advance any of our product candidates through clinical trials and regulatory approval.

Additionally, several of our planned and ongoing clinical trials utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

If we enter into clinical trials, the results from nonclinical testing or early or late stage clinical trials of a product candidate may not predict the results that will be obtained in subsequent subjects or in subsequent human clinical trials of that product candidate or any other product candidate. For example, we are conducting the APOLLO-B and HELIOS-B Phase 3 clinical trials of patisiran and vutrisiran, respectively, which are investigating the potential of patisiran and vutrisiran to treat the cardiac manifestations of disease in patients with ATTR amyloidosis with cardiomyopathy. We announced positive topline results from the APOLLO-B study in August 2022, and patients enrolled in the study are receiving patisiran as part of an open-label extension period. While both patisiran and vutrisiran have demonstrated positive results in patients with hATTR amyloidosis with polyneuropathy, we cannot be certain that the results from HELIOS-B will be positive or that the results from APOLLO-B and/or HELIOS-B will support approval of patisiran and/or vutrisiran for the treatment of patients with ATTR amyloidosis with cardiomyopathy. There is a high failure rate for drugs proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development, including with respect to patisiran and/or vutrisiran, could have a material adverse effect on our business and operating results. Moreover, our approved products and our current product candidates, employ novel delivery technologies that, with the exception of inclisiran, have yet to be extensively evaluated in human clinical trials and proven safe and effective.

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

Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the age and condition of the patients, the stage and severity of disease, the availability of clinical trials for other investigational drugs for the same disease or condition, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial. For example, we or our partners may experience difficulty enrolling our clinical trials, including, but not limited to, the ongoing clinical trials for fitusiran, due to the availability of existing approved treatments, as well as other investigational treatments in development. In addition, in November 2018 we announced that due to recruitment challenges, we had discontinued a Phase 2 study of cemdisiran in atypical hemolytic uremic syndrome and are focusing our cemdisiran clinical development efforts in a different indication. Delays or difficulties in patient enrollment, including the enrollment delays in our KARDIA-1 Phase 2 monotherapy study of zilebesiran resulting from the ongoing situation in Ukraine, or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments or safety concerns, including the impact of public health emergencies such as the COVID-19 pandemic, can result in increased costs, longer development times or termination of a clinical trial.

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

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

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

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

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

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

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

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

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

Our and our partnered product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, pricing, marketing and distribution of drugs. Rigorous nonclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the U.S. and in many foreign jurisdictions before a new drug can be

marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that the product candidates we and our partners are developing will not obtain the regulatory approvals necessary for us or our collaborators to begin selling them, or, in the case of patisiran and vutrisiran, will not obtain regulatory approval to be sold for broader indications than are currently approved. It is also possible that the FDA or other regulatory authorities may determine that the data generated in clinical trials for a product candidate, including patisiran, while positive, is not sufficient to support the review or approval of an application for regulatory approval.

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

Because the drugs we or our partners are developing represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these drugs. The lack of policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we or our partners may submit. Moreover, the FDA may respond to these submissions by defining requirements we or our partners may not have anticipated. Such responses could lead to significant delays and increased costs in the development of our or our partnered product candidates. In addition, because there may be approved treatments for some of the diseases for which we or our partners may seek approval, including patisiran and vutrisiran for the treatment of ATTR amyloidosis with cardiomyopathy, or treatments in development which are approved by the time we or they apply for approval, in order to receive regulatory approval, we or they may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Interruption or delays in the operations of the FDA, EMA and comparable foreign regulatory agencies due to the COVID-19 pandemic, may impact the review, inspection and approval timelines for our or our partnered product candidates. During the COVID-19 public health emergency, the FDA has worked to ensure timely reviews of applications for medical products in line with its user fee performance goals and conduct mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. 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 complete response letter regarding Novartis' NDA for inclisiran, stating that the agency could not approve the NDA by the PDUFA action date due to unresolved facility inspection-related conditions. In July 2021, Novartis announced that the resubmission to the FDA of the inclisiran NDA to address the complete response letter was filed, and the FDA approved Leqvio (which is the trade name under which inclisiran is marketed in the U.S.) in December 2021. The 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 agency could have a material adverse effect on our efforts to obtain regulatory approval for our product candidates, which could have a material adverse effect on our financial results. For instance, the FDA may request additional clinical or other data or information in connection with the regulatory review of our or our partners' product candidates, including patisiran, including by issuing a complete response letter which may require that we or our partners' submit additional clinical or other data or impose other conditions that must be met in order to secure final approval of our or our partners' 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.

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

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

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

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

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

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

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

The CMO and manufacturing facilities we use to make our approved products and certain of our current product candidates, including our Cambridge facility, our Norton facility, 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 facilities or our CMOs, or our or their manufacturing processes or facilities, may result in restrictions on the drug or CMO or facility, including delay in approval or, in the future, withdrawal of the drug from the market. 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, which delayed our PDUFA goal date and AMVUTTRA's FDA approval. We have developed cGMP capabilities and processes for the manufacture of patisiran formulated bulk drug product for commercial use. In addition, in 2020, we completed construction of a cGMP manufacturing facility for drug substance for clinical and, eventually, commercial use. We may not have the ability or capacity to manufacture material at a broader commercial scale in the future. We may manufacture clinical trial materials, or we may contract a third party to manufacture 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 CMO for regulatory compliance.

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

seizures, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

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

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

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

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

As described above, we remain focused on our global compliance program, which is designed to support the execution of these programs and activities in compliance with applicable laws.

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

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

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

- the timing of our receipt of any marketing approvals, the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our product candidates, as demonstrated in clinical trials and as compared with alternative treatments, if any;

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

For example, one of our two commercially approved therapeutics for the treatment of the polyneuropathy of hATTR amyloidosis in adults, ONPATTRO, utilizes an intravenous mode of administration with pre-medication that physicians and/or patients may not readily adopt, or which may not compete favorably with other available options, including inotersen, marketed by Ionis in several countries, which is administered subcutaneously, or tafamidis, marketed by Pfizer in several countries, which is in pill form. In addition, fitusiran represents a new approach to treating hemophilia which may not be readily accepted by patients and their caregivers. Patisiran, if approved for the treatment of ATTR amyloidosis with cardiomyopathy, could face similar challenges in market acceptance.

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. Even if we successfully scale our commercial capabilities, the market may not be receptive to our commercial products.

Having received our first product approval only four years ago, we have established our capabilities for marketing, sales, market access and distribution over the last several years. We currently expect to rely on third parties to launch and market certain of our product candidates in certain geographies, if approved. However, we are commercializing ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA, and intend to commercialize several of our late-stage 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, and will continue to, require significant financial and management resources. For those products for which we will perform marketing, sales, market access and distribution functions ourselves, including ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA, and for future products we successfully develop where we may retain certain product development and commercialization rights, we could face a number of additional risks, including:

- 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.

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

Our estimates regarding the potential market size for ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA or any future products at the time we commence commercialization, may be materially different from the actual market size, including as a result of the indication approved by regulatory authorities, which could result in significant changes in our business plan and may have a material adverse effect on our results of operations and financial condition. For example, the initial indication approved by the FDA for ONPATTRO is for the treatment of the polyneuropathy of hATTR amyloidosis and not for the treatment of cardiomyopathy or other manifestations of the disease. In addition, the U.S. label does not include cardiac data included in our APOLLO-B Phase 3 study results. This had an adverse impact on the market opportunity for ONPATTRO in the U.S. While data from the APOLLO-B study of patisiran in ATTR amyloidosis patients with cardiomyopathy was positive, the FDA may determine that the data is not supportive of a label expansion of ONPATTRO for the treatment of cardiomyopathy, which would further impact ONPATTRO's market opportunity. In addition, our efforts to raise disease awareness and improve diagnosis of our relevant disease states have been and may in the future be impacted by the COVID-19 pandemic. For example, in 2020 and 2021, we saw a reduction in peer to peer educational opportunities, reduced physician

attendance at congresses and symposia and overall opportunities for physician engagement. As is the case with most orphan diseases, if we cannot successfully raise awareness of these diseases and improve diagnosis, it will be more difficult or impossible to achieve profitability.

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

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

Our ability to commercialize our approved products or any future products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. One or more of our approved products and other products for which we are able to obtain marketing approval may not be considered cost-effective, and the amount reimbursed may be insufficient to allow us to sell such product(s) or any future products on a competitive basis. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for drug products. In the U.S., we have entered into at least 40 value-based agreements, or VBAs, and are negotiating additional VBAs with commercial health insurers. The goal of these agreements is to ensure that we are paid based on the ability of our commercially approved products to deliver results in the real world setting comparable to those demonstrated in clinical trials, and the agreements are structured to link the performance of our approved products in real-world use to financial terms. Partnering with payers on these agreements is also intended to provide more certainty to them for their investment 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 development and other costs, or if reimbursement is denied, our return on investment could be adversely affected. In addition, we have stated publicly that we intend to grow through continued scientific innovation rather than arbitrary price increases. Specifically, we have stated that we will not raise the price of any product for which we receive marketing approval over the rate of inflation, as determined by the consumer price index for urban consumers (approximately 9.1% currently) absent a significant value driver. Our patient access philosophy could also negatively impact the revenues we are able to generate from the sale of one or more of our products in the future.

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

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

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

President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drugs, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs the U.S.

Department of Health and Human Services, or HHS, to provide a report on actions to combat excessive pricing of prescription drugs, continue to clarify and improve the approval framework for generic drugs and identify and address any efforts to impede generic drug competition, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. The FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. In response, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the Most Favored Nation, or MFN, Model may materially and adversely affect the price we receive for any of our commercially approved products. Further, on November 20, 2020, the Centers for Medicare and Medicaid Services, or CMS, issued an Interim Final Rule implementing the MFN Model under which Medicare Part B reimbursement rates will be calculated for certain drugs based on the lowest price drug manufacturers receive in OECD countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, on December 29, 2021, CMS rescinded the proposed MFN rule. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors have been delayed until January 1, 2023, requiring manufacturers to ensure the full value of co-pay assistance is passed on to the patient or these dollars will count toward the Average Manufacturer Price and Best Price calculation of the drug. On May 17, 2022, the U.S. District Court for the District of Columbia granted the Pharmaceutical Research and Manufacturers of America's motion for summary judgement invalidating the accumulator adjustment rule. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the current U.S. presidential administration may reverse or otherwise change these measures, both the current U.S. presidential administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

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

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

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

- Mandatory rebates for drugs sold into the Medicaid program were increased, and the rebate requirement was extended to drugs used in risk-based Medicaid managed care plans.
- The 340B Drug Pricing Program under the Public Health Service Act was extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.
- Pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the "donut hole."
- Pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company's market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.
- The law provides that approval of an application for a follow-on biologic product may not become effective until 12 years after the date on which the reference innovator biologic product was first licensed by the FDA, with a possible six-month extension for pediatric products. After this exclusivity ends, it will be easier for generic manufacturers to enter the market, which is likely to reduce the pricing for such products and could affect our profitability.

- The law creates a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected.
- The law expands eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability.
- The law expands the entities eligible for discounts under the Public Health Service Act pharmaceutical pricing program.
- The law expands healthcare fraud and abuse laws, including the civil FCA and the federal Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance.
- The law establishes new requirements to report financial arrangements with physicians and teaching hospitals and to annually report drug samples that manufacturers and distributors provide to physicians.
- The law establishes a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.
- The law established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery methods.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the suspension, a 1% payment reduction began April 1, 2022, lasting through June 30, 2022. The 2% payment reduction resumed on July 1, 2022. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for our approved products or any of our product candidates for which we may obtain regulatory approval, or the frequency with which our products or any future product is prescribed or used.

Further, there have been several changes to the 340B Drug Pricing Program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain healthcare facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B Drug Pricing Program, and CMS subsequently altered the fiscal years 2019 and 2018 reimbursement formula on specified covered outpatient drugs. The court ruled this change was not an "adjustment" which was within the Secretary's discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court's decision and found that the changes were within the Secretary's authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), and the court denied this petition on October 16, 2020. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021. On July 2, 2021, the Supreme Court granted the petition. On June 15, 2022, the Supreme Court unanimously reversed the Court of Appeals' decision, holding that HHS's 2018 and 2019 reimbursement rates for 340B hospitals were contrary to the statute and unlawful. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

On August 16, 2022, the Inflation Reduction Act of 2022 was passed, which among other things, allows for CMS to negotiate prices for certain single-source drugs and biologics reimbursed under Medicare Part B and Part D, beginning with ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. The legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. Further, the legislation caps Medicare beneficiaries' annual out-of-pocket drug expenses at $2,000. The effect of Inflation Reduction Act of 2022 on our business and the healthcare industry in general is not yet known

The full effects of the U.S. healthcare reform legislation cannot be known until the law is fully implemented through regulations or guidance issued by CMS and other federal and state healthcare agencies. The financial impact of the U.S. healthcare reform legislation over the next few years will depend on a number of factors, including, but not limited, to the policies reflected in implementing regulations and guidance, and changes in sales volumes for products affected by the new

system of rebates, discounts and fees. This legislation may also have a positive impact on our future net sales, if any, by increasing the aggregate number of persons with healthcare coverage in the U.S.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for the purpose of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing. Some of these measures include price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. In addition, regional 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 ultimate demand for our products, once approved, or put pressure on our product pricing.

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

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

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

We remain focused on these laws and the activities they regulate and, as detailed above, 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. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

In some countries, including Member States of the EU, or Japan, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels,

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

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

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

- The U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchase, lease, order, arrangement, or recommendation of any good, facility, item 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. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal FCA or federal civil money penalties.
- The U.S. federal false claims laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government-funded programs such as Medicare or Medicaid that are false or fraudulent, making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery.
- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program 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 a state healthcare program, unless an exception applies.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which imposes requirements relating to the privacy, security, and transmission of individually identifiable health information; and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information.
- Federal "sunshine" requirements imposed by the ACA on drug, device, biological and medical supply manufacturers when payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS under the Open Payments Program, information regarding any payment or other "transfer of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and

chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.

- Federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products.
- Federal statutory and regulatory requirements applicable to pricing and sales of product to Federal Government Agencies.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- State and foreign laws comparable to each of the above federal laws, including in the EU laws prohibiting giving healthcare professionals any gift or benefit in kind as an inducement to prescribe our products, national transparency laws requiring the public disclosure of payments made to healthcare professionals and institutions, and data privacy laws, in addition to anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to government reimbursement programs, patient data privacy and security.
- European Privacy Laws including Regulation 2016/679, known as the General Data Protection Regulation, or the EU GDPR, as transposed into the laws of the UK, the UK GDPR, collectively referred to as the GDPR, and the e-Privacy Directive (202/58/EC), and the national laws implementing each of them, as well as the privacy laws of Japan and other territories. Failure to comply with our obligations under the privacy regime could expose us to significant fines and/or adverse publicity, which could have material adverse effects on our reputation and business.
- The California Consumer Privacy Act of 2018, or CCPA, effective as of January 1, 2020, that gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation.

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

If our operations are found to be in violation of any of the aforementioned requirements, we may be subject to penalties, including civil or criminal penalties (including individual imprisonment), criminal prosecution, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, or the imposition of a corporate integrity agreement with the Office of Inspector General of the Department of Health and Human Services, any of which could adversely affect our financial results. We remain focused on enhancing our global compliance infrastructure following the commercial launch of our four products over the last four years in the U.S., EU and multiple other geographies, and as we prepare for the launch of our products in additional countries, assuming regulatory approvals. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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

- adverse regulatory inspection findings;
- untitled letters or warning letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;

- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- product seizures;
- injunctions; and
- civil and criminal penalties, up to and including criminal prosecution resulting in fines, exclusion from healthcare reimbursement programs and imprisonment.

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

Third party patient assistance programs that receive financial support from companies have become the subject of enhanced government and regulatory scrutiny. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria and do not link aid to use of a donor's product. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of their patient assistance programs under a variety of federal and state laws. It is possible that we may make grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, we could be subject to damages, fines, penalties, or other criminal, civil, or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies, and procedures will be sufficient to protect against acts of our employees, business partners, or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could impact our business practices, harm our reputation, divert the attention of management, increase our expenses, and reduce the availability of foundation support for our patients who need assistance.

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

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

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

Significantly, the GDPR imposes strict rules on the transfer of personal data out of the EU to the U.S. or other regions that have not been deemed to offer "adequate" privacy protections. In the past, companies in the U.S. were able to rely upon the EU-U.S. and the Swiss-U.S. Privacy Shield frameworks to legitimize data transfers from the EU and the UK to the U.S. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C-311/18 (Data Protection Commissioner v Facebook Ireland and Maximillian Schrems, or Schrems II) invalidated the EU-U.S. Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the U.S. The CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the EC are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case-by-case basis to ensure the law in the recipient country provides "essentially equivalent" protections to safeguard the transferred personal data as the EU, and required businesses to adopt supplementary measures if such standard is not met. Subsequent guidance published by the European Data Protection Board in June 2021 described what such supplementary measures must be, and stated that businesses should avoid or cease transfers of personal data if, in the absence of supplementary measures, equivalent protections cannot be afforded. On June 4, 2021, the EC published new versions of the SCCs, which seek to address the issues identified by the CJEU's Schrems II decision and provide further details regarding the transfer assessments that the parties are required to conduct when implementing the New SCCs. However, there continue to be concerns about whether the SCCs and other mechanisms will face additional challenges. Similarly, the Swiss data protection authority determined the Swiss-U.S. Privacy Shield framework was no longer a valid mechanism for Swiss-U.S. data transfers and also raised questions about the validity of the SCCs as a mechanism for transferring personal data from Switzerland. While 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 personal data from the EU to the U.S. in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. The UK is not subject to the EC's new SCCs but has published its own transfer mechanism, the International Transfer Agreement, which enables transfers from the UK. On March 25, 2022, The EC and the US announced to have reached a political agreement on a new "Trans-Atlantic Data Privacy Framework", which will replace the invalidated Privacy Shield. However, no formal text has been issued yet.

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

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

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

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

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

If other federal spending is reduced, any budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health, or NIH, to continue to function. Amounts allocated to federal grants and contracts

may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell our approved products and any other products we may develop. Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

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

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

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

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with governmental regulations, comply with healthcare fraud and abuse and anti-kickback laws and regulations in the U.S. and abroad, or failure to report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including improper trading based upon, information obtained in the course of clinical studies, which could result in regulatory sanctions and serious harm to our reputation. We 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 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 and results of operations, including the imposition of significant fines or other sanctions.

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

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

Health Administration of the U.S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials.

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

Risks Related to Patents, Licenses and Trade Secrets

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

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

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

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

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

protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.

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

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

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

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

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

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

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

As the field of RNAi therapeutics is maturing, patent applications are being fully processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference, re-examination and opposition proceedings, as well as *inter partes* and post-grant review proceedings introduced by provisions of the AIA, which became available to third party challengers on September 16, 2012, in various patent offices relating to patent rights in the RNAi field. In addition, third parties may challenge the validity of our patents. For example, a third party has filed an opposition in the European Patent Office, or EPO, against our owned patent EP 2723758, with claims directed to compositions and methods of ANGPTL3, arguing that the granted claims are invalid. An oral hearing was held at the EPO on February 17, 2021, where the patent was revoked. A notice of appeal of the EPO's decision was filed on June 23, 2021. We expect that additional oppositions will be filed in the EPO and elsewhere, and other challenges will be raised relating to other patents and patent applications in our portfolio. In many cases, the possibility of appeal exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business if we are not successful in defending the patentability and scope of our pending and issued patent claims. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need for our siRNA products marketed by us or our licensees, our late-stage therapeutic candidates being developed by us or our licensees, 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 licensees. Thus, it is possible that one or more organizations will hold patent rights to which we may need a license, or hold patent rights which could be asserted against us. If those organizations refuse to grant us a license to such patent rights on reasonable terms and/or a court rules that we need such patent rights that have been asserted against us and we are not able to obtain a license on reasonable terms, we may be unable to market products, including ONPATTRO, GIVLAARI, OXLUMO or AMVUTTRA, or perform research and development or other activities covered by such patents. For example, during 2017 and 2018, Silence Therapeutics, plc, or Silence, filed claims in several jurisdictions, including the High Court of England and Wales, and named us and our wholly owned subsidiary Alnylam UK Ltd. as co-defendants. Silence alleged various claims, including that ONPATTRO infringed one or more Silence patents. There were also a number of related actions brought by us or Silence in connection with this intellectual property dispute. In December 2018, we entered into a Settlement and License Agreement with Silence, resolving all ongoing claims, administrative proceedings, and regulatory proceedings worldwide between us regarding, among other issues, patent infringement, patent invalidity and breach of contract.

If we become involved in 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, in October 2017 Silence sued us in the UK alleging that ONPATTRO and other investigational RNAi therapeutics we or MDCO are developing infringed one or more Silence patents. In December 2018 we and Silence settled all ongoing litigation between us. A third party may also claim that we have improperly obtained or used its confidential or proprietary information.

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

We may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others or protect our proprietary information and trade secrets. For example, during the second quarter of 2015, we filed a trade secret misappropriation lawsuit against Dicerna to protect our rights in the RNAi assets we purchased from Merck Sharp & Dohme Corp., or Merck. We and Dicerna settled the ongoing litigation between us in April 2018. In March 2022, we announced that we separately filed suit in United States District Court for the District of Delaware against Pfizer and Moderna, Inc., seeking damages for infringement of U.S. Patent No. 11,246,933 in the parties' manufacture and sale of their messenger RNA, or mRNA, COVID-19 vaccines. In July 2022, we filed a new lawsuit in United States District Court for the District of Delaware against each of Pfizer and Moderna seeking damages for infringing our newly granted U.S. Patent No. 11,382,979. The aforementioned patents relate to our biodegradable cationic lipids that are foundational to the success of the mRNA COVID-19 vaccines.

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

In addition, in connection with certain license and collaboration agreements, we have agreed to indemnify certain third parties for certain costs incurred in connection with litigation relating to intellectual property rights or the subject matter of the agreements. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and litigation would divert our management's efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation or legal proceeding could delay our research, development and commercialization efforts and limit our ability to continue our operations.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon or otherwise violates their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties' patent rights. In addition to any damages we might have to pay, a court could issue an injunction requiring us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially reasonable terms, if at all. In addition, such licenses are likely to be non-exclusive and,

therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Moreover, we expect that a number of our collaborations will provide that royalties payable to us for licenses to our intellectual property may be offset by amounts paid by our collaborators to third parties who have competing or superior intellectual property positions in the relevant fields, which could result in significant reductions in our revenues from products developed through collaborations.

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

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

Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we will be required to pay on sales of each of our approved products or future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in such products. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, 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, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Risks Related to Competition

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

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

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;

- product candidates that are based on previously tested or accepted technologies;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. For example, if approved by the FDA, patisiran, our RNAi therapeutic in development for ATTR amyloidosis patients with cardiomyopathy, would compete with tafamidis, marketed by Pfizer, which is currently approved to treat this disease. We also expect to face competition from new drugs that enter the market. There are a number of drugs currently under development, which may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. These drugs may be more effective, safer, less expensive, or marketed and sold more effectively, than any products we develop and commercialize. For example, we developed ONPATTRO for the treatment of hATTR amyloidosis. In August 2018, the FDA approved ONPATTRO lipid complex injection for the treatment of the polyneuropathy of hATTR amyloidosis in adults, and the EC granted marketing authorization for ONPATTRO for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. We are aware of other approved products used to treat this disease, including tafamidis, and inotersen, developed and marketed by Ionis, as well as product candidates in various stages of clinical development, including eplontersen, an additional investigational drug developed by Ionis in partnership with AstraZeneca, which recently met co-primary and secondary endpoints in an interim analysis of a Phase 3 study for the polyneuropathy of hATTR amyloidosis. Finally, we are aware that BridgeBio Pharma, Inc. (formerly Eidos Therapeutics, Inc.), or BridgeBio, announced topline results from Part A of its Phase 3 clinical trial of acoramidis, a TTR stabilizer, in ATTR-CM in December 2021, which did not meet the primary endpoint of the study at month 12. BridgeBio initiated enrollment in Part B of its Phase 3 clinical trial of acoramidis in ATTR-PN patients in the fourth quarter of 2020, and anticipates topline results in 2023. While we believe that ONPATTRO has and will continue to have a competitive product profile for the treatment of patients with hATTR amyloidosis with polyneuropathy, and that AMVUTTRA has a competitive product profile in this indication, it is possible that ONPATTRO and/or AMVUTTRA may not compete favorably with these products and product candidates, or others, and, as a result, may not achieve commercial success. Moreover, positive or negative data and/or the commercial success or failure of competitive products could negatively impact our stock price. For example, our stock price was negatively impacted by the results of Part A of BridgeBio's Phase 3 clinical trial.

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

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

We are aware of product candidates in various stages of clinical development for the treatment of PH1 which would compete with OXLUMO, our RNAi therapeutic approved in the U.S. and EU for the treatment of this disease, including Oxabact®, a bacteria-based investigational therapy in development by OxThera AB, reloxaliase an investigational enzyme therapy in Phase 3 development for primary or severe secondary hyperoxaluria by Allena Pharmaceuticals, Inc., and nedosiran, an investigational RNAi therapeutic in development by Dicerna for the treatment of primary hyperoxaluria. In July 2019, the FDA granted a Breakthrough Therapy Designation to nedosiran for the treatment of patients with primary hyperoxaluria, and in August 2021, Dicerna reported positive topline results from its PHYOX2 pivotal clinical trial of nedosiran for the treatment of primary hyperoxaluria. Based on the results of the trial, Novo Nordisk expects to submit an NDA to the FDA in 2022 for the treatment of PH1 in patients aged six years and older. In April 2020, we and Dicerna granted each other a non-exclusive cross-license to our respective intellectual property related to lumasiran, and Dicerna’s nedosiran product candidate. Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above or on other factors. In addition, our competitors may develop strategic alliances with or receive funding from larger pharmaceutical or biotechnology companies, providing them with an advantage over us. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and the ability to execute on our business plan. Furthermore, we also face competition from existing and new treatment methods that reduce or eliminate the need for drugs, such as the use of advanced

medical devices. The development of new medical devices or other treatment methods for the diseases we are targeting could make our product candidates noncompetitive, obsolete or uneconomical.

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

In addition to the competition we face from competing drugs in general, we also face competition from other companies working to develop novel drugs using technology that competes more directly with our own. We are aware of several other companies that are working to develop RNAi therapeutic products. Some of these companies are seeking, as we are, to develop chemically synthesized siRNAs as drugs. Others are following a gene therapy approach, with the goal of treating patients not with synthetic siRNAs but with synthetic, exogenously-introduced genes designed to produce siRNA-like molecules within cells. Companies working on chemically synthesized siRNAs include, but are not limited to, Takeda Pharmaceutical Company Ltd., or Takeda, Marina Biotech, Inc., Arrowhead Pharmaceuticals Inc, Inc., or Arrowhead, Quark Pharmaceuticals, Inc., or Quark, Silence, Arbutus, Sylentis, S.A.U, or Sylentis, Dicerna and its collaborators, WAVE Life Sciences Ltd., Arcturus Therapeutics Inc., and Genevant Sciences, launched by Arbutus and Roivant Sciences. In addition, we granted licenses or options for licenses to Ionis, Benitec Biopharma Ltd., or Benitec, Arrowhead, Arbutus, Quark, Sylentis and others under which these companies may independently develop RNAi therapeutics against a limited number of targets. Any one of these companies may develop its RNAi technology more rapidly and more effectively than us.

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

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

Risks Related to Our Common Stock

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

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

We may incur significant costs from class action litigation.

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development and commercialization efforts or the development and commercialization efforts of our collaborators and/or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. When the market price of a stock has been volatile as our stock

price has been, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock.

For example, on September 12, 2019, the Chester County Employees Retirement Fund, individually and on behalf of all others similarly situated, filed a purported securities class action complaint alleging violation of federal securities laws against us, certain of our current and former directors and officers, and the underwriters of our November 14, 2017 public stock offering, in the Supreme Court of the State of New York, New York County. While we believe the allegations in the New York State Securities Litigation are without merit, in August 2021 the parties reached an agreement in principle to resolve the matter. At a hearing on April 12, 2022, the Supreme Court of the State of New York granted final approval to the settlement. Proceedings in the First Department were adjourned until April 2022, pending final approval of any settlement, and were withdrawn as a result of final approval on April 18, 2022. Future litigation could result in substantial costs and divert our management's attention and resources, which could cause serious harm to our business, operating results and financial condition. We maintain liability insurance; however, if any costs or expenses associated with litigation exceed our insurance coverage, we may be forced to bear some or all of these costs and expenses directly, which could be substantial. In addition, we have obligations to indemnify third parties in connection with certain litigation, and such obligations are not covered by insurance.

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

A small number of our stockholders beneficially own a substantial amount of our common stock. As of September 30, 2022, our six largest stockholders beneficially owned in excess of 50% of our outstanding shares of common stock. If our significant stockholders, or we or our officers and directors, sell substantial amounts of our common stock in the public market, or there is a perception that such sales may occur, the market price of our common stock could be adversely affected. Sales of common stock by our significant stockholders might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

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

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

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

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

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

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

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

Risks Related to Our Convertible Notes

Servicing our debt may require a significant amount of cash. We may not have sufficient cash flow from our business to pay our indebtedness.

On September 12, 2022, we commenced a private offering of $900.0 million in aggregate principal amount of 1% Convertible Senior Notes due 2027, or the Initial Notes. On September 13, 2022, the initial purchasers in such offering exercised their option to purchase an additional $135.0 million in aggregate principal amount of our 1% Convertible Senior Notes due 2027, or the Additional Notes, and together with the Initial Notes, collectively referred to as the Notes, bringing the total aggregate principal amount of the Notes to $1.04 billion. The interest rate for the Notes is fixed at 1.00% per annum and is payable semi-annually in arrears on May 15 and September 15 of each year, beginning on March 15, 2023. 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, any of our future debt agreements may contain restrictive covenants that may prohibit us from adopting any of these alternatives. Our failure to comply with these covenants could result in an event of default which, if not cured or waived, could result in the acceleration of our debt.

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, and our future debt may contain limitations on our ability to pay cash upon conversion of the Notes or to repurchase the Notes.

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.

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, results of operations 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.

The conditional conversion feature of the Notes, if triggered, may adversely affect our financial condition and operating results.

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 rather than long-term liability, which would result in a material reduction of our net working capital.

Transactions relating to our 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. Our Notes may become in the future convertible at the option of their holders under certain circumstances. If holders of our 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 we will be 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 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.

In August 2020, the Financial Accounting Standards Board published an Accounting Standards Update, which we refer to as ASU 2020-06, which simplified certain of the accounting standards that apply to convertible notes. ASU 2020-06 became effective for us beginning January 1, 2022.

In accordance with ASU 2020-06, the Notes will be reflected as a liability on our consolidated balance sheets, with the initial carrying amount equal to the principal amount of the Notes, net of issuance costs. The issuance costs will be treated as a debt discount for accounting purposes, which will be 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, we expect that the shares of common stock underlying the Notes will be reflected in our diluted earnings per share using the “if converted” method, in accordance with ASU 2020-06. Under that method, diluted earnings per share would generally be 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 convert their notes and could materially reduce our reported working capital.

ITEM 6. EXHIBITS

4.1*	Indenture, dated as of September 15, 2022, between the Registrant and The Bank of New York Mellon, as trustee.
4.2	Form of 1.00% Convertible Senior notes due 2027 (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, File No. 001-36407, filed on September 16, 2022)
10.1	Form of Capped Call Transaction Confirmation (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, File No. 001-36407, filed on September 16, 2022)
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: October 27, 2022

/s/ Yvonne L. Greenstreet, MBChB, MBA

Yvonne L. Greenstreet, MBChB, MBA
Chief Executive Officer
(Principal Executive Officer)

Date: October 27, 2022

/s/ Jeffrey V. Poulton

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

Exhibit 4.1

ALNYLAM PHARMACEUTICALS, INC.

AND

THE BANK OF NEW YORK MELLON,

as Trustee

INDENTURE

Dated as of September 15, 2022

1.00% Convertible Senior Notes due 2027

TABLE OF CONTENTS

PAGE

ARTICLE 1
Definitions

Section 1.01. *Definitions* 1
Section 1.02. *References to Interest* 15

ARTICLE 2
Issue, Description, Execution, Registration and Exchange of Notes

Section 2.01. *Designation and Amount* 15
Section 2.02. *Form of Notes* 15
Section 2.03. *Date and Denomination of Notes; Payments of Interest and Defaulted Amounts* 16
Section 2.04. *Execution, Authentication and Delivery of Notes* 17
Section 2.05. *Exchange and Registration of Transfer of Notes; Restrictions on Transfer; Depositary* 18
Section 2.06. *Mutilated, Destroyed, Lost or Stolen Notes* 25
Section 2.07. *Temporary Notes* 27
Section 2.08. *Cancellation of Notes Paid, Converted, Etc* 27
Section 2.09. *CUSIP Numbers* 27
Section 2.10. *Additional Notes; Repurchases* 27

ARTICLE 3
Satisfaction and Discharge

Section 3.01. *Satisfaction and Discharge* 28

ARTICLE 4
Particular Covenants of the Company

Section 4.01. *Payment of Principal and Interest* 29
Section 4.02. *Maintenance of Office or Agency* 29
Section 4.03. *Appointments to Fill Vacancies in Trustee's Office* 29
Section 4.04. *Provisions as to Paying Agent* 30
Section 4.05. *Existence* 31
Section 4.06. *Rule 144A Information Requirement and Annual Reports* 31
Section 4.07. *Stay, Extension and Usury Laws* 34
Section 4.08. *Compliance Certificate; Statements as to Defaults* 34
Section 4.09. *Further Instruments and Acts* 34

ARTICLE 5
Lists of Holders and Reports by the Company and the Trustee

Section 5.01. *Lists of Holders* 35
Section 5.02. *Preservation and Disclosure of Lists* 35

ARTICLE 6
Defaults and Remedies

Section 6.01. *Events of Default* 35

Section 6.02. *Acceleration; Rescission and Annulment* 36
Section 6.03. *Additional Interest* 37
Section 6.04. *Payments of Notes on Default; Suit Therefor* 39
Section 6.05. *Application of Monies Collected by Trustee* 40
Section 6.06. *Proceedings by Holders* 41
Section 6.07. *Proceedings by Trustee* 42
Section 6.08. *Remedies Cumulative and Continuing* 42
Section 6.09. *Direction of Proceedings and Waiver of Defaults by Majority of Holders* 43
Section 6.10. *Notice of Defaults* 43
Section 6.11. *Undertaking to Pay Costs* 44

ARTICLE 7
Concerning the Trustee

Section 7.01. *Duties and Responsibilities of Trustee* 44
Section 7.02. *Rights of the Trustee* 46
Section 7.03. *No Responsibility for Recitals, Etc* 48
Section 7.04. *Trustee, Paying Agents, Conversion Agents, Bid Solicitation Agent or Note Registrar May Own Notes* 48
Section 7.05. *Monies and Shares of Common Stock to Be Held in Trust* 48
Section 7.06. *Compensation and Expenses of Trustee* 48
Section 7.07. *Officer's Certificate as Evidence* 49
Section 7.08. *Eligibility of Trustee* 49
Section 7.09. *Resignation or Removal of Trustee* 49
Section 7.10. *Acceptance by Successor Trustee* 51
Section 7.11. *Succession by Merger, Etc* 51

ARTICLE 8
Concerning the Holders

Section 8.01. *Action by Holders* 52
Section 8.02. *Proof of Execution by Holders* 52
Section 8.03. *Who Are Deemed Absolute Owners* 52
Section 8.04. *Company-Owned Notes Disregarded* 53
Section 8.05. *Revocation of Consents; Future Holders Bound* 53

ARTICLE 9
Holders' Meetings

Section 9.01. *Purpose of Meetings* 53
Section 9.02. *Call of Meetings by Trustee or the Company* 54
Section 9.03. *Call of Meetings by Company or Holders* 54
Section 9.04. *Qualifications for Voting* 54
Section 9.05. *Regulations* 55
Section 9.06. *Voting* 55
Section 9.07. *No Delay of Rights by Meeting* 56

ARTICLE 10
Supplemental Indentures
Section 10.01. *Supplemental Indentures Without Consent of Holders* 56
Section 10.02. *Supplemental Indentures with Consent of Holders* 57
Section 10.03. *Effect of Supplemental Indentures* 58
Section 10.04. *Notation on Notes* 59
Section 10.05. *Evidence of Compliance of Supplemental Indenture to Be Furnished Trustee* 59
ARTICLE 11
Consolidation, Merger, Sale, Conveyance and Lease
Section 11.01. *Company May Consolidate, Etc. on Certain Terms* 59
Section 11.02. *Successor Corporation to Be Substituted* 60
Section 11.03. *Opinion of Counsel to Be Given to Trustee* 60
ARTICLE 12
Immunity of Incorporators, Stockholders, Officers and Directors
Section 12.01. *Indenture and Notes Solely Corporate Obligations* 61
ARTICLE 13
[Intentionally Omitted]
ARTICLE 14
Conversion of Notes
Section 14.01. *Conversion Privilege* 61
Section 14.02. *Conversion Procedure; Settlement Upon Conversion* 65
Section 14.03. *Increased Conversion Rate Applicable to Certain Notes Surrendered in Connection with Make-Whole Fundamental Changes or Redemption Notice* 71
Section 14.04. *Adjustment of Conversion Rate* 73
Section 14.05. *Adjustments of Prices* 84
Section 14.06. *Shares to Be Fully Paid* 84
Section 14.07. *Effect of Recapitalizations, Reclassifications and Changes of the Common Stock* 84
Section 14.08. *Certain Covenants* 86
Section 14.09. *Responsibility of Trustee* 87
Section 14.10. *Notice to Holders Prior to Certain Actions* 87
Section 14.11. *Stockholder Rights Plans* 88
Section 14.12. *Exchange in Lieu of Conversion* 88
ARTICLE 15
Repurchase of Notes at Option of Holders
Section 15.01. [Intentionally Omitted] 89
Section 15.02. *Repurchase at Option of Holders Upon a Fundamental Change* 89
Section 15.03. *Withdrawal of Fundamental Change Repurchase Notice* 93
Section 15.04. *Deposit of Fundamental Change Repurchase Price* 93

Section 15.05. *Covenant to Comply with Applicable Laws Upon Repurchase of Notes* 94

ARTICLE 16
Optional Redemption

Section 16.01. *Optional Redemption* 94
Section 16.02. *Notice of Optional Redemption; Selection of Notes* 95
Section 16.03. *Payment of Notes Called for Redemption* 96
Section 16.04. *Restrictions on Redemption* 97

ARTICLE 17
Miscellaneous Provisions

Section 17.01. *Provisions Binding on Company's Successors* 97
Section 17.02. *Official Acts by Successor Corporation* 97
Section 17.03. *Addresses for Notices, Etc* 97
Section 17.04. *Governing Law; Jurisdiction* 98
Section 17.05. *Evidence of Compliance with Conditions Precedent; Certificates and Opinions of Counsel to Trustee* 98
Section 17.06. *Legal Holidays* 99
Section 17.07. *No Security Interest Created* 99
Section 17.08. *Benefits of Indenture* 99
Section 17.09. *Table of Contents, Headings, Etc* 99
Section 17.10. *Authenticating Agent* 99
Section 17.11. *Execution in Counterparts* 100
Section 17.12. *Severability; Entire Agreement* 101
Section 17.13. *Waiver of Jury Trial* 101
Section 17.14. *Force Majeure* 101
Section 17.15. *Calculations* 101
Section 17.16. *USA PATRIOT Act* 102
Section 17.17. *Tax Withholding* 102
Section 17.18. *Electronic Signatures* 102
Section 17.19. *Electronic Means* 102

EXHIBIT

Exhibit A Form of Note A-1

INDENTURE dated as of September 15, 2022 between ALNYLAM PHARMACEUTICALS, INC., a Delaware corporation, as issuer (the "**Company**," as more fully set forth in Section 1.01) and THE BANK OF NEW YORK MELLON, a New York banking corporation, as trustee (the "**Trustee**," as more fully set forth in Section 1.01).

W I T N E S E T H:

WHEREAS, for its lawful corporate purposes, the Company has duly authorized the issuance of its 1.00% Convertible Senior Notes due 2027 (the "**Notes**"), initially in an aggregate principal amount not to exceed $1,035,000,000, and in order to provide the terms and conditions upon which the Notes are to be authenticated, issued and delivered, the Company has duly authorized the execution and delivery of this Indenture; and

WHEREAS, the Form of Note, the certificate of authentication to be borne by each Note, the Form of Notice of Conversion, the Form of Fundamental Change Repurchase Notice and the Form of Assignment and Transfer to be borne by the Notes are to be substantially in the forms hereinafter provided; and

WHEREAS, all acts and things necessary to make the Notes, when executed by the Company and authenticated and delivered by the Trustee or a duly authorized authenticating agent, as provided in this Indenture, the valid, binding and legal obligations of the Company, and this Indenture the valid, binding and legal agreement of the Company and the Trustee, have been done and performed, and the execution of this Indenture and the issuance hereunder of the Notes have in all respects been duly authorized.

NOW, THEREFORE, THIS INDENTURE WITNESSETH:

That in order to declare the terms and conditions upon which the Notes are, and are to be, authenticated, issued and delivered, and in consideration of the premises and of the purchase and acceptance of the Notes by the Holders thereof, the Company covenants and agrees with the Trustee for the equal and proportionate benefit of the respective Holders from time to time of the Notes (except as otherwise provided below), as follows:

ARTICLE 1
DEFINITIONS

Section 1.01. *Definitions.* The terms defined in this Section 1.01 (except as herein otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section 1.01. The words "herein," "hereof," "hereunder" and words of similar import refer to this Indenture as a whole and not to any particular Article, Section or other subdivision. The terms defined in this Article include the plural as well as the singular. "**1% Provision**" shall have the meaning specified in Section 14.04(k).

"**Additional Interest**" means all amounts, if any, payable pursuant to Section 4.06(d), Section 4.06(e) and Section 6.03, as applicable.

"**Additional Shares**" shall have the meaning specified in Section 14.03(a).

"**Affiliate**" of any specified Person means any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For the purposes of this definition, "control," when used with respect to any specified Person means the power to direct or cause the direction of the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise; and the terms "controlling" and "controlled" have meanings correlative to the foregoing. Notwithstanding anything to the contrary herein, the determination of whether one Person is an "**Affiliate**" of another Person for purposes of this Indenture shall be made based on the facts at the time such determination is made or required to be made, as the case may be, hereunder.

"**Applicable Procedures**" means, with respect to a Depositary, as to any matter at any time, the policies and procedures of such Depositary, if any, that are applicable to such matter at such time.

"**Authorized Officers**" shall have the meaning specified in Section 17.19.

"**Bid Solicitation Agent**" means the Company or the Person appointed by the Company to solicit bids for the Trading Price of the Notes in accordance with Section 14.01(b)(i). The Company shall initially act as the Bid Solicitation Agent.

"**Board of Directors**" means the board of directors of the Company or a committee of such board duly authorized to act for it hereunder.

"**Board Resolution**" means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company to have been duly adopted by the Board of Directors, and to be in full force and effect on the date of such certification, and delivered to the Trustee.

"**Business Day**" means any day other than a Saturday, a Sunday or a day on which the Federal Reserve Bank of New York is authorized or required by law or executive order to close or be closed.

"**Business Combination Event**" shall have the meaning specified in Section 11.01.

"**Capital Stock**" means, for any entity, any and all shares, interests, rights to purchase, warrants, options, participations or other equivalents of or interests in (however designated) stock issued by that entity; *provided* that debt securities that are convertible into or exchangeable for Capital Stock shall not constitute Capital Stock prior to their conversion or exchange, as the case may be.

"**Cash Settlement**" shall have the meaning specified in Section 14.02(a).

"**Certain Distributions Notification**" shall have the meaning specified in Section 14.01(b)(iii).

"**Certain Distributions Conversion Period End Date**" shall have the meaning specified in Section 14.01(b)(iii).

"**Clause A Distribution**" shall have the meaning specified in Section 14.04(c).

"**Clause B Distribution**" shall have the meaning specified in Section 14.04(c).

"**Clause C Distribution**" shall have the meaning specified in Section 14.04(c).

"**close of business**" means 5:00 p.m. (New York City time).

"**Combination Settlement**" shall have the meaning specified in Section 14.02(a).

"**Commission**" means the U.S. Securities and Exchange Commission.

"**Common Equity**" of any Person means Capital Stock of such Person that is generally entitled (a) to vote in the election of directors of such Person or (b) if such Person is not a corporation, to vote or otherwise participate in the selection of the governing body, partners, managers or others that will control the management or policies of such Person.

"**Common Stock**" means the common stock of the Company, par value $0.01 per share, at the date of this Indenture, subject to Section 14.07.

"**Company**" shall have the meaning specified in the first paragraph of this Indenture, and subject to the provisions of Article 11, shall include its successors and assigns.

"**Company Order**" means a written order of the Company, signed on behalf of the Company by an Officer.

"**Conversion Agent**" shall have the meaning specified in Section 4.02.

"**Conversion Date**" shall have the meaning specified in Section 14.02(c).

"**Conversion Obligation**" shall have the meaning specified in Section 14.01(a).

"**Conversion Price**" means as of any time, $1,000, *divided by* the Conversion Rate as of such time.

"**Conversion Rate**" shall have the meaning specified in Section 14.01(a).

"**Corporate Event**" shall have the meaning specified in Section 14.01(b)(iv).

"**Corporate Trust Office**" means the corporate trust office of the Trustee at which at any time its corporate trust business shall be administered, which office at the date hereof is located at The Bank of New York Mellon, 240 Greenwich Street, 7th Floor, New York, New York 10286, Attention: Corporate Trust Administration, or such other

address as the Trustee may designate from time to time by notice to the Holders and the Company, or the principal corporate trust office of any successor trustee (or such other address as such successor trustee may designate from time to time by notice to the Holders and the Company).

"**Custodian**" means the Trustee, as custodian for The Depository Trust Company, with respect to the Global Notes, or any successor entity thereto.

"**Daily Conversion Value**" means, for each of the 20 consecutive Trading Days during the Observation Period, 1/20th of the product of (a) the Conversion Rate on such Trading Day and (b) the Daily VWAP for such Trading Day.

"**Daily Measurement Value**" means the Specified Dollar Amount (if any), *divided by* 20.

"**Daily Settlement Amount**," for each of the 20 consecutive Trading Days during the Observation Period, shall consist of:

(a) cash in an amount equal to the lesser of (i) the Daily Measurement Value and (ii) the Daily Conversion Value on such Trading Day; and

(b) if the Daily Conversion Value on such Trading Day exceeds the Daily Measurement Value, a number of shares of Common Stock equal to (i) the difference between the Daily Conversion Value and the Daily Measurement Value, *divided by* (ii) the Daily VWAP for such Trading Day.

"**Daily VWAP**" means, for each of the 20 consecutive Trading Days during the relevant Observation Period, the per share volume-weighted average price as displayed under the heading "Bloomberg VWAP" on Bloomberg page "ALNY <equity> AQR" (or its equivalent successor if such page is not available) in respect of the period from the scheduled open of trading until the scheduled close of trading of the primary trading session on such Trading Day (or, if such volume-weighted average price is unavailable, the market value of one share of the Common Stock on such Trading Day determined, using a volume-weighted average method, by a nationally recognized independent investment banking firm retained for this purpose by the Company). The "**Daily VWAP**" shall be determined without regard to after-hours trading or any other trading outside of the regular trading session trading hours.

"**Default**" means any event that is, or after notice or passage of time, or both, would be, an Event of Default.

"**Defaulted Amounts**" means any amounts on any Note (including, without limitation, the Redemption Price, the Fundamental Change Repurchase Price, principal and interest) that are payable but are not punctually paid or duly provided for.

"**Default Settlement Method**" means, initially, Combination Settlement with a Specified Dollar Amount per $1,000 principal amount of Notes of $1,000; *provided* that the Company may, from time to time, change the Default Settlement Method by sending notice of the new Default Settlement Method to the Holders, the Trustee and the Conversion Agent (if other than the Trustee) prior to June 15, 2027, all in accordance with, and subject to, the last paragraph of Section 14.02(a)(iii).

"**Depositary**" means, with respect to each Global Note, the Person specified in Section 2.05(c) as the Depositary with respect to such Notes, until a successor shall have been appointed and become such pursuant to the applicable provisions of this Indenture, and thereafter, "**Depositary**" shall mean or include such successor.

"**Distributed Property**" shall have the meaning specified in Section 14.04(c).

"**Effective Date**" shall have the meaning specified in Section 14.03(c), except that, as used in Section 14.04 and Section 14.05, "**Effective Date**" means the first date on which shares of the Common Stock trade on the applicable exchange or in the applicable market, regular way, reflecting the relevant share split or share combination, as applicable. For the avoidance of doubt, any alternative trading convention on the applicable exchange or market in respect of shares of the Common Stock under a separate ticker symbol or CUSIP number will not be considered "regular way" for this purpose.

"**Electronic Means**" shall have the meaning specified in Section 17.19.

"**Event of Default**" shall have the meaning specified in Section 6.01.

"**Ex-Dividend Date**" means the first date on which shares of the Common Stock trade on the applicable exchange or in the applicable market, regular way, without the right to receive the issuance, dividend or distribution in question, from the Company or, if applicable, from the seller of Common Stock on such exchange or market (in the form of due bills or otherwise) as determined by such exchange or market. For the avoidance of doubt, any alternative trading convention on the applicable exchange or market in respect of shares of the Common Stock under a separate ticker symbol or CUSIP number will not be considered "regular way" for this purpose.

"**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"**Exchange Election**" shall have the meaning specified in Section 14.12.

"**Exempted Fundamental Change**" refers to any Fundamental Change with respect to which the Company does not offer to repurchase any Notes in accordance with Section 15.02(f).

"**Expiration Date**" shall have the meaning specified in Section 14.04(e).

"**Form of Assignment and Transfer**" means the "Form of Assignment and Transfer" attached as Attachment 3 to the Form of Note attached hereto as Exhibit A.

"**Form of Fundamental Change Repurchase Notice**" means the "Form of Fundamental Change Repurchase Notice" attached as Attachment 2 to the Form of Note attached hereto as Exhibit A.

"**Form of Note**" means the "Form of Note" attached hereto as Exhibit A.

"**Form of Notice of Conversion**" means the "Form of Notice of Conversion" attached as Attachment 1 to the Form of Note attached hereto as Exhibit A.

"**Fundamental Change**" shall be deemed to have occurred at the time after the Notes are originally issued if any of the following occurs:

(a) a "person" or "group" within the meaning of Section 13(d) of the Exchange Act, other than the Company, its Wholly Owned Subsidiaries and the employee benefit plans of the Company and its Wholly Owned Subsidiaries, files a Schedule TO or any schedule, form or report under the Exchange Act disclosing that such "person" or "group" has become the direct or indirect "beneficial owner," as defined in Rule 13d-3 under the Exchange Act, of the Common Stock representing more than 50% of the voting power of the Common Stock; unless such beneficial ownership arises solely as a result of a revocable proxy delivered in response to a public proxy or consent solicitation made pursuant to the applicable rules and regulations under the Exchange Act and is not also then reportable on Schedule 13D or Schedule 13G (or any successor schedule) under the Exchange Act regardless of whether such a filing has actually been made; *provided*, that no "person" or "group" shall be deemed to be the beneficial owner of any securities tendered pursuant to a tender or exchange offer made by or on behalf of such "person" or "group" until such tendered securities are accepted for purchase or exchange under such offer;

(b) the consummation of (A) any recapitalization, reclassification or change of the Common Stock (other than changes resulting from a subdivision, combination or a change in par value) as a result of which the Common Stock would be converted into, or exchanged for, stock, other securities, other property or assets; (B) any share exchange, consolidation or merger of the Company pursuant to which the Common Stock will be converted into cash, securities or other property or assets; or (C) any sale, lease or other transfer in one transaction or a series of transactions of all or substantially all of the consolidated assets of the Company and its Subsidiaries, taken as a whole, to any Person other than one or more of the Company's direct or indirect Wholly Owned Subsidiaries; *provided, however*, that a transaction described in clause (A) or (B) in which the holders of all classes of the Company's Common Equity immediately prior to such transaction own, directly or indirectly, more than 50% of all classes of Common Equity of the continuing or surviving corporation or transferee or the parent thereof immediately after such transaction in substantially the same proportions (relative to each other) as such ownership immediately prior to such transaction shall not be a Fundamental Change pursuant to this clause (b);

(c) the stockholders of the Company approve any plan or proposal for the liquidation or dissolution of the Company; or

(d) the Common Stock (or other Common Equity underlying the Notes) ceases to be listed or quoted on any of The New York Stock Exchange, The Nasdaq Global Select Market or The Nasdaq Global Market (or any of their respective successors);

provided, *however*, that a transaction or transactions described in clause (a) or clause (b) above shall not constitute a Fundamental Change, if at least 90% of the consideration received or to be received by the holders of the Common Stock, excluding cash payments for fractional shares and cash payments made in respect of dissenters' appraisal rights, in connection with such transaction or transactions consists of Common Equity that are listed or quoted on any of The New York Stock Exchange, The Nasdaq Global Select Market or The Nasdaq Global Market (or any of their respective successors) or will be so listed or quoted when issued or exchanged in connection with such transaction or transactions and as a result of such transaction or transactions such consideration, excluding cash payments for fractional shares and cash payments made in respect of dissenters' appraisal rights, becomes Reference Property for the Notes (subject to the provisions of Section 14.02(a)). Any event, transaction or series of related transactions that constitute a Fundamental Change under both clause (a) and clause (b) above (determined without regard to the proviso in clause (b) above) shall be deemed to be a Fundamental Change solely under clause (b) above (subject to such *proviso*). If any transaction in which the Common Stock is replaced by the Common Equity of another entity occurs, following completion of any related Make-Whole Fundamental Change Period (or, in the case of a transaction that would have been a Fundamental Change or a Make-Whole Fundamental Change but for the proviso immediately following clause (d) of this definition, following the effective date of such transaction) references to the Company in this definition shall instead be references to such other entity.

"**Fundamental Change Company Notice**" shall have the meaning specified in Section 15.02(c).

"**Fundamental Change Repurchase Date**" shall have the meaning specified in Section 15.02(a).

"**Fundamental Change Repurchase Notice**" shall have the meaning specified in Section 15.02(b)(i).

"**Fundamental Change Repurchase Price**" shall have the meaning specified in Section 15.02(a).

"**Global Note**" shall have the meaning specified in Section 2.05(b).

"**Holder**," as applied to any Note, means any Person in whose name at the time a particular Note is registered on the Note Register.

"**Indenture**" means this instrument as originally executed or, if amended or supplemented as herein provided, as so amended or supplemented.

"**Instructions**" shall have the meaning specified in Section 17.19.

"**Interest Payment Date**" means each March 15 and September 15 of each year, beginning on March 15, 2023.

"**Last Reported Sale Price**" of the Common Stock (or other security for which a closing sale price must be determined) on any date means the closing sale price per share (or if no closing sale price is reported, the average of the bid and ask prices or, if more than one in either case, the average of the average bid and the average ask prices) on that date as reported in composite transactions for the principal U.S. national or regional securities exchange on which the Common Stock (or such other security) is traded. If the Common Stock (or such other security) is not listed for trading on a U.S. national or regional securities exchange on the relevant date, the "**Last Reported Sale Price**" shall be the last quoted bid price per share for the Common Stock (or such other security) in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. or a similar organization. If the Common Stock (or such other security) is not so quoted, the "**Last Reported Sale Price**" shall be the average of the mid-point of the last bid and ask prices per share for the Common Stock (or such other security) on the relevant date from each of at least three nationally recognized independent investment banking firms selected by the Company for this purpose. The "**Last Reported Sale Price**" shall be determined without regard to after-hours trading or any other trading outside of regular trading session hours.

"**Legend Removal Deadline Date**" shall have the meaning specified in Section 4.06(e).

"**Make-Whole Fundamental Change**" means any transaction or event that constitutes a Fundamental Change (as defined above and determined after giving effect to any exceptions to or exclusions from such definition, but without regard to the *proviso* in clause (b) of the definition thereof).

"**Make-Whole Fundamental Change Period**" shall have the meaning specified in Section 14.03(a).

"**Market Disruption Event**" means, for the purposes of determining amounts due upon conversion (a) a failure by the primary U.S. national or regional securities exchange or market on which the Common Stock is listed or admitted for trading to open for trading during its regular trading session or (b) the occurrence or existence prior to 1:00 p.m., New York City time, on any Scheduled Trading Day for the Common Stock for more than one half-hour period in the aggregate during regular trading hours of any suspension or limitation imposed on trading (by reason of movements in price exceeding limits permitted by the relevant stock exchange or otherwise) in the Common Stock or in any options contracts or futures contracts traded on any U.S. exchange relating to the Common Stock.

"**Maturity Date**" means September 15, 2027.

"**Measurement Period**" shall have the meaning specified in Section 14.01(b)(i).

"**Note**" or "**Notes**" shall have the meaning specified in the first paragraph of the recitals of this Indenture.

"**Note Register**" shall have the meaning specified in Section 2.05(a).

"**Note Registrar**" shall have the meaning specified in Section 2.05(a).

"**Notice of Conversion**" shall have the meaning specified in Section 14.02(b).

"**Observation Period**" with respect to any Note surrendered for conversion means: (i) subject to clause (ii), if the relevant Conversion Date occurs prior to June 15, 2027, the 20 consecutive Trading Day period beginning on, and including, the second Trading Day immediately succeeding such Conversion Date; (ii) with respect to any Notes called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)), if the relevant Conversion Date occurs during a Redemption Period with respect to such Notes, the 20 consecutive Trading Days beginning on, and including, the 21st Scheduled Trading Day immediately preceding the relevant Redemption Date; and (iii) subject to clause (ii), if the relevant Conversion Date occurs on or after June 15, 2027, the 20 consecutive Trading Days beginning on, and including, the 21st Scheduled Trading Day immediately preceding the Maturity Date.

"**Offering Memorandum**" means the preliminary offering memorandum dated September 12, 2022, as supplemented by the related pricing term sheet dated September 12, 2022, relating to the offering and sale of the Notes.

"**Officer**" means, with respect to the Company, the President, the Chief Executive Officer, the Chief Financial Officer, the Treasurer, the Secretary, any assistant Treasurer, any assistant Secretary, any Executive or Senior Vice President or any Vice President (whether or not designated by a number or numbers or word or words added before or after the title "Vice President").

"**Officer's Certificate**," when used with respect to the Company, means a certificate that is delivered to the Trustee and that is signed on behalf of the Company by an Officer of the Company that meets the requirements of Section 17.05.

"**open of business**" means 9:00 a.m. (New York City time).

"**Opinion of Counsel**" means an opinion in writing signed by legal counsel, who may be an employee of or counsel to the Company, that is delivered to the Trustee.

"**Optional Redemption**" shall have the meaning specified in Section 16.01.

"**outstanding**," when used with reference to Notes, shall, subject to the provisions of Section 8.04, mean, as of any particular time, all Notes authenticated and delivered by the Trustee under this Indenture, except:

(a) Notes theretofore canceled by the Trustee or accepted by the Trustee for cancellation;

(b) Notes, or portions thereof, that have become due and payable and in respect of which monies in the necessary amount shall have been deposited in trust with the Trustee or with any Paying Agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own Paying Agent);

(c) Notes that have been paid pursuant to Section 2.06 or Notes in lieu of which, or in substitution for which, other Notes shall have been authenticated and delivered pursuant to the terms of Section 2.06 unless proof satisfactory to the Trustee is presented that any such Notes are held by protected purchasers in due course;

(d) Notes surrendered for purchase in accordance with Article 15 for which Paying Agent or tender agent holds money sufficient to pay the Fundamental Change Repurchase Price, in accordance with Section 15.04(b);

(e) Notes converted pursuant to Article 14 and required to be cancelled pursuant to Section 2.08;

(f) Notes redeemed pursuant to Article 16; and

(g) Notes repurchased by the Company pursuant to the last sentence of Section 2.10 after the Company surrenders them to the Trustee for cancellation in accordance with Section 2.08.

"**Partial Redemption Limitation**" shall have the meaning specified in Section 16.02(d).

"**Paying Agent**" shall have the meaning specified in Section 4.02.

"**Person**" means an individual, a corporation, a limited liability company, an association, a partnership, a joint venture, a joint stock company, a trust, an unincorporated organization or a government or an agency or a political subdivision thereof.

"**Physical Notes**" means permanent certificated Notes in registered form issued in minimum denominations of $1,000 principal amount and integral multiples in excess thereof.

"**Physical Settlement**" shall have the meaning specified in Section 14.02(a).

"**Predecessor Note**" of any particular Note means every previous Note evidencing all or a portion of the same debt as that evidenced by such particular Note; and, for the purposes of this definition, any Note authenticated and delivered under Section 2.06 in lieu of or in exchange for a mutilated, lost, destroyed or stolen Note shall be deemed to evidence the same debt as the mutilated, lost, destroyed or stolen Note that it replaces.

"**Qualified Successor Entity**" means, with respect to a Business Combination Event, a corporation; *provided*, *however*, that a limited liability company, limited partnership or other similar entity shall also constitute a Qualified Successor Entity with respect to such Business Combination Event if either (i) such Business Combination Event is an Exempted Fundamental Change; or (ii) both of the following conditions are satisfied: (1) either (x) such limited liability company, limited partnership or other similar entity, as applicable, is treated as a corporation or is a direct or indirect, wholly owned subsidiary of, and disregarded as an entity separate from, a corporation, in each case for U.S. federal income tax purposes; or (y) the Company has received an opinion of a nationally recognized tax counsel to the effect that such Business Combination Event will not be treated as an exchange under Section 1001 of the U.S. Internal Revenue Code of 1986, as amended, for Holders or beneficial owners of the Notes; and (2) such Business Combination Event constitutes a Share Exchange Event whose Reference Property consists solely of any combination of cash in U.S. dollars and shares of common stock or other corporate Common Equity of an entity that is (x) treated as a corporation for U.S. federal income tax purposes; (y) duly organized and existing under the laws of the United States of America, any State thereof or the District of Columbia; and (z) the direct or indirect parent of the limited liability company, limited partnership or similar entity.

"**Record Date**" means, with respect to any dividend, distribution or other transaction or event in which the holders of Common Stock (or other applicable security) have the right to receive any cash, securities or other property or in which the Common Stock (or such other security) is exchanged for or converted into any combination of cash, securities or other property, the date fixed for determination of holders of the Common Stock (or such other security) entitled to receive such cash, securities or other property (whether such date is fixed by the Board of Directors, by statute, by contract or otherwise).

"**Redemption Date**" shall have the meaning specified in Section 16.02(a).

"**Redemption Notice**" shall have the meaning specified in Section 16.02(a).

"**Redemption Period**" means the period from, and including, the date of a Redemption Notice until the close of business on the second Scheduled Trading Day immediately preceding the related Redemption Date, or, if the Company defaults in the payment of the Redemption Price, until the Redemption Price has been paid or duly provided for.

"**Redemption Price**" means, for any Notes to be redeemed pursuant to Section 16.01, 100% of the principal amount of such Notes, *plus* accrued and unpaid interest, if any, to, but excluding, the Redemption Date (unless the Redemption Date falls after a Regular Record Date but on or prior to the immediately succeeding Interest Payment Date, in which case interest accrued to the Interest Payment Date will be paid to Holders of record of such Notes as of the close of business on such Regular Record Date, and the Redemption Price will be equal to 100% of the principal amount of such Notes).

"**Reference Property**" shall have the meaning specified in Section 14.07(a).

"**Regular Record Date**," with respect to any Interest Payment Date, means the March 1 or September 1 (whether or not such day is a Business Day) immediately preceding the applicable March 15 or September 15 Interest Payment Date, respectively.

"**Resale Restriction Termination Date**" shall have the meaning specified in Section 2.05(c).

"**Responsible Officer**" means, when used with respect to the Trustee, any officer within the Corporate Trust Office of the Trustee, including any vice president, assistant vice president, assistant secretary, assistant treasurer, trust officer or any other officer of the Trustee who customarily performs functions similar to those performed by the Persons who at the time shall be such officers, respectively, or to whom any corporate trust matter relating to this Indenture is referred because of such person's knowledge of and familiarity with the particular subject and, in each case, who shall have direct responsibility for the administration of this Indenture.

"**Restricted Securities**" shall have the meaning specified in Section 2.05(c).

"**Restrictive Legend**" shall have the meaning specified in Section 2.05(c).

"**Rule 144**" means Rule 144 as promulgated under the Securities Act.

"**Rule 144A**" means Rule 144A as promulgated under the Securities Act.

"**Scheduled Trading Day**" means a day that is scheduled to be a Trading Day on the principal U.S. national or regional securities exchange or market on which the Common Stock is listed or admitted for trading. If the Common Stock is not so listed or admitted for trading, "**Scheduled Trading Day**" means a Business Day.

"**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"**Settlement Amount**" shall have the meaning specified in Section 14.02(a)(iv) .

"**Settlement Method**" means, with respect to any conversion of Notes, Physical Settlement, Cash Settlement or Combination Settlement, as elected (or deemed to have been elected) by the Company.

"**Settlement Method Election Deadline**" shall have the meaning specified in Section 14.02(a)(iii).

"**Settlement Notice**" shall have the meaning specified in Section 14.02(a)(iii).

"**Share Exchange Event**" shall have the meaning specified in Section 14.07(a).

"**Significant Subsidiary**" means a Subsidiary of the Company that meets the definition of "significant subsidiary" in Article 1, Rule 1-02(w) of Regulation S-X under the Exchange Act as in effect on the date of this Indenture; *provided* that, in the case of a Subsidiary of the Company that meets the criteria of clause (1)(iii) of such definition of "significant subsidiary" but not clause (1)(i) or (1)(ii) thereof, in each case, as such rule is

in effect on the date of this Indenture, such Subsidiary shall not be deemed to be a Significant Subsidiary unless such Subsidiary's income from continuing operations before income taxes, exclusive of amounts attributable to any non-controlling interests, for the last completed fiscal year prior to the date of such determination exceeds $100,000,000. For the avoidance of doubt, to the extent any such Subsidiary would not be deemed to be a "significant subsidiary" under the relevant definition set forth in Article 1, Rule 1-02(w) of Regulation S-X under the Exchange Act (or any successor rule) as in effect on the relevant date of determination, such Subsidiary shall not be deemed to be a Significant Subsidiary under this Indenture irrespective of whether such Subsidiary would otherwise be deemed to be a Significant Subsidiary pursuant to the immediately preceding sentence.

"**Specified Dollar Amount**" means the maximum cash amount per $1,000 principal amount of Notes to be received upon conversion as specified in the Settlement Notice related to any converted Notes.

"**Spin-Off**" shall have the meaning specified in Section 14.04(c).

"**Stock Price**" shall have the meaning specified in Section 14.03(c).

"**Subsidiary**" means, with respect to any Person, any corporation, association, partnership or other business entity of which more than 50% of the total voting power of shares of Capital Stock or other interests (including partnership interests) entitled (without regard to the occurrence of any contingency) to vote in the election of directors, managers, general partners or trustees thereof is at the time owned or controlled, directly or indirectly, by (i) such Person; (ii) such Person and one or more Subsidiaries of such Person; or (iii) one or more Subsidiaries of such Person.

"**Successor Company**" shall have the meaning specified in Section 11.01(a).

"**Trading Day**" means a day on which (i) trading in the Common Stock (or other security for which a closing sale price must be determined) generally occurs on The Nasdaq Global Select Market or, if the Common Stock (or such other security) is not then listed on The Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which the Common Stock (or such other security) is then listed or, if the Common Stock (or such other security) is not then listed on a U.S. national or regional securities exchange, on the principal other market on which the Common Stock (or such other security) is then traded and (ii) a Last Reported Sale Price for the Common Stock (or closing sale price for such other security) is available on such securities exchange or market; *provided* that if the Common Stock (or such other security) is not so listed or traded, "**Trading Day**" means a Business Day; and *provided*, *further*, that for purposes of determining amounts due upon conversion only, "**Trading Day**" means a day on which (x) there is no Market Disruption Event and (y) trading in the Common Stock generally occurs on The Nasdaq Global Select Market or, if the Common Stock is not then listed on The Nasdaq Global Select Market, on the principal other U.S. national or regional securities exchange on which the Common Stock is then listed or, if the Common Stock is not then listed on a U.S. national or regional securities

exchange, on the principal other market on which the Common Stock is then listed or admitted for trading, except that if the Common Stock is not so listed or admitted for trading, "**Trading Day**" means a Business Day.

"**Trading Price**" per $1,000 principal amount of the Notes on any date of determination means the average of the secondary market bid quotations obtained by the Bid Solicitation Agent for $5,000,000 principal amount of Notes at approximately 3:30 p.m., New York City time, on such determination date from three independent nationally recognized securities dealers the Company selects for this purpose; *provided* that if three such bids cannot reasonably be obtained by the Bid Solicitation Agent but two such bids are obtained, then the average of the two bids shall be used, and if only one such bid can reasonably be obtained by the Bid Solicitation Agent, that one bid shall be used. If the Bid Solicitation Agent cannot reasonably obtain at least one bid for $5,000,000 principal amount of Notes from a nationally recognized securities dealer on any determination date, then the Trading Price per $1,000 principal amount of Notes on such determination date shall be deemed to be less than 98% of the product of the Last Reported Sale Price of the Common Stock and the Conversion Rate. Any such determination will be conclusive absent manifest error.

"**Trading Price Condition**" shall have the meaning specified in Section 14.01(b)(i).

"**transfer**" shall have the meaning specified in Section 2.05(c).

"**Trigger Event**" shall have the meaning specified in Section 14.04(c).

"**Trust Indenture Act**" means the Trust Indenture Act of 1939, as amended, as it was in force at the date of execution of this Indenture; *provided*, *however*, that in the event the Trust Indenture Act of 1939 is amended after the date hereof, the term "Trust Indenture Act" shall mean, to the extent required by such amendment, the Trust Indenture Act of 1939, as so amended.

"**Trustee**" means the Person named as the "**Trustee**" in the first paragraph of this Indenture until a successor trustee shall have become such pursuant to the applicable provisions of this Indenture, and thereafter "**Trustee**" shall mean or include each Person who is then a Trustee hereunder.

"**unit of Reference Property**" shall have the meaning specified in Section 14.07(a).

"**Valid Payment Date**" means any day other than a Saturday, a Sunday or a day on which banking institutions in the place of payment are authorized or required by law or executive order to close or be closed.

"**Valuation Period**" shall have the meaning specified in Section 14.04(c).

"**Wholly Owned Subsidiary**" means, with respect to any Person, any Subsidiary of such Person, except that, solely for purposes of this definition, the reference to "more than 50%" in the definition of "Subsidiary" shall be deemed replaced by a reference to "100%".

Section 1.02. *References to Interest.* Unless the context otherwise requires, any reference to interest on, or in respect of, any Note in this Indenture shall be deemed to include Additional Interest if, in such context, Additional Interest is, was or would be payable pursuant to any of Section 4.06(d), Section 4.06(e) and Section 6.03. Unless the context otherwise requires, any express mention of Additional Interest in any provision hereof shall not be construed as excluding Additional Interest in those provisions hereof where such express mention is not made.

ARTICLE 2
ISSUE, DESCRIPTION, EXECUTION, REGISTRATION AND EXCHANGE OF NOTES

Section 2.01. *Designation and Amount.* The Notes shall be designated as the "1.00% Convertible Senior Notes due 2027." The aggregate principal amount of Notes that may be authenticated and delivered under this Indenture is initially limited to $1,035,000,000, subject to Section 2.10 and except for Notes authenticated and delivered upon registration or transfer of, or in exchange for, or in lieu of other Notes to the extent expressly permitted hereunder.

Section 2.02. *Form of Notes.* The Notes and the Trustee's certificate of authentication to be borne by such Notes shall be substantially in the respective forms set forth in Exhibit A, the terms and provisions of which shall constitute, and are hereby expressly incorporated in and made a part of this Indenture. To the extent applicable, the Company and the Trustee, by their execution and delivery of this Indenture, expressly agree to such terms and provisions and to be bound thereby. In the case of any conflict between this Indenture and a Note, the provisions of this Indenture shall control and govern to the extent of such conflict.

Any Global Note may be endorsed with or have incorporated in the text thereof such legends or recitals or changes not inconsistent with the provisions of this Indenture as may be required by the Custodian or the Depositary, or as may be required to comply with any applicable law or any regulation thereunder or with the rules and regulations of any securities exchange or automated quotation system upon which the Notes may be listed or traded or designated for issuance or to conform with any usage with respect thereto, or to indicate any special limitations or restrictions to which any particular Notes are subject.

Any of the Notes may have such letters, numbers or other marks of identification and such notations, legends or endorsements as the Officer executing the same may approve (execution thereof to be conclusive evidence of such approval) and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, or to conform to usage or to indicate any special limitations or restrictions to which any particular Notes are subject.

Each Global Note shall represent such principal amount of the outstanding Notes as shall be specified therein and shall provide that it shall represent the aggregate principal amount of outstanding Notes from time to time endorsed thereon and that the aggregate principal amount of outstanding Notes represented thereby may from time to time be increased or reduced to reflect redemptions, repurchases, cancellations, conversions, transfers or exchanges permitted hereby. Any endorsement of a Global Note to reflect the amount of any increase or decrease in the amount of outstanding Notes represented thereby shall be made by the Trustee or the Custodian, at the direction of the Trustee, in such manner and upon instructions given by the Holder of such Notes in accordance with this Indenture. Payment of principal (including the Redemption Price, the Fundamental Change Repurchase Price, if applicable) of, and accrued and unpaid interest on, a Global Note shall be made to the Holder of such Note on the date of payment, unless a record date or other means of determining Holders eligible to receive payment is provided for herein.

Section 2.03. *Date and Denomination of Notes; Payments of Interest and Defaulted Amounts.* (a) The Notes shall be issuable in registered form without coupons in minimum denominations of $1,000 principal amount and integral multiples in excess thereof. Each Note shall be dated the date of its authentication and shall bear interest from the date specified on the face of such Note. Accrued interest on the Notes shall be computed on the basis of a 360-day year composed of twelve 30-day months and, for partial months, on the basis of the number of days actually elapsed in a 30-day month.

(b) The Person in whose name any Note (or its Predecessor Note) is registered on the Note Register at the close of business on any Regular Record Date with respect to any Interest Payment Date shall be entitled to receive the interest payable on such Interest Payment Date. The principal amount of any Note (x) in the case of any Physical Note, shall be payable at the office or agency of the Company maintained by the Company for such purposes in the United States of America, which shall initially be the Corporate Trust Office in the United States of America and (y) in the case of any Global Note, shall be payable by wire transfer of immediately available funds to the account of the Depositary or its nominee. The Company shall pay, or cause the Paying Agent to pay, interest (i) on any Physical Notes (A) to Holders holding Physical Notes having an aggregate principal amount of $5,000,000 or less, by check mailed to the Holders of these Notes at their address as it appears in the Note Register and (B) to Holders holding Physical Notes having an aggregate principal amount of more than $5,000,000, either by check mailed to each Holder or, upon application by such a Holder to the Note Registrar not later than the relevant Regular Record Date, by wire transfer in immediately available funds to that Holder's account within the United States of America if such Holder has provided the Trustee or Paying Agent with the requisite information necessary to make such wire transfer, which application shall remain in effect until the Holder notifies, in writing, the Note Registrar to the contrary or (ii) on any Global Note by wire transfer of immediately available funds to the account of the Depositary or its nominee.

(c) Any Defaulted Amounts shall forthwith cease to be payable to the Holder on the relevant payment date but shall accrue interest per annum at the rate borne by the Notes, subject to the enforceability thereof under applicable law, from, and including, such relevant payment date, and such Defaulted Amounts together with such interest thereon shall be paid by the Company, at its election in each case, as provided in clause (i) or (ii) below:

(i) The Company may elect to make payment of any Defaulted Amounts to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on a special record date for the payment of such Defaulted Amounts, which shall be fixed in the following manner. The Company shall notify the Trustee in writing of the amount of the Defaulted Amounts proposed to be paid on each Note and the date of the proposed payment (which shall be not less than 25 days after the receipt by the Trustee of such notice, unless the Trustee shall consent to an earlier date), and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount to be paid in respect of such Defaulted Amounts or shall make arrangements satisfactory to the Trustee for such deposit on or prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Amounts as in this clause provided. Thereupon the Company shall fix a special record date for the payment of such Defaulted Amounts which shall be not more than 15 days and not less than 10 days prior to the date of the proposed payment, and not less than 10 days after the receipt by the Trustee of the notice of the proposed payment. The Company shall promptly notify the Trustee of such special record date in writing and the Trustee, in the name and at the expense of the Company, shall cause notice of the proposed payment of such Defaulted Amounts and the special record date therefor to be delivered to each Holder not less than 10 days prior to such special record date. Notice of the proposed payment of such Defaulted Amounts and the special record date therefor having been so delivered, such Defaulted Amounts shall be paid to the Persons in whose names the Notes (or their respective Predecessor Notes) are registered at the close of business on such special record date and shall no longer be payable pursuant to the following clause (ii) of this Section 2.03(c). The Trustee shall have no responsibility for the calculation of Defaulted Amounts.

(ii) The Company may make payment of any Defaulted Amounts in any other lawful manner not inconsistent with the requirements of any securities exchange or automated quotation system on which the Notes may be listed or designated for issuance, and upon such notice as may be required by such exchange or automated quotation system, if, after written notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

Section 2.04. *Execution, Authentication and Delivery of Notes.* The Notes shall be signed in the name and on behalf of the Company by the manual, facsimile or other electronic signature of one of its Officers.

At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Notes executed by the Company to the Trustee for authentication, together with a Company Order for the authentication and delivery of such Notes, and the Trustee in accordance with such Company Order shall authenticate and deliver such Notes, without any further action by the Company hereunder; *provided*, *however*, that the Trustee shall be entitled to receive an Officer's Certificate and an Opinion of Counsel of the Company with respect to the issuance, authentication and delivery of the Notes.

Only such Notes as shall bear thereon a certificate of authentication substantially in the form set forth on the Form of Note attached as Exhibit A hereto, executed manually, electronically or by facsimile by an authorized signatory of the Trustee (or an authenticating agent appointed by the Trustee as provided by Section 17.10), shall be entitled to the benefits of this Indenture or be valid or obligatory for any purpose. Such certificate by the Trustee (or such an authenticating agent) upon any Note executed by the Company shall be conclusive evidence that the Note so authenticated has been duly authenticated and delivered hereunder and that the Holder is entitled to the benefits of this Indenture.

In case any Officer of the Company who shall have signed any of the Notes shall cease to be such Officer before the Notes so signed shall have been authenticated and delivered by the Trustee, or disposed of by the Company, such Notes nevertheless may be authenticated and delivered or disposed of as though the person who signed such Notes had not ceased to be such Officer of the Company; and any Note may be signed on behalf of the Company by such persons as, at the actual date of the execution of such Note, shall be the Officers of the Company, although at the date of the execution of this Indenture any such person was not such an Officer.

Section 2.05. *Exchange and Registration of Transfer of Notes; Restrictions on Transfer; Depositary.* (a) The Company shall cause to be kept at the Corporate Trust Office a register (the register maintained in such office or in any other office or agency of the Company designated pursuant to Section 4.02, the "**Note Register**") in which, subject to such reasonable regulations as it may prescribe, the Company shall provide for the registration of Notes and of transfers of Notes. Such register shall be in written form or in any form capable of being converted into written form within a reasonable period of time. The Trustee is hereby initially appointed the "**Note Registrar**" for the purpose of registering Notes and transfers of Notes as herein provided. The Company may appoint one or more co-Note Registrars in accordance with Section 4.02.

Upon surrender for registration of transfer of any Note to the Note Registrar or any co-Note Registrar, and satisfaction (as determined by the Company) of the requirements for such transfer set forth in this Section 2.05, the Company shall execute, and the Trustee shall authenticate and deliver, in the name of the designated transferee or transferees, one or more new Notes of any authorized denominations and of a like aggregate principal amount and bearing such legends as may be required by this Indenture.

Notes may be exchanged for other Notes of any authorized denominations and of a like aggregate principal amount, upon surrender of the Notes to be exchanged at any such office or agency maintained by the Company pursuant to Section 4.02. Whenever any Notes are so surrendered for exchange, the Company shall execute, and the Trustee shall authenticate and deliver, the Notes that the Holder making the exchange is entitled to receive, bearing registration numbers not contemporaneously outstanding.

All Notes presented or surrendered for registration of transfer or for exchange, repurchase or conversion shall (if so required by the Company, the Trustee, the Note Registrar or any co-Note Registrar) be duly endorsed, or be accompanied by a written instrument or instruments of transfer in form satisfactory to the Note Registrar and duly executed, by the Holder thereof or its attorney-in-fact duly authorized in writing.

No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent for any exchange or registration of transfer of Notes, but the Company may require a Holder to pay a sum sufficient to cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of new Notes issued upon such exchange or registration of transfer being different from the name of the Holder of the old Notes surrendered for exchange or registration of transfer.

None of the Company, the Trustee, the Note Registrar or any co-Note Registrar shall be required to exchange or register a transfer of (i) any Notes surrendered for conversion or, if a portion of any Note is surrendered for conversion, such portion thereof surrendered for conversion, (ii) any Notes, or a portion of any Note, surrendered for repurchase (and not withdrawn) in accordance with Article 15 or (iii) any Notes selected for redemption in accordance with Article 16, except the unredeemed portion of any Note being redeemed in part.

All Notes issued upon any registration of transfer or exchange of Notes in accordance with this Indenture shall be the valid obligations of the Company, evidencing the same debt, and entitled to the same benefits under this Indenture as the Notes surrendered upon such registration of transfer or exchange.

(b) So long as the Notes are eligible for book-entry settlement with the Depositary, unless otherwise required by law, subject to the fourth paragraph from the end of Section 2.05(c) all Notes shall be represented by one or more Notes in global form (each, a "**Global Note**") registered in the name of the Depositary or the nominee of the Depositary. The transfer and exchange of beneficial interests in a Global Note that does not involve the issuance of a Physical Note shall be effected through the Depositary (but not the Trustee or the Custodian) in accordance with this Indenture (including the restrictions on transfer set forth herein) and the Applicable Procedures.

(c) Every Note that bears or is required under this Section 2.05(c) to bear the legend set forth in this Section 2.05(c) (together with any Common Stock issued upon conversion of the Notes that is required to bear the legend set forth in Section 2.05(d), collectively, the "**Restricted Securities**") shall be subject to the restrictions on transfer

set forth in this Section 2.05(c) (including the legend set forth below), unless such restrictions on transfer shall be eliminated or otherwise waived by written consent of the Company, and the Holder of each such Restricted Security, by such Holder's acceptance thereof, agrees to be bound by all such restrictions on transfer. As used in this Section 2.05(c) and Section 2.05(d), the term "**transfer**" encompasses any sale, pledge, transfer or other disposition whatsoever of any Restricted Security.

Until the date (the "**Resale Restriction Termination Date**") that is the later of (1) the date that is one year after the last date of original issuance of the Notes, or such shorter period of time as permitted by Rule 144 or any successor provision thereto, and (2) such later date, if any, as may be required by applicable law, any certificate evidencing such Note (and all securities issued in exchange therefor or substitution thereof, other than Common Stock, if any, issued upon conversion thereof, which shall bear the legend set forth in Section 2.05(d), if applicable) shall bear a legend in substantially the following form (the "**Restrictive Legend**") (unless such Notes have been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that continues to be effective at the time of such transfer, or sold pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or unless otherwise agreed by the Company in writing, with notice thereof to the Trustee):

THIS SECURITY AND THE COMMON STOCK, IF ANY, ISSUABLE UPON CONVERSION OF THIS SECURITY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS A "QUALIFIED INSTITUTIONAL BUYER" (WITHIN THE MEANING OF RULE 144A UNDER THE SECURITIES ACT) AND THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND

(2) AGREES FOR THE BENEFIT OF ALNYLAM PHARMACEUTICALS, INC. (THE "**COMPANY**") THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO THE COMPANY OR ANY SUBSIDIARY THEREOF, OR

(B) PURSUANT TO A REGISTRATION STATEMENT THAT HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT AND IS EFFECTIVE AT THE TIME OF SUCH TRANSFER, OR

(C) TO A PERSON THAT YOU REASONABLY BELIEVE TO BE A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY RESERVES THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

NO AFFILIATE (AS DEFINED IN RULE 144 UNDER THE SECURITIES ACT) OF THE COMPANY OR PERSON THAT HAS BEEN AN AFFILIATE (AS DEFINED IN RULE 144 UNDER THE SECURITIES ACT) OF THE COMPANY DURING THE IMMEDIATELY PRECEDING THREE MONTHS MAY PURCHASE, OTHERWISE ACQUIRE OR HOLD THIS SECURITY OR A BENEFICIAL INTEREST HEREIN.

No transfer of any Note prior to the Resale Restriction Termination Date will be registered by the Note Registrar unless the applicable box on the Form of Assignment and Transfer has been checked.

Any Note (or security issued in exchange or substitution therefor) (i) as to which such restrictions on transfer shall have expired in accordance with their terms, (ii) that has been transferred pursuant to a registration statement that has become effective or been declared effective under the Securities Act and that continues to be effective at the time of such transfer or (iii) that has been sold pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, may, upon surrender of such Note for exchange to the Note Registrar in accordance with the provisions of this Section 2.05, be exchanged for a new Note or Notes, of like tenor and aggregate principal amount, which shall not bear the Restrictive Legend required by this Section 2.05(c) and shall not be assigned (or deemed assigned) a restricted CUSIP number. The Restrictive Legend set forth above and affixed on any Note will be deemed, in accordance with the terms of the certificate representing such Note, to be removed

therefrom upon the Company's delivery to the Trustee of an Officer's Certificate to such effect; at such time, such Note will be deemed to be assigned an unrestricted CUSIP number as provided in the certificate representing such Note, it being understood that the Depositary of any Global Note may require a mandatory exchange or other process to cause such Global Note to be identified by an unrestricted CUSIP number in the facilities of such Depositary. Without limiting the generality of any other provision of this Indenture, the Trustee will be entitled to receive an instruction letter, together with the documents contemplated under Section 17.05 hereof, from the Company before taking any action with respect to effecting any such mandatory exchange or other process. The Company reserves the right to require the delivery of such legal opinions, certifications or other evidence as may reasonably be required in order to determine that any proposed transfer of any Note is being made in compliance with the Securities Act and applicable state securities laws.

The Company shall be entitled to instruct the Custodian in writing to so surrender any Global Note as to which any of the conditions set forth in clause (i) through (iii) of the immediately preceding sentence have been satisfied, and, upon such instruction, the Custodian shall so surrender such Global Note for exchange; and any new Global Note so exchanged therefor shall not bear the Restrictive Legend specified in this Section 2.05(c) and shall not be assigned (or deemed assigned) a restricted CUSIP number. The Company shall promptly notify the Trustee in writing upon the occurrence of the Resale Restriction Termination Date and promptly after a registration statement, if any, with respect to the Notes or any Common Stock issued upon conversion of the Notes has been declared effective under the Securities Act.

Notwithstanding any other provisions of this Indenture (other than the provisions set forth in this Section 2.05(c)), a Global Note may not be transferred as a whole or in part except (i) by the Depositary to a nominee of the Depositary or by a nominee of the Depositary to the Depositary or another nominee of the Depositary or by the Depositary or any such nominee to a successor Depositary or a nominee of such successor Depositary and (ii) for exchange of a Global Note or a portion thereof for one or more Physical Notes in accordance with the second immediately succeeding paragraph.

The Depositary shall be a clearing agency registered under the Exchange Act. The Company initially appoints The Depository Trust Company to act as Depositary with respect to each Global Note. Initially, each Global Note shall be issued to the Depositary, registered in the name of Cede & Co., as the nominee of the Depositary, and deposited with the Trustee as custodian for Cede & Co.

If (i) the Depositary notifies the Company at any time that the Depositary is unwilling or unable to continue as depositary for the Global Notes and a successor depositary is not appointed within 90 days, (ii) the Depositary ceases to be registered as a clearing agency under the Exchange Act and a successor depositary is not appointed within 90 days or (iii) an Event of Default with respect to the Notes has occurred and is continuing and a beneficial owner of any Note requests that its beneficial interest therein be issued as a Physical Note, the Company shall execute, and the Trustee, upon receipt of an Officer's Certificate and a Company Order for the authentication and delivery of

Notes, shall authenticate and deliver (x) in the case of clause (iii), a Physical Note to such beneficial owner in a principal amount equal to the principal amount of such Note corresponding to such beneficial owner's beneficial interest and (y) in the case of clause (i) or (ii), Physical Notes to each beneficial owner of the related Global Notes (or a portion thereof) in an aggregate principal amount equal to the aggregate principal amount of such Global Notes in exchange for such Global Notes, and upon delivery of the Global Notes to the Trustee such Global Notes shall be canceled.

Physical Notes issued in exchange for all or a part of the Global Note pursuant to this Section 2.05(c) shall be registered in such names and in such authorized denominations as the Depositary, pursuant to instructions from its direct or indirect participants or otherwise, or, in the case of clause (iii) of the immediately preceding paragraph, the relevant beneficial owner, shall instruct the Trustee. Upon execution and authentication, the Trustee shall deliver such Physical Notes to the Persons in whose names such Physical Notes are so registered.

At such time as all interests in a Global Note have been converted, canceled, repurchased, redeemed or transferred, such Global Note shall be, upon receipt thereof, canceled by the Trustee in accordance with standing procedures and existing instructions between the Depositary and the Custodian. At any time prior to such cancellation, if any interest in a Global Note is exchanged for Physical Notes, converted, canceled, repurchased, redeemed or transferred to a transferee who receives Physical Notes therefor or any Physical Note is exchanged or transferred for part of such Global Note, the principal amount of such Global Note shall, in accordance with the standing procedures and instructions existing between the Depositary and the Custodian, be appropriately reduced or increased, as the case may be, and an endorsement shall be made on such Global Note, by the Trustee or the Custodian, at the direction of the Trustee, to reflect such reduction or increase.

None of the Company, the Trustee, the Paying Agent, the Conversion Agent or any agent of the Company or the Trustee shall have any responsibility or liability for the payment of amounts to owners of beneficial interest in a Global Note, for any aspect of the records relating to or payments made on account of beneficial ownership interests of a Global Note or maintaining, supervising or reviewing any records relating to such beneficial ownership interests.

Neither the Company nor the Trustee, Paying Agent, Note Registrar or Conversion Agent (nor the Company's or their agents) shall have any responsibility or liability for any act or omission of the Depositary. All notices and communications to be given to the Holders and all payments to be made to Holders in respect of the Notes shall be given or made only to, or upon the order of, the registered Holder(s) (which shall be the Depositary or its nominee in the case of a Global Note).

The rights of beneficial owners in any Global Note shall be exercised only through the Depositary subject to the Applicable Procedures of the Depositary. The Trustee may rely and shall be fully protected in relying upon information furnished by the Depositary with respect to its members, participants and any beneficial owners.

(d) Until the Resale Restriction Termination Date, any stock certificate representing Common Stock issued upon conversion of a Note shall bear a legend in substantially the following form (unless such Common Stock has been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that continues to be effective at the time of such transfer, or pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or such Common Stock has been issued upon conversion of a Note that has transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that continues to be effective at the time of such transfer, or pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, or unless otherwise agreed by the Company with written notice thereof to the Trustee and any transfer agent for the Common Stock):

THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**SECURITIES ACT**"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS A "QUALIFIED INSTITUTIONAL BUYER" (WITHIN THE MEANING OF RULE 144A UNDER THE SECURITIES ACT) AND THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND

(2) AGREES FOR THE BENEFIT OF ALNYLAM PHARMACEUTICALS, INC. (THE "**COMPANY**") THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE OF THE SERIES OF NOTES UPON THE CONVERSION OF WHICH THIS SECURITY WAS ISSUED OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO THE COMPANY OR ANY SUBSIDIARY THEREOF, OR

(B) PURSUANT TO A REGISTRATION STATEMENT THAT HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT AND IS EFFECTIVE AT THE TIME OF SUCH TRANSFER, OR

(C) TO A PERSON THAT YOU REASONABLY BELIEVE TO BE A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY AND THE TRANSFER AGENT FOR THE COMPANY'S COMMON STOCK RESERVE THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

Any such Common Stock (i) as to which such restrictions on transfer shall have expired in accordance with their terms, (ii) that has been transferred pursuant to a registration statement that has become or been declared effective under the Securities Act and that continues to be effective at the time of such transfer or (iii) that has been sold pursuant to the exemption from registration provided by Rule 144 or any similar provision then in force under the Securities Act, may, upon surrender of the certificates representing such shares of Common Stock for exchange in accordance with the procedures of the transfer agent for the Common Stock, be exchanged for a new certificate or certificates for a like aggregate number of shares of Common Stock, which shall not bear the restrictive legend required by this Section 2.05(d).

(e) Any Note that is owned by the Company or any Affiliate of the Company (or any Person who was an Affiliate of the Company at any time during the three months immediately preceding) may not be resold by the Company or such Affiliate (or such Person, as the case may be) unless registered under the Securities Act or resold pursuant to an exemption from the registration requirements of the Securities Act in a transaction that results in such Note no longer being a "restricted security" (as defined under Rule 144).

(f) Notwithstanding anything contained herein to the contrary, neither the Trustee nor the Note Registrar shall be responsible for ascertaining whether any transfer complies with the registration provisions of, or exemptions from, the Securities Act, applicable state securities laws or other applicable law, or for monitoring any Holder's compliance with the provisions of this Section 2.05 or for verifying any Holder's representations made in accordance with this Section 2.05. Neither the Trustee nor the Note Registrar shall have any responsibility for any actions taken or not taken by the Depositary.

Section 2.06. *Mutilated, Destroyed, Lost or Stolen Notes.* In case any Note shall become mutilated or be destroyed, lost or stolen, the Company in its discretion may execute, and upon receipt of a Company Order, the Trustee or an authenticating agent

appointed by the Trustee shall authenticate and deliver, a new Note, bearing a registration number not contemporaneously outstanding, in exchange and substitution for the mutilated Note, or in lieu of and in substitution for the Note so destroyed, lost or stolen. In every case the applicant for a substituted Note shall furnish to the Company, to the Trustee and, if applicable, to such authenticating agent such security or indemnity as may be required by them to save each of them harmless from any loss, liability, cost or expense caused by or connected with such substitution, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company, to the Trustee and, if applicable, to such authenticating agent evidence to their satisfaction of the destruction, loss or theft of such Note and of the ownership thereof.

The Trustee or such authenticating agent may authenticate any such substituted Note and deliver the same upon the receipt of such security or indemnity as the Trustee, the Company and, if applicable, such authenticating agent may require. No service charge shall be imposed by the Company, the Trustee, the Note Registrar, any co-Note Registrar or the Paying Agent upon the issuance of any substitute Note, but the Company may require a Holder to pay a sum sufficient to cover any documentary, stamp or similar issue or transfer tax required in connection therewith as a result of the name of the Holder of the new substitute Note being different from the name of the Holder of the old Note that became mutilated or was destroyed, lost or stolen. In case any Note that has matured or is about to mature or has been surrendered for required repurchase or is about to be converted in accordance with Article 14 shall become mutilated or be destroyed, lost or stolen, the Company may, in its sole discretion, instead of issuing a substitute Note, pay or authorize the payment of or convert or authorize the conversion of the same (without surrender thereof except in the case of a mutilated Note), as the case may be, if the applicant for such payment or conversion shall furnish to the Company, to the Trustee and, if applicable, to such authenticating agent such security or indemnity as may be required by them to save each of them harmless for any loss, liability, cost or expense caused by or connected with such substitution, and, in every case of destruction, loss or theft, evidence satisfactory to the Company, the Trustee and, if applicable, any Paying Agent or Conversion Agent of the destruction, loss or theft of such Note and of the ownership thereof.

Every substitute Note issued pursuant to the provisions of this Section 2.06 by virtue of the fact that any Note is destroyed, lost or stolen shall constitute an additional contractual obligation of the Company, whether or not the destroyed, lost or stolen Note shall be found at any time, and shall be entitled to all the benefits of (but shall be subject to all the limitations set forth in) this Indenture equally and proportionately with any and all other Notes duly issued hereunder. To the extent permitted by law, all Notes shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the replacement, payment, redemption, conversion or repurchase of mutilated, destroyed, lost or stolen Notes and shall preclude any and all other rights or remedies notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement, payment, redemption, conversion or repurchase of negotiable instruments or other securities without their surrender.

Section 2.07. *Temporary Notes.* Pending the preparation of Physical Notes, the Company may execute and the Trustee or an authenticating agent appointed by the Trustee shall, upon receipt of a Company Order, authenticate and deliver temporary Notes (printed or lithographed). Temporary Notes shall be issuable in any authorized denomination, and substantially in the form of the Physical Notes but with such omissions, insertions and variations as may be appropriate for temporary Notes, all as may be determined by the Company. Every such temporary Note shall be executed by the Company and authenticated by the Trustee or such authenticating agent upon the same conditions and in substantially the same manner, and with the same effect, as the Physical Notes. Without unreasonable delay, the Company shall execute and deliver to the Trustee or such authenticating agent Physical Notes (other than any Global Note) and thereupon any or all temporary Notes (other than any Global Note) may be surrendered in exchange therefor, at each office or agency maintained by the Company pursuant to Section 4.02 and the Trustee or such authenticating agent shall, upon receipt of a Company Order, authenticate and deliver in exchange for such temporary Notes an equal aggregate principal amount of Physical Notes. Such exchange shall be made by the Company at its own expense and without any charge therefor. Until so exchanged, the temporary Notes shall in all respects be entitled to the same benefits and subject to the same limitations under this Indenture as Physical Notes authenticated and delivered hereunder.

Section 2.08. *Cancellation of Notes Paid, Converted, Etc.* The Company shall cause all Notes surrendered for the purpose of payment at maturity, registration of transfer or exchange or conversion, if surrendered to the Company or any Person that the Company controls, to be surrendered to the Trustee for cancellation and they will no longer be considered outstanding under this Indenture upon their payment at maturity, registration of transfer or exchange or conversion. All Notes delivered to the Trustee shall be canceled promptly by it. Except for any Notes surrendered for registration of transfer or exchange, or as otherwise expressly permitted by any of the provisions of this Indenture, no Notes shall be authenticated in exchange for any Notes surrendered to the Trustee for cancellation. The Trustee shall dispose of canceled Notes in accordance with its customary procedures. After such cancellation, the Trustee shall deliver a certificate of such cancellation to the Company, at the Company's written request in a Company Order.

Section 2.09. *CUSIP Numbers.* The Company in issuing the Notes may use CUSIP numbers (if then generally in use), and, if so, the Trustee shall use CUSIP numbers in all notices issued to Holders as a convenience to such Holders; *provided* that the Trustee shall have no liability for any defect in the CUSIP numbers as they appear on any Note, notice or elsewhere and that any such notice may state that no representation is made as to the correctness of such numbers either as printed on the Notes or on such notice and that reliance may be placed only on the other identification numbers printed on the Notes. The Company shall promptly notify the Trustee in writing of any change in the CUSIP numbers.

Section 2.10. *Additional Notes; Repurchases.* The Company may, without the consent of, or notice to, the Holders and notwithstanding Section 2.01, issue additional

Notes hereunder with the same terms as the Notes initially issued hereunder (other than differences in the issue date, the issue price, interest accrued prior to the issue date of such additional Notes and, if applicable, restrictions on transfer in respect of such additional Notes) in an unlimited aggregate principal amount; *provided* that if any such additional Notes are not fungible with the Notes initially issued hereunder for U.S. federal income tax or securities law purposes, such additional Notes shall have a separate CUSIP number or no CUSIP number. Prior to the issuance of any such additional Notes, the Company shall deliver to the Trustee a Company Order, an Officer's Certificate and an Opinion of Counsel, such Officer's Certificate and Opinion of Counsel to cover such matters, in addition to those required by Section 17.05, as the Trustee shall reasonably request. In addition, the Company may, to the extent permitted by law and without notice to or the consent of Holders, and directly or indirectly (regardless of whether such Notes are surrendered to the Company), repurchase Notes in the open market or otherwise, whether by the Company or its Subsidiaries or through a private or public tender or exchange offer or through counterparties to private agreements, including by cash-settled swaps or other derivatives. The Company may, to the extent permitted by applicable law, reissue, resell or surrender to the Trustee for cancellation in accordance with Section 2.08 any Notes that the Company may repurchase, in the case of a reissuance or resale, so long as such Notes do not constitute "restricted securities" (as defined under Rule 144) upon such reissuance or resale; *provided* that, if any such Notes are not fungible with the Notes initially issued hereunder for U.S. federal income tax law purposes, such reissued or resold Notes shall have a separate CUSIP number or no CUSIP number. Any Notes that the Company may repurchase shall be considered outstanding for all purposes under this Indenture (for the avoidance of doubt, other than, at any time when such Notes are held by the Company, any of the Company's Subsidiaries or Affiliates or any Subsidiary of any of the Company's Affiliates, for the purpose of determining whether Holders of the requisite aggregate principal amount of Notes have concurred in any direction, consent, waiver or other action under this Indenture) unless and until such time the Company surrenders them to the Trustee for cancellation in accordance with Section 2.08 and, upon receipt of a written order from the Company, the Trustee shall cancel all Notes so surrendered.

ARTICLE 3
SATISFACTION AND DISCHARGE

Section 3.01. *Satisfaction and Discharge.* This Indenture and the Notes shall upon request of the Company contained in an Officer's Certificate cease to be of further effect, and the Trustee, at the expense of the Company, shall execute such instruments reasonably requested by the Company acknowledging satisfaction and discharge of this Indenture and the Notes, when (a) (i) all Notes theretofore authenticated and delivered (other than Notes which have been destroyed, lost or stolen and which have been replaced, paid or converted as provided in Section 2.06) have been delivered to the Trustee for cancellation; or (ii) after the Notes have (x) become due and payable, whether on the Maturity Date, on any Redemption Date, on any Fundamental Change Repurchase Date or otherwise and/or (y) been converted (and the related consideration due upon conversion has been determined), the Company has deposited with the Trustee cash and/

or has delivered to Holders shares of Common Stock, as applicable, (in the case of Common Stock, solely to satisfy the Company's Conversion Obligation) sufficient, without consideration of reinvestment, to pay all of the outstanding Notes and all other sums due and payable under this Indenture by the Company; and (b) the Company has delivered to the Trustee an Officer's Certificate and an Opinion of Counsel, each stating that all conditions precedent herein provided for relating to the satisfaction and discharge of this Indenture have been complied with. Notwithstanding the satisfaction and discharge of this Indenture, the obligations of the Company to the Trustee under Section 7.06 shall survive.

ARTICLE 4
PARTICULAR COVENANTS OF THE COMPANY

Section 4.01. *Payment of Principal and Interest.* The Company covenants and agrees that it will cause to be paid the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, the Settlement Amounts owed upon conversion on, and accrued and unpaid interest on, each of the Notes at the places, at the respective times and in the manner provided herein and in the Notes.

Section 4.02. *Maintenance of Office or Agency.* The Company will maintain in the United States of America an office or agency where the Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase ("**Paying Agent**") or for conversion ("**Conversion Agent**") and where notices in respect of the Notes and this Indenture may be made. The Company will give prompt written notice to the Trustee of the location, and any change in the location, of such office or agency. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, surrenders, notices and demands may be made at the Corporate Trust Office.

The Company may also from time to time designate a Paying Agent one or more other offices or agencies where the Notes may be presented or surrendered for any or all such purposes and may from time to time rescind such designations; *provided* that no such designation or rescission shall in any manner relieve the Company of its obligation to maintain an office or agency in the United States of America for such purposes. The Company will give prompt written notice to the Trustee of any such designation or rescission and of any change in the location of any such other office or agency. The terms "**Paying Agent**" and "**Conversion Agent**" include any such additional or other offices or agencies, as applicable.

The Company hereby initially designates the Trustee as the Paying Agent, Note Registrar, Custodian and Conversion Agent and the Corporate Trust Office as a place where Notes may be surrendered for registration of transfer or exchange or for presentation for payment or repurchase (if applicable) or for conversion and where notices in respect of the Notes and this Indenture may be made; provided, that the Trustee shall not be considered an agent of the Company for service of legal process.

Section 4.03. *Appointments to Fill Vacancies in Trustee's Office.* The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the

manner provided in Section 7.09, a Trustee, so that there shall at all times be a Trustee hereunder.

Section 4.04. *Provisions as to Paying Agent.* (a) If the Company shall appoint a Paying Agent other than the Trustee, the Company will cause such Paying Agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section 4.04:

(i) that it will hold all sums held by it as such agent for the payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and accrued and unpaid interest on, the Notes in trust for the benefit of the Holders of the Notes;

(ii) that it will give the Trustee prompt written notice of any failure by the Company to make any payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and accrued and unpaid interest on, the Notes when the same shall be due and payable; and

(iii) that at any time during the continuance of an Event of Default, upon request of the Trustee, it will forthwith pay to the Trustee all sums so held in trust;

provided, that a Paying Agent appointed as contemplated under Section 15.02(f) shall not be required to deliver any such instrument.

The Company shall, on or before each due date of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, or accrued and unpaid interest on, the Notes, deposit with the Paying Agent a sum sufficient to pay such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) or accrued and unpaid interest, and (unless such Paying Agent is the Trustee) the Company will promptly notify the Trustee in writing of any failure to take such action; *provided* that if such deposit is made on the due date, such deposit must be received by the Paying Agent by 11:00 a.m., New York City time, on such date.

(b) If the Company shall act as its own Paying Agent, it will, on or before each due date of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, and accrued and unpaid interest on, the Notes, set aside, segregate and hold in trust for the benefit of the Holders of the Notes a sum sufficient to pay such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) and accrued and unpaid interest so becoming due and will promptly notify the Trustee in writing of any failure to take such action and of any failure by the Company to make any payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, or accrued and unpaid interest on, the Notes when the same shall become due and payable.

(c) Anything in this Section 4.04 to the contrary notwithstanding, the Company may, at any time, for the purpose of obtaining a satisfaction and discharge of this Indenture, or for any other reason, pay, cause to be paid or deliver to the Trustee all sums or amounts held in trust by the Company or any Paying Agent hereunder as required by this Section 4.04, such sums or amounts to be held by the Trustee upon the trusts herein contained and upon such payment or delivery by the Company or any Paying Agent to the Trustee, the Company or such Paying Agent shall be released from all further liability but only with respect to such sums or amounts.

(d) Subject to applicable law, any money deposited with the Trustee, the Conversion Agent or any Paying Agent, or any money and shares of Common Stock then held by the Company, in trust for the payment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, accrued and unpaid interest on and the consideration due upon conversion of any Note and remaining unclaimed for two years after such principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable), interest or consideration due upon conversion has become due and payable shall be paid to the Company on request of the Company contained in an Officer's Certificate, or (if then held by the Company) shall be discharged from such trust; and the Holder of such Note shall thereafter, as an unsecured general creditor, look only to the Company for payment thereof, and all liability of the Trustee, the Conversion Agent or such Paying Agent with respect to such trust money, and all liability of the Company as trustee with respect to such trust money and shares of Common Stock, shall thereupon cease; *provided*, *however*, that the Trustee, Conversion Agent or such Paying Agent, before being required to make any such repayment, may at the expense of the Company cause to be published once, in a newspaper published in the English language, customarily published on each Business Day and of general circulation in The Borough of Manhattan, The City of New York, notice that such money and shares of Common Stock remain unclaimed and that, after a date specified therein, which shall not be less than 30 days from the date of such publication, any unclaimed balance of such money and shares of Common Stock then remaining will be repaid or delivered to the Company.

Section 4.05. *Existence.* Subject to Article 11, the Company shall do or cause to be done all things necessary to preserve and keep in full force and effect its corporate existence.

Section 4.06. *Rule 144A Information Requirement and Annual Reports.* (a) At any time the Company is not subject to Section 13 or 15(d) of the Exchange Act, the Company shall, so long as any of the Notes or any shares of Common Stock issuable upon conversion thereof shall, at such time, constitute "restricted securities" within the meaning of Rule 144(a)(3) under the Securities Act, promptly provide to the Trustee and, upon written request, any Holder, beneficial owner or prospective purchaser of such Notes or any shares of Common Stock issuable upon conversion of such Notes, the information required to be delivered pursuant to Rule 144A(d)(4) under the Securities Act to facilitate the resale of such Notes or shares of Common Stock pursuant to Rule 144A.

(b) The Company shall file with the Trustee, within 15 days after the same are required to be filed with the Commission, copies of any documents or reports that the Company is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act (giving effect to any grace period provided by Rule 12b-25 under the Exchange Act). Notwithstanding the foregoing, the Company shall in no event be required to file with, or otherwise provide or disclose to, the Trustee or any Holder any information for which the Company is requesting (assuming such request has not been denied), or has received, confidential treatment from the Commission, or any correspondence with the Commission. Any such document or report that the Company files with the Commission via the Commission's EDGAR system (or any successor thereto) shall be deemed to be filed with the Trustee for purposes of this Section 4.06(b) at the time such documents are filed via the EDGAR system (or any successor thereto); provided that the Trustee shall have no obligation to determine whether such documents or reports have been filed via the EDGAR system.

(c) Delivery of the reports and documents described in subsection (a) and (b) above to the Trustee is for informational purposes only, and the Trustee's receipt of such shall not constitute constructive or actual notice of any information contained therein or determinable from information contained therein, including the Company's compliance with any of its covenants hereunder (as to which the Trustee is entitled to conclusively rely on an Officer's Certificate).

(d) If, at any time during the six-month period beginning on, and including, the date that is six months after the last date of original issuance of the Notes, the Company fails to timely file any document or report that it is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act, as applicable (after giving effect to all applicable grace periods thereunder and other than reports on Form 8-K), or the Notes are not otherwise freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates or Holders that were the Company's Affiliates at any time during the three months immediately preceding (as a result of restrictions pursuant to U.S. securities laws or the terms of this Indenture or the Notes), the Company shall pay Additional Interest on the Notes. Such Additional Interest shall accrue on the Notes at the rate of (i) 0.25% per annum of the principal amount of the Notes outstanding for each day during the first 90 calendar days of such period for which the Company's failure to file has occurred and is continuing or the Notes are not otherwise freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates (or Holders that were the Company's Affiliates at any time during the three months immediately preceding) and (ii) 0.50% per annum of the principal amount of the Notes outstanding for each day after the 90th day of such period for which the Company's failure to file has occurred and is continuing or the Notes are not otherwise freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates (or Holders that were the Company's Affiliates at any time during the three months immediately preceding). As used in this Section 4.06(d), documents or reports that the Company is required to "file" with the Commission pursuant to Section 13 or 15(d) of the Exchange Act does not include documents or reports that the Company furnishes to the Commission pursuant to Section 13 or 15(d) of the Exchange Act. For purposes of this Section 4.06(d), "as a result of restrictions

pursuant to U.S. securities laws or the terms of this Indenture or the Notes" shall not include, for the avoidance of doubt, the assignment of a restricted CUSIP number or the existence of a Restrictive Legend on the Notes in compliance with the Indenture, in either case, during the six-month period described in this Section 4.06(d).

(e) If, and for so long as, the Restrictive Legend on the Notes specified in Section 2.05(c) has not been removed, the Notes are assigned a restricted CUSIP number or the Notes are not otherwise freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates or Holders that were the Company's Affiliates at any time during the three months immediately preceding (without restrictions pursuant to U.S. securities laws or the terms of this Indenture or the Notes) as of the 380th day after the last date of original issuance of the Notes (the "**Legend Removal Deadline Date**"), the Company shall pay Additional Interest on the Notes at a rate equal to (i) 0.25% per annum of the principal amount of Notes outstanding for each day during the period beginning on, and including, the Legend Removal Deadline Date and ending on the earlier of (x) the 90th day immediately following the Legend Removal Deadline Date and (y) the date on which the Restrictive Legend on the Notes has been removed in accordance with Section 2.05(c), the Notes are assigned an unrestricted CUSIP number and the Notes are freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates (or Holders that were the Company's Affiliates at any time during the three months immediately preceding) without restrictions pursuant to U.S. securities laws or the terms of this Indenture or the Notes and (ii) 0.50% per annum of the principal amount of Notes outstanding for each day during the period beginning on, and including, the 91st day immediately following the Legend Removal Deadline Date and ending on the date on which the Restrictive Legend on the Notes has been removed in accordance with Section 2.05(c), the Notes are assigned an unrestricted CUSIP number and the Notes are freely tradable pursuant to Rule 144 by Holders other than the Company's Affiliates (or Holders that were the Company's Affiliates at any time during the three months immediately preceding) without restrictions pursuant to U.S. securities laws or the terms of this Indenture or the Notes. The Restrictive Legend on the Notes shall be deemed removed pursuant to the terms of this Indenture as provided in Section 2.05(c), and, at such time, the Notes will, pursuant to, and subject to the provisions of, such Section, be deemed assigned an unrestricted CUSIP number. However, for the avoidance of doubt, Global Notes will continue to bear Additional Interest pursuant to this paragraph until such time as they are identified by an unrestricted CUSIP number in the facilities of the Depositary therefor, as a result of completion of such Depositary's mandatory exchange process or otherwise.

(f) Additional Interest will be payable in arrears on each Interest Payment Date following accrual in the same manner as regular interest on the Notes.

(g) The Additional Interest that is payable in accordance with Section 4.06(d) or Section 4.06(e) shall be in addition to, and not in lieu of, any Additional Interest that may be payable as a result of the Company's election pursuant to Section 6.03. However, in no event shall any Additional Interest that may accrue as a result of the Company's failure to timely file any document or report that it is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act, as applicable, after

giving effect to all applicable grace periods thereunder and other than reports on Form 8-K, as described in Section 4.06(d), together with any Additional Interest payable at the Company's election as the remedy for an Event of Default relating to the Company's failure to comply with its obligations as set forth Section 4.06(b), accrue at a rate in excess of 0.50% per annum pursuant to this Indenture, regardless of the number of events or circumstances giving rise to the requirement to pay such Additional Interest.

(h) If Additional Interest is payable by the Company pursuant to Section 4.06(d) or Section 4.06(e), the Company shall deliver to the Trustee an Officer's Certificate to that effect stating (i) the amount of such Additional Interest that is payable and (ii) the date on which such Additional Interest is payable. Unless and until a Responsible Officer of the Trustee receives at the Corporate Trust Office such a certificate, the Trustee may assume without inquiry that no such Additional Interest is payable.

Section 4.07. *Stay, Extension and Usury Laws.* The Company covenants (to the extent that it may lawfully do so) that it shall not at any time insist upon, plead, or in any manner whatsoever claim or take the benefit or advantage of, any stay, extension or usury law or other law that would prohibit or forgive the Company from paying all or any portion of the principal of or interest on the Notes as contemplated herein, wherever enacted, now or at any time hereafter in force, or that may affect the covenants or the performance of this Indenture; and the Company (to the extent it may lawfully do so) hereby expressly waives all benefit or advantage of any such law, and covenants that it will not, by resort to any such law, hinder, delay or impede the execution of any power herein granted to the Trustee, but will suffer and permit the execution of every such power as though no such law had been enacted.

Section 4.08. *Compliance Certificate; Statements as to Defaults.* The Company shall deliver to the Trustee within 120 days after the end of each fiscal year of the Company (beginning with the fiscal year ending on December 31, 2022) an Officer's Certificate stating whether the signers thereof have knowledge of any failure by the Company to comply with all conditions and covenants then required to be performed under this Indenture and, if so, specifying each such failure and the nature thereof.

In addition, the Company shall deliver to the Trustee within 30 days after an officer of the Company becomes aware of the occurrence of any Event of Default or Default, an Officer's Certificate setting forth the details of such Event of Default or Default, its status and the action that the Company is taking or proposing to take in respect thereof; *provided* that the Company is not required to deliver such notice if such Event of Default or Default has been cured.

Section 4.09. *Further Instruments and Acts.* Upon request of the Trustee, Paying Agent or Conversion Agent, the Company will execute and deliver such further instruments and do such further acts as may be reasonably necessary or proper to carry out more effectively the purposes of this Indenture.

ARTICLE 5
LISTS OF HOLDERS AND REPORTS BY THE COMPANY AND THE TRUSTEE

Section 5.01. *Lists of Holders.* The Company covenants and agrees that it will furnish or cause to be furnished to the Trustee, semi-annually, no later than March 1 and September 1 in each year beginning with March 1, 2023, and at such other times as the Trustee may request in writing, within 15 days after receipt by the Company of any such request (or such lesser time as the Trustee may reasonably request in order to enable it to timely provide any notice to be provided by it hereunder), a list in such form as the Trustee may reasonably require of the names and addresses of the Holders as of a date not more than 15 days (or such other date as the Trustee may reasonably request in order to so provide any such notices) prior to the time such information is furnished, except that no such list need be furnished so long as the Trustee is acting as Note Registrar.

Section 5.02. *Preservation and Disclosure of Lists.* The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the Holders contained in the most recent list furnished to it as provided in Section 5.01 or maintained by the Trustee in its capacity as Note Registrar, if so acting. The Trustee may destroy any list furnished to it as provided in Section 5.01 upon receipt of a new list so furnished.

ARTICLE 6
DEFAULTS AND REMEDIES

Section 6.01. *Events of Default.* Each of the following events shall be an "**Event of Default**" with respect to the Notes:

(a) default in any payment of interest on any Note when due and payable, and the default continues for a period of 30 days;

(b) default in the payment of principal of any Note when due and payable on the Maturity Date, upon Optional Redemption, upon any required repurchase, upon declaration of acceleration or otherwise;

(c) failure by the Company to comply with its obligation to convert the Notes in accordance with this Indenture upon exercise of a Holder's conversion right, and such failure continues for three Business Days;

(d) failure by the Company to issue (i) a Fundamental Change Company Notice in accordance with Section 15.02(c) or notice of a Make-Whole Fundamental Change in accordance with Section 14.03, in either case when due, and such failure continues for five Business Days, (ii) notice of a specified corporate event in accordance with Section 14.01(b)(iv) when due, and such failure continues for two Business Days or (iii) notice of a specified corporate event in accordance with Section 14.01(b)(iii) when due;

(e) failure by the Company to comply with its obligations under Article 11;

(f) failure by the Company for 60 days after written notice from the Trustee or the Holders of at least 25% in principal amount of the Notes then outstanding has been received by the Company to comply with any of its other agreements contained in the Notes or this Indenture;

(g) default by the Company or any Significant Subsidiary of the Company with respect to any mortgage, agreement or other instrument under which there may be outstanding, or by which there may be secured or evidenced, any indebtedness for money borrowed in excess of $100,000,000 (or its foreign currency equivalent) in the aggregate of the Company and/or any such Significant Subsidiary, whether such indebtedness now exists or shall hereafter be created (i) resulting in such indebtedness becoming or being declared due and payable prior to its stated maturity or (ii) constituting a failure to pay the principal of any such debt when due and payable at its stated maturity, upon required repurchase, upon declaration of acceleration or otherwise, in each case, after the expiration of any applicable grace period, in each case of the events described in clause (i) or (ii) of this Section 6.01(g), as applicable, if such acceleration shall not have been rescinded or annulled or such failure to pay or default shall not have been cured or waived, or such indebtedness shall not have been paid or discharged, as the case may be, within 30 days after written notice to the Company by the Trustee or to the Company and the Trustee by Holders of at least 25% in aggregate principal amount of Notes then outstanding in accordance with this Indenture;

(h) the Company or any Significant Subsidiary shall commence a voluntary case or other proceeding seeking liquidation, reorganization or other relief with respect to the Company or any such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of the Company or any such Significant Subsidiary or any substantial part of its property, or shall consent to any such relief or to the appointment of or taking possession by any such official in an involuntary case or other proceeding commenced against it, or shall make a general assignment for the benefit of creditors, or shall publicly admit in writing that it generally is not paying, or is unable to pay, its debts as they become due; or

(i) an involuntary case or other proceeding shall be commenced against the Company or any Significant Subsidiary seeking liquidation, reorganization or other relief with respect to the Company or such Significant Subsidiary or its debts under any bankruptcy, insolvency or other similar law now or hereafter in effect or seeking the appointment of a trustee, receiver, liquidator, custodian or other similar official of the Company or such Significant Subsidiary or any substantial part of its property, and such involuntary case or other proceeding shall remain undismissed and unstayed for a period of 60 consecutive days.

Section 6.02. *Acceleration; Rescission and Annulment*. If one or more Events of Default shall have occurred and be continuing (whatever the reason for such Event of Default and whether it shall be voluntary or involuntary or be effected by operation of law or pursuant to any judgment, decree or order of any court or any order, rule or regulation of any administrative or governmental body), then, and in each and every such case (other than an Event of Default specified in Section 6.01(h) or Section 6.01(i) with respect to the Company), unless the principal of all of the Notes shall have already become due and payable, either the Trustee or the Holders of at least 25% in aggregate principal amount of the Notes then outstanding determined in accordance with Section 8.04, by notice in writing to the Company (and to the Trustee if given by Holders), may

declare 100% of the principal of, and accrued and unpaid interest on, all the Notes to be due and payable immediately, and upon any such declaration the same shall become and shall automatically be immediately due and payable, anything contained in this Indenture or in the Notes to the contrary notwithstanding. If an Event of Default specified in Section 6.01(h) or Section 6.01(i) with respect to the Company occurs and is continuing, 100% of the principal of, and accrued and unpaid interest, if any, on, all Notes shall become and shall automatically be immediately due and payable.

The immediately preceding paragraph, however, is subject to the conditions that if, at any time after the principal of the Notes shall have been so declared due and payable, and before any judgment or decree for the payment of the monies due shall have been obtained or entered as hereinafter provided, the Company shall pay or shall deposit with the Trustee a sum sufficient to pay installments of accrued and unpaid interest upon all Notes and the principal of any and all Notes that shall have become due otherwise than by acceleration (with interest on overdue installments of accrued and unpaid interest to the extent that payment of such interest is enforceable under applicable law, and on such principal at the rate borne by the Notes at such time) and amounts due to the Trustee pursuant to Section 7.06, and if (1) rescission would not conflict with any judgment or decree of a court of competent jurisdiction and (2) any and all existing Events of Default under this Indenture, other than any continuing Events of Default relating to the nonpayment of the principal of and accrued and unpaid interest, if any, on Notes that shall have become due solely by such acceleration, shall have been cured or waived pursuant to Section 6.09, then and in every such case (except as provided in the immediately succeeding sentence) the Holders of a majority in aggregate principal amount of the Notes then outstanding, by written notice to the Company and to the Trustee, may waive all Defaults or Events of Default with respect to the Notes and rescind and annul such declaration and its consequences and such Default shall cease to exist, and any Event of Default arising therefrom shall be deemed to have been cured for every purpose of this Indenture; but no such waiver or rescission and annulment shall extend to or shall affect any subsequent Default or Event of Default, or shall impair any right consequent thereon. Notwithstanding anything to the contrary herein, no such waiver or rescission and annulment shall extend to or shall affect any Default or Event of Default resulting from (i) the nonpayment of the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, or accrued and unpaid interest on, any Notes, (ii) a failure to repurchase any Notes when required or (iii) a failure to pay or deliver, as the case may be, the consideration due upon conversion of the Notes.

Section 6.03. *Additional Interest*. Notwithstanding anything in this Indenture or in the Notes to the contrary, to the extent the Company elects, the sole remedy for an Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 4.06(b) shall after the occurrence of such an Event of Default consist exclusively of the right to receive Additional Interest on the Notes at a rate equal to: (i) 0.25% per annum of the principal amount of the Notes outstanding for each day during the period beginning on, and including, the date on which such Event of Default first occurs and ending on the earlier of (x) the date on which such Event of Default is cured

or validly waived in accordance with this Article 6 and (y) the 180th day immediately following, and including, the date on which such Event of Default first occurs and (ii) if such Event of Default has not been cured or validly waived prior to the 181st day immediately following, and including, the date on which such Event of Default first occurs, 0.50% per annum of the principal amount of Notes outstanding for each day during the period beginning on, and including, the 181st day immediately following, and including, the date on which such Event of Default first occurs and ending on the earlier of (x) the date on which the Event of Default is cured or validly waived in accordance with this Article 6 and (y) the 365th day immediately following, and including, the date on which such Event of Default first occurs. Additional Interest payable pursuant to this Section 6.03 shall be in addition to, not in lieu of, any Additional Interest payable pursuant to Section 4.06(d) or Section 4.06(e), subject to the second immediately succeeding paragraph. If the Company so elects, such Additional Interest shall be payable in the same manner and on the same dates as the stated interest payable on the Notes and shall accrue on all outstanding Notes from, and including, the date on which the Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 4.06(b) first occurs to, and including, the 365th day thereafter (or such earlier date on which such Event of Default is cured or validly waived in accordance with this Article 6). On the 366th day after such Event of Default (if the Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 4.06(b) is not cured or validly waived in accordance with this Article 6 prior to such 366th day), such Additional Interest shall cease to accrue and the Notes shall be immediately subject to acceleration as provided in Section 6.02. The provisions of this paragraph will not affect the rights of Holders of Notes in the event of the occurrence of any Event of Default other than the Company's failure to comply with its obligations as set forth in Section 4.06(b). In the event the Company does not elect to pay Additional Interest following an Event of Default in accordance with this Section 6.03 or the Company has elected to make such payment but does not pay the Additional Interest when due, the Notes shall be immediately subject to acceleration as provided in Section 6.02.

In order to elect to pay Additional Interest as the sole remedy during the first 365 days after the occurrence of any Event of Default described in the immediately preceding paragraph, the Company must notify all Holders of the Notes, the Trustee and the Paying Agent in an Officer's Certificate (consistent with Section 4.06(h)) of such election on or before the open of business on the date on which such Event of Default first occurs. Upon the failure to timely give such notice, the Notes shall be immediately subject to acceleration as provided in Section 6.02.

In no event shall Additional Interest payable at the Company's election as the remedy for an Event of Default relating to the Company's failure to comply with its obligations as set forth in Section 4.06(b), together with any Additional Interest that may accrue as a result of the Company's failure to timely file any document or report that it is required to file with the Commission pursuant to Section 13 or 15(d) of the Exchange Act, as applicable, after giving effect to all applicable grace periods thereunder and other than reports on Form 8-K, pursuant to Section 4.06(d), accrue at a rate in excess of 0.50%

per annum pursuant to this Indenture, regardless of the number of events or circumstances giving rise to the requirement to pay such Additional Interest.

The Company shall send written notice to the Holder of each Note and the Trustee of the commencement and termination of any period on which Additional Interest accrues on such Note under any provision of this Indenture.

Section 6.04. *Payments of Notes on Default; Suit Therefor.* If an Event of Default described in clause (a) or (b) of Section 6.01 shall have occurred, the Company shall, upon demand of the Trustee, pay to the Trustee, for the benefit of the Holders of the Notes, the whole amount then due and payable on the Notes for principal and interest, if any, with interest on any overdue principal and interest, if any, at the rate borne by the Notes at such time, and, in addition thereto, such further amount as shall be sufficient to cover any amounts due to the Trustee under Section 7.06. If the Company shall fail to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, may institute a judicial proceeding for the collection of the sums so due and unpaid, may prosecute such proceeding to judgment or final decree and may enforce the same against the Company or any other obligor upon the Notes and collect the moneys adjudged or decreed to be payable in the manner provided by law out of the property of the Company or any other obligor upon the Notes, wherever situated.

In the event there shall be pending proceedings for the bankruptcy or for the reorganization of the Company or any other obligor on the Notes under Title 11 of the United States Code, or any other applicable law, or in case a receiver, assignee or trustee in bankruptcy or reorganization, liquidator, sequestrator or similar official shall have been appointed for or taken possession of the Company, the property of the Company, or in the event of any other judicial proceedings relative to the Company, or to the creditors or property of the Company, the Trustee, irrespective of whether the principal of the Notes shall then be due and payable as therein expressed or by declaration or otherwise and irrespective of whether the Trustee shall have made any demand pursuant to the provisions of this Section 6.04, shall be entitled and empowered, by intervention in such proceedings or otherwise, to file and prove a claim or claims for the whole amount of principal and accrued and unpaid interest, if any, in respect of the Notes, and, in case of any judicial proceedings, to file such proofs of claim and other papers or documents and to take such other actions as it may deem necessary or advisable in order to have the claims of the Trustee (including any claim for the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel) and of the Holders allowed in such judicial proceedings relative to the Company, its creditors, or its property, and to collect and receive any monies or other property payable or deliverable on any such claims, and to distribute the same after the deduction of any amounts due to the Trustee under Section 7.06; and any receiver, assignee or trustee in bankruptcy or reorganization, liquidator, custodian or similar official is hereby authorized by each of the Holders to make such payments to the Trustee, as administrative expenses, and, in the event that the Trustee shall consent to the making of such payments directly to the Holders, to pay to the Trustee any amount due it for reasonable compensation, expenses, advances and disbursements, including agents and counsel fees, and including any other amounts due to the Trustee under Section 7.06, incurred by it up to the date of such

distribution. To the extent that such payment of reasonable compensation, expenses, advances and disbursements out of the estate in any such proceedings shall be denied for any reason, payment of the same shall be secured by a lien on, and shall be paid out of, any and all distributions, dividends, monies, securities and other property that the Holders of the Notes may be entitled to receive in such proceedings, whether in liquidation or under any plan of reorganization or arrangement or otherwise.

Nothing herein contained shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Holder any plan of reorganization, arrangement, adjustment or composition affecting such Holder or the rights of any Holder thereof, or to authorize the Trustee to vote in respect of the claim of any Holder in any such proceeding.

All rights of action and of asserting claims under this Indenture, or under any of the Notes, may be enforced by the Trustee without the possession of any of the Notes, or the production thereof at any trial or other proceeding relative thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for the payment of the reasonable compensation, expenses, disbursements and advances of the Trustee, its agents and counsel, be for the ratable benefit of the Holders of the Notes.

In any proceedings brought by the Trustee (and in any proceedings involving the interpretation of any provision of this Indenture to which the Trustee shall be a party) the Trustee shall be held to represent all the Holders of the Notes, and it shall not be necessary to make any Holders of the Notes parties to any such proceedings.

In case the Trustee shall have proceeded to enforce any right under this Indenture and such proceedings shall have been discontinued or abandoned because of any waiver pursuant to Section 6.09 or any rescission and annulment pursuant to Section 6.02 or for any other reason or shall have been determined adversely to the Trustee, then and in every such case the Company, the Holders and the Trustee shall, subject to any determination in such proceeding, be restored respectively to their several positions and rights hereunder, and all rights, remedies and powers of the Company, the Holders and the Trustee shall continue as though no such proceeding had been instituted.

Section 6.05. *Application of Monies Collected by Trustee.* Any monies or property collected by the Trustee pursuant to this Article 6 with respect to the Notes shall be applied in the following order, at the date or dates fixed by the Trustee for the distribution of such monies or property, upon presentation of the several Notes, and stamping thereon the payment, if only partially paid, and upon surrender thereof, if fully paid:

First, to the payment of all amounts due the Trustee, including its agents and counsel, under Section 7.06;

Second, in case the principal of the outstanding Notes shall not have become due and be unpaid, to the payment of interest on, and any cash due upon conversion of, the Notes in default in the order of the date due of the payments of such interest and cash due upon conversion, as the case may be, with interest (to the extent that such interest has

been collected by the Trustee) upon such overdue payments at the rate borne by the Notes at such time, such payments to be made ratably to the Persons entitled thereto;

Third, in case the principal of the outstanding Notes shall have become due, by declaration or otherwise, and be unpaid to the payment of the whole amount (including, if applicable, the payment of the Redemption Price, the Fundamental Change Repurchase Price and any cash due upon conversion) then owing and unpaid upon the Notes for principal and interest, if any, with interest on the overdue principal and, to the extent that such interest has been collected by the Trustee, upon overdue installments of interest at the rate borne by the Notes at such time, and in case such monies shall be insufficient to pay in full the whole amounts so due and unpaid upon the Notes, then to the payment of such principal (including, if applicable, the Redemption Price, the Fundamental Change Repurchase Price and any cash due upon conversion) and interest without preference or priority of principal over interest, or of interest over principal or of any installment of interest over any other installment of interest, or of any Note over any other Note, ratably to the aggregate of such principal (including, if applicable, the Redemption Price, the Fundamental Change Repurchase Price and any cash due upon conversion) and accrued and unpaid interest; and

Fourth, to the payment of the remainder, if any, to the Company.

Section 6.06. *Proceedings by Holders.* Except to enforce the right to receive payment of principal (including, if applicable, the Redemption Price and the Fundamental Change Repurchase Price) or interest when due, or the right to receive payment or delivery of the consideration due upon conversion, no Holder of any Note shall have any right by virtue of or by availing of any provision of this Indenture to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture, or for the appointment of a receiver, trustee, liquidator, custodian or other similar official, or for any other remedy hereunder, unless:

(a) such Holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof, as herein provided;

(b) Holders of at least 25% in aggregate principal amount of the Notes then outstanding shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as Trustee hereunder;

(c) such Holders shall have offered and, if requested, provided to the Trustee such security or indemnity satisfactory to Trustee in its reasonable judgment against any loss, liability or expense to be incurred therein or thereby;

(d) the Trustee for 60 days after its receipt of such notice, request and offer of such security or indemnity, shall have neglected or refused to institute any such action, suit or proceeding; and

(e) no direction that, in the opinion of the Trustee, is inconsistent with such written request shall have been given to the Trustee by the Holders of a majority of the

aggregate principal amount of the Notes then outstanding within such 60-day period pursuant to Section 6.09,

it being understood and intended, and being expressly covenanted by the taker and Holder of every Note with every other taker and Holder and the Trustee that no one or more Holders shall have any right in any manner whatever by virtue of or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of any other Holder, or to obtain or seek to obtain priority over or preference to any other such Holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all Holders (except as otherwise provided herein). For the protection and enforcement of this Section 6.06, each and every Holder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Notwithstanding any other provision of this Indenture and any provision of any Note, each Holder shall have the contractual right to receive payment or delivery, as the case may be, of (x) the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, (y) accrued and unpaid interest, if any, on, and (z) the consideration due upon conversion of, such Note, on or after the respective due dates expressed or provided for in such Note or in this Indenture, and the contractual right to institute suit for the enforcement of any such payment or delivery, as the case may be, on or after such respective dates, shall not be amended without the consent of each Holder.

Section 6.07. *Proceedings by Trustee.* In case of an Event of Default, the Trustee may in its discretion proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as are necessary to protect and enforce any of such rights, either by suit in equity or by action at law or by proceeding in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in this Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law. The Trustee may maintain a proceeding even if it does not possess the Notes or does not produce the Notes in the proceeding.

Section 6.08. *Remedies Cumulative and Continuing.* Except as provided in the last paragraph of Section 2.06, all powers and remedies given by this Article 6 to the Trustee or to the Holders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any thereof or of any other powers and remedies available to the Trustee or the Holders of the Notes, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture, and no delay or omission of the Trustee or of any Holder of any of the Notes to exercise any right or power accruing upon any Default or Event of Default shall impair any such right or power, or shall be construed to be a waiver of any such Default or Event of Default or any acquiescence therein; and, subject to the provisions of Section 6.06, every power and remedy given by this Article 6 or by law to the Trustee or to the Holders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Holders.

Section 6.09. *Direction of Proceedings and Waiver of Defaults by Majority of Holders.* The Holders of a majority of the aggregate principal amount of the Notes at the time outstanding determined in accordance with Section 8.04 shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee or exercising any trust or power conferred on the Trustee with respect to the Notes; *provided*, *however*, that (a) such direction shall not be in conflict with any rule of law or with this Indenture, and (b) the Trustee may take any other action deemed proper by the Trustee that is not inconsistent with such direction. The Trustee may refuse to follow any direction that it determines is unduly prejudicial to the rights of any other Holder or that would involve the Trustee in personal liability (it being understood that the Trustee does not have an affirmative duty to determine whether any direction is prejudicial to any Holder) or for which it has not received indemnity or security satisfactory to the Trustee in its reasonable judgement against any loss, liability or expense. The Holders of a majority in aggregate principal amount of the Notes at the time outstanding determined in accordance with Section 8.04 may on behalf of the Holders of all of the Notes (x) waive any past Default or Event of Default hereunder and its consequences except (i) a default in the payment of accrued and unpaid interest, if any, on, or the principal (including any Redemption Price and any Fundamental Change Repurchase Price) of, the Notes when due that has not been cured pursuant to the provisions of Section 6.01, (ii) a failure by the Company to pay or deliver, as the case may be, the consideration due upon conversion of the Notes or (iii) a default in respect of a covenant or provision hereof which under Article 10 cannot be modified or amended without the consent of each Holder of an outstanding Note affected; and (y) rescind any resulting acceleration of the Notes and its consequences if (i) such rescission would not conflict with any judgment or decree of a court of competent jurisdiction and (ii) all existing Events of Default (other than nonpayment of the principal of, and interest on, the Notes that have become due solely by such acceleration) have been cured or waived. Upon any such waiver the Company, the Trustee and the Holders of the Notes shall be restored to their former positions and rights hereunder; but no such waiver shall extend to any subsequent or other Default or Event of Default or impair any right consequent thereon. Whenever any Default or Event of Default hereunder shall have been waived as permitted by this Section 6.09, said Default or Event of Default shall for all purposes of the Notes and this Indenture be deemed to have been cured and to be not continuing; but no such waiver shall extend to any subsequent or other Default or Event of Default or impair any right consequent thereon.

Section 6.10. *Notice of Defaults.* The Trustee shall, after the occurrence and continuance of a Default of which a Responsible Officer has actual knowledge, deliver to all Holders notice of such Default within 90 days after such Responsible Officer obtains such knowledge, unless such Defaults shall have been cured or waived before the giving of such notice; *provided* that, except in the case of a Default in the payment of the principal of (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable), or accrued and unpaid interest on, any of the Notes or a Default in the payment or delivery of the consideration due upon conversion, the Trustee shall be protected in withholding such notice if and so long as a Responsible Officer of the

Trustee in good faith determines that the withholding of such notice is in the interests of the Holders.

Section 6.11. *Undertaking to Pay Costs.* All parties to this Indenture agree, and each Holder of any Note by its acceptance thereof shall be deemed to have agreed, that any court may, in its discretion, require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees and expenses, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; *provided* that the provisions of this Section 6.11 (to the extent permitted by law) shall not apply to any suit instituted by the Trustee, to any suit instituted by any Holder, or group of Holders, holding in the aggregate more than 10% in principal amount of the Notes at the time outstanding determined in accordance with Section 8.04, or to any suit instituted by any Holder for the enforcement of the payment of the principal of or accrued and unpaid interest, if any, on any Note (including, but not limited to, the Redemption Price and the Fundamental Change Repurchase Price, if applicable) on or after the due date expressed or provided for in such Note or to any suit for the enforcement of the right to convert any Note, or receive the consideration due upon conversion, in accordance with the provisions of Article 14.

ARTICLE 7
CONCERNING THE TRUSTEE

Section 7.01. *Duties and Responsibilities of Trustee.* The Trustee, prior to the occurrence of an Event of Default of which a Responsible Officer of the Trustee has actual knowledge and after the curing or waiver of all Events of Default that may have occurred, undertakes to perform such duties and only such duties as are specifically set forth in this Indenture. If an Event of Default has occurred and is continuing, the Trustee shall exercise such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in its exercise, as a prudent person would exercise or use under the circumstances in the conduct of such person's own affairs under the same circumstances; *provided* that the Trustee will be under no obligation to exercise any of the rights or powers under this Indenture at the request or direction of any of the Holders unless such Holders have offered to the Trustee indemnity or security satisfactory to Trustee in its reasonable judgment against any loss, liability or expense that might be incurred by it in compliance with such request or direction.

No provision of this Indenture shall be construed to relieve the Trustee from liability for its own grossly negligent action, its own grossly negligent failure to act or its own willful misconduct, except that:

(a) prior to the occurrence of an Event of Default and after the curing or waiving of all Events of Default that may have occurred:

(i) the duties and obligations of the Trustee shall be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable

except for the performance of such duties and obligations as are specifically set forth in this Indenture and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(ii) in the absence of gross negligence or willful misconduct on the part of the Trustee, the Trustee may conclusively rely, without investigation, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture, but need not verify the contents thereof; however, in the case of any such certificates or opinions that by any provisions hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine whether or not they conform on their face to the requirements of this Indenture (but need not confirm or investigate the accuracy of any mathematical calculations or other facts stated therein);

(b) the Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer or Officers of the Trustee, unless it shall be proved that the Trustee was grossly negligent in ascertaining the pertinent facts;

(c) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the direction of the Holders of not less than a majority of the aggregate principal amount of the Notes at the time outstanding determined as provided in Section 8.04 relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee, under this Indenture;

(d) whether or not therein provided, every provision of this Indenture relating to the conduct or affecting the liability of, or affording protection to, the Trustee shall be subject to the provisions of this Section;

(e) the Trustee shall not be liable in respect of any payment (as to the correctness of amount, entitlement to receive or any other matters relating to payment) or notice effected by the Company or any Paying Agent or any records maintained by any co-Note Registrar with respect to the Notes;

(f) if any party fails to deliver a notice relating to an event the fact of which, pursuant to this Indenture, requires notice to be sent to the Trustee, the Trustee may conclusively rely on its failure to receive such notice as reason to act as if no such event occurred;

(g) in the absence of written investment direction from the Company, all cash received by the Trustee shall be placed in a non-interest bearing trust account, and in no event shall the Trustee be liable for the selection of investments or for investment losses incurred thereon or for losses incurred as a result of the liquidation of any such investment prior to its maturity date or the failure of the party directing such investments prior to its maturity date or the failure of the party directing such investment to provide timely written investment direction, and the Trustee shall have no obligation to invest or

reinvest any amounts held hereunder in the absence of such written investment direction from the Company; and

(h) in the event that the Trustee is also acting as Custodian, Note Registrar, Paying Agent, Conversion Agent or transfer agent hereunder, the rights and protections afforded to the Trustee pursuant to this Article 7 shall also be afforded to such Custodian, Note Registrar, Paying Agent, Conversion Agent or transfer agent.

None of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers.

Section 7.02. *Rights of the Trustee.* Except as otherwise provided in Section 7.01:

(a) The Trustee may conclusively rely and shall be fully protected in acting upon any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, judgment, bond, note, coupon or other paper or document (whether in original or facsimile form) believed by it in good faith to be genuine and to have been signed or presented by the proper party or parties.

(b) Any request, direction, order or demand of the Company mentioned herein shall be sufficiently evidenced by an Officer's Certificate (unless other evidence in respect thereof be herein specifically prescribed); and any Board Resolution may be evidenced to the Trustee by a copy thereof certified by the Secretary or an Assistant Secretary of the Company. Before the Trustee acts or refrains from acting, it may require an Officer's Certificate or an Opinion of Counsel or both. The Trustee shall not be liable for any action it takes or omits to take in good faith in reliance on such Officer's Certificate or Opinion of Counsel.

(c) The Trustee may consult with counsel and require an Opinion of Counsel and any advice of such counsel or Opinion of Counsel shall be full and complete authorization and protection in respect of any action taken or omitted by it hereunder in good faith and in reliance on such advice or Opinion of Counsel.

(d) The Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, direction, consent, order, judgment, bond, debenture or other paper or document, but the Trustee, in its discretion, may make such further inquiry or investigation into such facts or matters as it may see fit, and, if the Trustee shall determine in its reasonable judgment to make such further inquiry or investigation, it shall be entitled, at a reasonable time on any Business Day after reasonable notice, to examine the books, records and premises of the Company, personally or by agent or attorney at the expense of the Company and shall incur no liability of any kind by reason of such inquiry or investigation.

(e) The Trustee may execute any of the trusts or powers hereunder or perform any duties hereunder either directly or by or through agents, custodians, nominees or

attorneys and the Trustee shall not be responsible for any misconduct or negligence on the part of any agent, custodian, nominee or attorney appointed by it with due care hereunder, and the permissive rights of the Trustee enumerated herein shall not be construed as duties.

(f) The Trustee shall not be required to give any bond or surety in respect of the execution of the trusts and powers under this Indenture.

(g) The Trustee may request that the Company deliver an Officer's Certificate setting forth the names of individuals and/or titles of officers authorized at such time to take specified actions pursuant to this Indenture, which Officer's Certificate may be signed by any Person authorized to sign an Officer' Certificate, including any Person specified as so authorized in any such certificate previously delivered and not superseded.

(h) The Trustee shall not be deemed to have notice or knowledge of any Default or Event of Default, unless written notice of any event which is in fact such a Default or Event of Default (and stating the occurrence of a Default or Event of Default) is actually received by the Trustee at the Corporate Trust Office of the Trustee, and such notice references the Notes and this Indenture and states that it is a notice of Default or Event of Default.

(i) Reserved.

(j) Reserved.

(k) Neither the Trustee nor any of its directors, officers, employees, agents or affiliates shall be responsible for nor have any duty to monitor the performance or any action of the Company, or any of their respective directors, members, officers, agents, affiliates or employee, nor shall it have any liability in connection with the malfeasance or nonfeasance by such party. The Trustee shall not be responsible for any inaccuracy in the information obtained from the Company or for any inaccuracy or omission in the records which may result from such information or any failure by the Trustee to perform its duties as set forth herein as a result of any inaccuracy or incompleteness.

(l) In no event shall the Trustee be responsible or liable for punitive, special, indirect, incidental or any consequential loss or damage of any kind whatsoever (including but not limited to lost profits), even if the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action.

(m) Neither the Trustee nor any agent shall have any responsibility or liability for any actions taken or not taken by the Depositary.

Section 7.03. *No Responsibility for Recitals, Etc.* The recitals contained herein and in the Notes (except in the Trustee's certificate of authentication) shall be taken as the statements of the Company, and the Trustee assumes no responsibility for the correctness of the same. The Trustee makes no representations as to the validity or sufficiency of this Indenture or of the Notes or other transaction documents relating to the Notes and this Indenture. The Trustee shall not be accountable for the use or application

by the Company of any Notes or the proceeds of any Notes authenticated and delivered by the Trustee in conformity with the provisions of this Indenture or for any money paid to the Company or upon the Company's direction under any provision of this Indenture.

Section 7.04. *Trustee, Paying Agents, Conversion Agents, Bid Solicitation Agent or Note Registrar May Own Notes.* The Trustee, any Paying Agent, any Conversion Agent, Bid Solicitation Agent or Note Registrar (in each case, if other than an Affiliate of the Company), in its individual or any other capacity, may become the owner or pledgee of Notes with the same rights it would have if it were not the Trustee, Paying Agent, Conversion Agent, Bid Solicitation Agent or Note Registrar.

Section 7.05. *Monies and Shares of Common Stock to Be Held in Trust.* All monies and shares of Common Stock, if any, received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received. Money and shares of Common Stock, if any, held by the Trustee in trust hereunder need not be segregated from other funds except to the extent required by law. The Trustee shall be under no liability for interest on any money received by it hereunder except as may be agreed from time to time by the Company and the Trustee.

Section 7.06. *Compensation and Expenses of Trustee.* The Company covenants and agrees to pay to the Trustee from time to time, and the Trustee shall be entitled to, compensation for all services rendered by it hereunder in any capacity (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust) as mutually agreed to in writing between the Trustee and the Company, and the Company will pay or reimburse the Trustee upon its request for all expenses, disbursements and advances incurred or made by the Trustee in accordance with any of the provisions of this Indenture in any capacity thereunder (including the compensation and the reasonable expenses and disbursements of its agents and counsel and of all Persons not regularly in its employ and including costs in connection with enforcement of its right to indemnity hereunder) except any such expense, disbursement or advance as shall have been caused by its gross negligence or willful misconduct as determined by a final order of a court of competent jurisdiction. The Company also covenants to indemnify the Trustee in any capacity under this Indenture and any other document or transaction entered into in connection herewith and its agents and any authenticating agent for, and to hold them harmless against, any loss, claim, damage, liability or expense (including attorneys' fees) incurred without gross negligence or willful misconduct on the part of the Trustee, its officers, directors or employees, as the case may be, as determined by a final order of a court of competent jurisdiction, and arising out of or in connection with the acceptance or administration of this Indenture or in any other capacity hereunder (whether such claims arise by or against the Company or a third person), including the reasonable costs and expenses of defending themselves against any claim of liability in the premises or enforcing the Company's obligations hereunder, including under this Section 7.06. The obligations of the Company under this Section 7.06 to compensate or indemnify the Trustee and to pay or reimburse the Trustee for expenses, disbursements and advances shall be secured by a senior claim to which the Notes are hereby made subordinate on all money or property held or collected by the Trustee, except, subject to

the effect of Section 6.05, funds held in trust herewith for the benefit of the Holders of particular Notes. The Trustee's right to receive payment of any amounts due under this Section 7.06 shall not be subordinate to any other liability or indebtedness of the Company. The obligation of the Company under this Section 7.06 shall survive the satisfaction and discharge of this Indenture, the payment or conversion of the Notes and the earlier resignation or removal of the Trustee. The Company need not pay for any settlement made without its consent, which consent shall not be unreasonably withheld. The indemnification provided in this Section 7.06 shall extend to the officers, directors, agents and employees of the Trustee.

Without prejudice to any other rights available to the Trustee under applicable law, when the Trustee and its agents and any authenticating agent incur expenses or render services after an Event of Default specified in Section 6.01(h) or Section 6.01(i) occurs, the expenses and the compensation for the services are intended to constitute administrative expenses for the purpose of priority under any bankruptcy, insolvency or similar laws.

Section 7.07. *Officer's Certificate as Evidence.* Except as otherwise provided in Section 7.01, whenever in the administration of the provisions of this Indenture the Trustee shall deem it necessary or desirable that a matter be proved or established prior to taking or omitting any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of gross negligence or willful misconduct on the part of the Trustee, be deemed to be conclusively proved and established by an Officer's Certificate delivered to the Trustee, and such Officer's Certificate, in the absence of gross negligence or willful misconduct on the part of the Trustee, shall be full warrant to the Trustee for any action taken or omitted by it under the provisions of this Indenture upon the faith thereof.

Section 7.08. *Eligibility of Trustee.* There shall at all times be a Trustee hereunder which shall be a Person that is eligible pursuant to the Trust Indenture Act (as if the Trust Indenture Act were applicable hereto) to act as such and has a combined capital and surplus of at least $50,000,000. If such Person publishes reports of condition at least annually, pursuant to law or to the requirements of any supervising or examining authority, then for the purposes of this Section, the combined capital and surplus of such Person shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. If at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section, it shall resign immediately in the manner and with the effect hereinafter specified in this Article.

Section 7.09. *Resignation or Removal of Trustee.* (a) The Trustee may at any time resign by giving written notice of such resignation to the Company. Upon receiving such notice of resignation, the Company shall promptly notify all Holders and appoint a successor trustee by written instrument, in duplicate, executed by order of the Board of Directors, one copy of which instrument shall be delivered to the resigning Trustee and one copy to the successor trustee. If no successor trustee shall have been so appointed and have accepted appointment within 30 days after the giving of such notice of resignation to the Company, the resigning Trustee may, upon ten Business Days' notice

to the Company and the Holders, and at the expense of the Company petition any court of competent jurisdiction for the appointment of a successor trustee, or any Holder who has been a bona fide holder of a Note or Notes for at least six months (or since the date of this Indenture) may, subject to the provisions of Section 6.11, on behalf of himself or herself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(b) In case at any time any of the following shall occur:

(i) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.08 and shall fail to resign after written request therefor by the Company or by any such Holder, or

(ii) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or a receiver of the Trustee or of its property shall be appointed, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation,

then, in either case, the Company may by a Board Resolution remove the Trustee and appoint a successor trustee by written instrument, in duplicate, executed by order of the Board of Directors, one copy of which instrument shall be delivered to the Trustee so removed and one copy to the successor trustee, or, subject to the provisions of Section 6.11, any Holder who has been a bona fide holder of a Note or Notes for at least six months (or since the date of this Indenture) may, on behalf of himself or herself and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon, after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(c) The Holders of a majority in aggregate principal amount of the Notes at the time outstanding, as determined in accordance with Section 8.04, may, at any time upon 30 days' prior written notice, remove the Trustee and nominate a successor trustee that shall be deemed appointed as successor trustee unless within ten days after notice to the Company of such nomination the Company objects thereto, in which case the Trustee so removed or any Holder, upon the terms and conditions and otherwise as in Section 7.09(a) provided, may petition any court of competent jurisdiction for an appointment of a successor trustee.

(d) Any resignation or removal of the Trustee and appointment of a successor trustee pursuant to any of the provisions of this Section 7.09 shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.10.

Section 7.10. *Acceptance by Successor Trustee.* Any successor trustee appointed as provided in Section 7.09 shall execute, acknowledge and deliver to the Company and to its predecessor trustee an instrument accepting such appointment hereunder, and thereupon the resignation or removal of the predecessor trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become

vested with all the rights, powers, duties and obligations of its predecessor hereunder, with like effect as if originally named as Trustee herein; but, nevertheless, on the written request of the Company or of the successor trustee, the trustee ceasing to act shall, upon payment of any amounts then due it pursuant to the provisions of Section 7.06, execute and deliver an instrument transferring to such successor trustee all the rights and powers of the trustee so ceasing to act. Upon request of any such successor trustee, the Company shall execute any and all instruments in writing for more fully and certainly vesting in and confirming to such successor trustee all such rights and powers. Any trustee ceasing to act shall, nevertheless, retain a senior lien to which the Notes are hereby made subordinate on all money or property held or collected by such trustee as such, except for funds held in trust for the benefit of Holders of particular Notes, to secure any amounts then due it pursuant to the provisions of Section 7.06.

No successor trustee shall accept appointment as provided in this Section 7.10 unless at the time of such acceptance such successor trustee shall be eligible under the provisions of Section 7.08.

Upon acceptance of appointment by a successor trustee as provided in this Section 7.10, each of the Company and the successor trustee, at the written direction and at the expense of the Company shall deliver or cause to be delivered notice of the succession of such trustee hereunder to the Holders. If the Company fails to deliver such notice within ten days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be delivered at the expense of the Company.

Section 7.11. *Succession by Merger, Etc.* Any corporation or other entity into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee (including the administration of this Indenture), shall be the successor to the Trustee hereunder without the execution or filing of any paper or any further act on the part of any of the parties hereto; *provided* that in the case of any corporation or other entity succeeding to all or substantially all of the corporate trust business of the Trustee such corporation or other entity shall be eligible under the provisions of Section 7.08.

In case at the time such successor to the Trustee shall succeed to the trusts created by this Indenture, any of the Notes shall have been authenticated but not delivered, any such successor to the Trustee may adopt the certificate of authentication of any predecessor trustee or authenticating agent appointed by such predecessor trustee, and deliver such Notes so authenticated; and in case at that time any of the Notes shall not have been authenticated, any successor to the Trustee or an authenticating agent appointed by such successor trustee may authenticate such Notes either in the name of any predecessor trustee hereunder or in the name of the successor trustee; and in all such cases such certificates shall have the full force which it is anywhere in the Notes or in this Indenture provided that the certificate of the Trustee shall have; *provided*, *however*, that the right to adopt the certificate of authentication of any predecessor trustee or to

authenticate Notes in the name of any predecessor trustee shall apply only to its successor or successors by merger, conversion or consolidation.

ARTICLE 8
CONCERNING THE HOLDERS

Section 8.01. *Action by Holders.* Whenever in this Indenture it is provided that the Holders of a specified percentage of the aggregate principal amount of the Notes may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action, the Holders of such specified percentage have joined therein may be evidenced (a) by any instrument or any number of instruments of similar tenor executed by Holders in person or by agent or proxy appointed in writing, or (b) by the record of the Holders voting in favor thereof at any meeting of Holders duly called and held in accordance with the provisions of Article 9, or (c) by a combination of such instrument or instruments and any such record of such a meeting of Holders. Whenever the Company solicits the taking of any action by the Holders of the Notes, the Company may, but shall not be required to, fix in advance of such solicitation, a date as the record date for determining Holders entitled to take such action. The record date if one is selected shall be not more than fifteen days prior to the date of commencement of solicitation of such action.

Section 8.02. *Proof of Execution by Holders.* Subject to the provisions of Section 7.01, Section 7.02 and Section 9.05, proof of the execution of any instrument by a Holder or its agent or proxy shall be sufficient if made in accordance with such reasonable rules and regulations as may be prescribed by the Trustee or in such manner as shall be satisfactory to the Trustee. The holding of Notes shall be proved by the Note Register or by a certificate of the Note Registrar. The record of any Holders' meeting shall be proved in the manner provided in Section 9.06.

Section 8.03. *Who Are Deemed Absolute Owners.* The Company, the Trustee, any authenticating agent, any Paying Agent, any Conversion Agent and any Note Registrar may deem the Person in whose name a Note shall be registered upon the Note Register to be, and may treat it as, the absolute owner of such Note (whether or not such Note shall be overdue and notwithstanding any notation of ownership or other writing thereon made by any Person other than the Company or any Note Registrar) for the purpose of receiving payment of or on account of the principal (including any Redemption Price and any Fundamental Change Repurchase Price) of and (subject to Section 2.03) accrued and unpaid interest on such Note, for conversion of such Note and for all other purposes; and neither the Company nor the Trustee nor any Paying Agent nor any Conversion Agent nor any Note Registrar shall be affected by any notice to the contrary. All such payments or deliveries so made to any Holder for the time being, or upon its order, shall be valid, and, to the extent of the sums or shares of Common Stock so paid or delivered, effectual to satisfy and discharge the liability for monies payable or shares deliverable upon any such Note. Notwithstanding anything to the contrary in this Indenture or the Notes following an Event of Default, any holder of a beneficial interest in a Global Note may directly enforce against the Company, without

the consent, solicitation, proxy, authorization or any other action of the Depositary or any other Person, such holder's right to exchange such beneficial interest for a Note in certificated form in accordance with the provisions of this Indenture.

Section 8.04. *Company-Owned Notes Disregarded.* In determining whether the Holders of the requisite aggregate principal amount of Notes have concurred in any direction, consent, waiver or other action under this Indenture, Notes that are owned by the Company, by any Subsidiary thereof or by any Affiliate of the Company or any Subsidiary thereof shall be disregarded and deemed not to be outstanding for the purpose of any such determination; *provided* that for the purposes of determining whether the Trustee shall be protected in relying on any such direction, consent, waiver or other action only Notes that a Responsible Officer actually knows are so owned shall be so disregarded. Notes so owned that have been pledged in good faith may be regarded as outstanding for the purposes of this Section 8.04 if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right to so act with respect to such Notes and that the pledgee is not the Company, a Subsidiary thereof or an Affiliate of the Company or a Subsidiary thereof. Upon request of the Trustee, the Company shall furnish to the Trustee promptly an Officer's Certificate listing and identifying all Notes, if any, known by the Company to be owned or held by or for the account of any of the above described Persons; and, subject to Section 7.01, the Trustee shall be entitled to accept such Officer's Certificate as conclusive evidence of the facts therein set forth and of the fact that all Notes not listed therein are outstanding for the purpose of any such determination.

Section 8.05. *Revocation of Consents; Future Holders Bound.* At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.01, of the taking of any action by the Holders of the percentage of the aggregate principal amount of the Notes specified in this Indenture in connection with such action, any Holder of a Note that is shown by the evidence to be included in the Notes the Holders of which have consented to such action may, by filing written notice with the Trustee at the Corporate Trust Office and upon proof of holding as provided in Section 8.02, revoke such action so far as concerns such Note. Except as aforesaid, any such action taken by the Holder of any Note shall be conclusive and binding upon such Holder and upon all future Holders and owners of such Note and of any Notes issued in exchange or substitution therefor or upon registration of transfer thereof, irrespective of whether any notation in regard thereto is made upon such Note or any Note issued in exchange or substitution therefor or upon registration of transfer thereof.

ARTICLE 9
HOLDERS' MEETINGS

Section 9.01. *Purpose of Meetings.* A meeting of Holders may be called at any time and from time to time pursuant to the provisions of this Article 9 for any of the following purposes:

(a) to give any notice to the Company or to the Trustee or to give any directions to the Trustee permitted under this Indenture, or to consent to the waiving of any Default or Event of Default hereunder (in each case, as permitted under this

Indenture) and its consequences, or to take any other action authorized to be taken by Holders pursuant to any of the provisions of Article 6;

(b) to remove the Trustee and nominate a successor trustee pursuant to the provisions of Article 7;

(c) to consent to the execution of an indenture or indentures supplemental hereto pursuant to the provisions of Section 10.02; or

(d) to take any other action authorized to be taken by or on behalf of the Holders of any specified aggregate principal amount of the Notes under any other provision of this Indenture or under applicable law.

Section 9.02. *Call of Meetings by Trustee or the Company.* The Trustee or the Company may at any time call a meeting of Holders to take any action specified in Section 9.01, to be held at such time and at such place the party who called the meeting shall determine. Notice of every meeting of the Holders, setting forth the time and the place of such meeting and in general terms the action proposed to be taken at such meeting and the establishment of any record date pursuant to Section 8.01, shall be delivered to Holders of such Notes. Such notice shall also be delivered to the Company. Such notices shall be delivered not less than 20 nor more than 90 days prior to the date fixed for the meeting.

Any meeting of Holders shall be valid without notice if the Holders of all Notes then outstanding are present in person or by proxy or if notice is waived before or after the meeting by the Holders of all Notes then outstanding, and if the Company and the Trustee are either present by duly authorized representatives or have, before or after the meeting, waived notice.

Section 9.03. *Call of Meetings by Company or Holders.* In case at any time the Company, pursuant to a Board Resolution, or the Holders of at least 10% of the aggregate principal amount of the Notes then outstanding, shall have requested the Trustee to call a meeting of Holders, by written request setting forth in reasonable detail the action proposed to be taken at the meeting, and the Trustee shall not have delivered the notice of such meeting within 20 days after receipt of such request, then the Company or such Holders may determine the time and the place for such meeting and may call such meeting to take any action authorized in Section 9.01, by delivering notice thereof as provided in Section 9.02.

Section 9.04. *Qualifications for Voting.* To be entitled to vote at any meeting of Holders a Person shall (a) be a Holder of one or more Notes on the record date pertaining to such meeting or (b) be a Person appointed by an instrument in writing as proxy by a Holder of one or more Notes on the record date pertaining to such meeting. The only Persons who shall be entitled to be present or to speak at any meeting of Holders shall be the Persons entitled to vote at such meeting and their counsel and any representatives of the Trustee and its counsel and any representatives of the Company and its counsel.

Section 9.05. *Regulations.* Notwithstanding any other provisions of this Indenture, the Trustee or the Company may make such reasonable regulations as it may

deem advisable for any meeting of Holders, in regard to proof of the holding of Notes and of the appointment of proxies, and in regard to the appointment and duties of inspectors of votes, the submission and examination of proxies, certificates and other evidence of the right to vote, and such other matters concerning the conduct of the meeting as it shall think fit.

The Trustee shall, by an instrument in writing, appoint a temporary chairman of the meeting, unless the meeting shall have been called by the Company or by Holders as provided in Section 9.03, in which case the Company or the Holders calling the meeting, as the case may be, shall in like manner appoint a temporary chairman. A permanent chairman and a permanent secretary of the meeting shall be elected by vote of the Holders of a majority in aggregate principal amount of the Notes represented at the meeting and entitled to vote at the meeting.

Subject to the provisions of Section 8.04, at any meeting of Holders each Holder or proxyholder shall be entitled to one vote for each $1,000 principal amount of Notes held or represented by him or her; *provided*, *however*, that no vote shall be cast or counted at any meeting in respect of any Note challenged as not outstanding and ruled by the chairman of the meeting to be not outstanding. The chairman of the meeting shall have no right to vote other than by virtue of Notes held by it or instruments in writing as aforesaid duly designating it as the proxy to vote on behalf of other Holders. Any meeting of Holders duly called pursuant to the provisions of Section 9.02 or Section 9.03 may be adjourned from time to time by the Holders of a majority of the aggregate principal amount of Notes represented at the meeting, whether or not constituting a quorum, and the meeting may be held as so adjourned without further notice.

Section 9.06. *Voting.* The vote upon any resolution submitted to any meeting of Holders shall be by written ballot on which shall be subscribed the signatures of the Holders or of their representatives by proxy and the outstanding aggregate principal amount of the Notes held or represented by them. The permanent chairman of the meeting shall appoint two inspectors of votes who shall count all votes cast at the meeting for or against any resolution and who shall make and file with the secretary of the meeting their verified written reports in duplicate of all votes cast at the meeting. A record in duplicate of the proceedings of each meeting of Holders shall be prepared by the secretary of the meeting and there shall be attached to said record the original reports of the inspectors of votes on any vote by ballot taken thereat and affidavits by one or more Persons having knowledge of the facts setting forth a copy of the notice of the meeting and showing that said notice was delivered as provided in Section 9.02. The record shall show the aggregate principal amount of the Notes voting in favor of or against any resolution. The record shall be signed and verified by the affidavits of the permanent chairman and secretary of the meeting and one of the duplicates shall be delivered to the Company and the other to the Trustee to be preserved by the Trustee, the latter to have attached thereto the ballots voted at the meeting.

Any record so signed and verified shall be conclusive evidence of the matters therein stated.

Section 9.07. *No Delay of Rights by Meeting.* Nothing contained in this Article 9 shall be deemed or construed to authorize or permit, by reason of any call of a meeting of Holders or any rights expressly or impliedly conferred hereunder to make such call, any hindrance or delay in the exercise of any right or rights conferred upon or reserved to the Trustee or to the Holders under any of the provisions of this Indenture or of the Notes.

ARTICLE 10
SUPPLEMENTAL INDENTURES

Section 10.01. *Supplemental Indentures Without Consent of Holders.* The Company (when authorized by the resolutions of the Board of Directors) and the Trustee, at the Company's expense, may from time to time and at any time amend or supplement this Indenture or the Notes for one or more of the following purposes:

(a) to cure any ambiguity, omission, defect or inconsistency;

(b) to provide for the assumption by a Successor Company of the obligations of the Company under this Indenture pursuant to Article 11;

(c) to add guarantees with respect to the Notes;

(d) to secure the Notes;

(e) to add to the covenants or Events of Default of the Company for the benefit of the Holders or surrender any right or power conferred upon the Company;

(f) to make any change that does not adversely affect the rights of any Holder under this Indenture or the Notes;

(g) in connection with any Share Exchange Event, to provide that the notes are convertible into Reference Property, subject to the provisions of Section 14.02, and make such related changes to the terms of the Notes to the extent expressly required by Section 14.07;

(h) comply with any requirement of the Commission in connection with the qualification of this Indenture under the Trust Indenture Act to the extent this Indenture is qualified thereunder;

(i) provide for the issuance of additional Notes as permitted under this Indenture;

(j) provide for the appointment of a successor Trustee, Note Registrar, Paying Agent, Bid Solicitation Agent or Conversion Agent;

(k) comply with the rules of any applicable securities depositary in a manner that does not adversely affect the rights of any Holder under the Indenture or the Notes in any material respect;

(l) irrevocably elect or eliminate one of the Settlement Methods and/or irrevocably elect a Specified Dollar Amount;

(m) increase the Conversion Rate as provided in this Indenture; or

(n) to conform the provisions of this Indenture or the Notes to the "Description of notes" section of the Offering Memorandum.

Upon the written request of the Company, the Trustee is hereby authorized to join with the Company in the execution of any such supplemental indenture, to make any further appropriate agreements and stipulations that may be therein contained, but the Trustee shall not be obligated to, but may in its discretion, enter into any supplemental indenture that affects the Trustee's own rights, duties or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section 10.01 may be executed by the Company and the Trustee without the consent of the Holders of any of the Notes at the time outstanding, notwithstanding any of the provisions of Section 10.02.

Section 10.02. *Supplemental Indentures with Consent of Holders.* With the consent (evidenced as provided in Article 8) of the Holders of at least a majority of the aggregate principal amount of the Notes then outstanding (determined in accordance with Article 8 and including, without limitation, consents obtained in connection with a repurchase of, or tender or exchange offer for, Notes), the Company, when authorized by the resolutions of the Board of Directors and the Trustee, at the Company's expense, may from time to time and at any time enter into an indenture or indentures supplemental hereto for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture, any supplemental indenture or the Notes or of modifying in any manner the rights of the Holders; *provided*, *however*, that, without the consent of each Holder of an outstanding Note affected, no such supplemental indenture shall:

(a) reduce the principal amount of Notes whose Holders must consent to an amendment;

(b) reduce the rate of or extend the stated time for payment of interest on any Note;

(c) reduce the principal of or extend the Maturity Date of any Note;

(d) make any change that adversely affects the conversion rights of any Notes other than as permitted or required by this Indenture;

(e) reduce the Redemption Price or the Fundamental Change Repurchase Price of any Note or amend or modify in any manner adverse to the Holders the Company's obligation to make such payments, whether through an amendment or waiver of provisions in the covenants, definitions or otherwise;

(f) make any Note payable in a currency, or at a place of payment, other than that stated in the Note;

(g) change the ranking of the Notes;

(h) eliminate the contractual right of any Holder to institute suit for the enforcement of its right to receive payment or delivery, as the case may be, of the principal (including the Fundamental Change Repurchase Price or Redemption Price, if applicable) of, accrued and unpaid interest, if any, on, and the consideration due upon conversion of, its Notes, on or after the respective due dates expressed or provided for in the Notes or this Indenture; or

(i) make any change in this Article 10 that requires each Holder's consent or in the waiver provisions in Section 6.02 or Section 6.09.

Upon the written request of the Company, and upon the filing with the Trustee of evidence of the consent of Holders as aforesaid and subject to Section 10.05, the Trustee shall join with the Company in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may in its discretion, but shall not be obligated to, enter into such supplemental indenture.

Holders do not need under this Section 10.02 to approve the particular form of any proposed supplemental indenture. It shall be sufficient if such Holders approve the substance thereof. After any such supplemental indenture becomes effective, the Company shall deliver to the Holders (with a copy to the Trustee) a notice briefly describing such supplemental indenture. However, the failure to give such notice to all the Holders, or any defect in the notice, will not impair or affect the validity of the supplemental indenture.

Section 10.03. *Effect of Supplemental Indentures.* Upon the execution of any supplemental indenture pursuant to the provisions of this Article 10, this Indenture shall be and be deemed to be modified and amended in accordance therewith and the respective rights, limitation of rights, obligations, duties and immunities under this Indenture of the Trustee, the Company and the Holders shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 10.04. *Notation on Notes.* Notes authenticated and delivered after the execution of any supplemental indenture pursuant to the provisions of this Article 10 may, at the Company's request and expense, bear a notation as to any matter provided for in such supplemental indenture. If the Company shall so determine, new Notes so modified as to conform, in the opinion of the Board of Directors, to any modification of this Indenture contained in any such supplemental indenture may, at the Company's expense, be prepared and executed by the Company, authenticated, upon receipt of a

Company Order, by the Trustee (or an authenticating agent duly appointed by the Trustee pursuant to Section 17.10) and delivered in exchange for the Notes then outstanding, upon surrender of such Notes then outstanding.

Section 10.05. *Evidence of Compliance of Supplemental Indenture to Be Furnished Trustee.* In addition to the documents required by Section 17.05, the Trustee shall receive an Officer's Certificate and an Opinion of Counsel as conclusive evidence that any supplemental indenture executed pursuant hereto complies with the requirements of this Article 10 and is permitted or authorized by this Indenture and such Opinion of Counsel shall include a customary legal opinion stating that such supplemental indenture is the valid and binding obligation of the Company, subject to customary exceptions and qualifications.

ARTICLE 11
CONSOLIDATION, MERGER, SALE, CONVEYANCE AND LEASE

Section 11.01. *Company May Consolidate, Etc. on Certain Terms.* Subject to the provisions of Section 11.02, the Company shall not consolidate with, merge with or into, or sell, convey, transfer or lease all or substantially all of the consolidated assets of the Company and the Company's Subsidiaries, taken as a whole, to another Person (a "**Business Combination Event**") (other than any such sale, conveyance, transfer or lease to one or more of the Company's direct or indirect Wholly Owned Subsidiaries), unless:

(a) the resulting, surviving or transferee Person (the "**Successor Company**"), if not the Company, shall be a Qualified Successor Entity organized and existing under the laws of the United States of America, any State thereof or the District of Columbia, and the Successor Company (if not the Company) shall expressly assume, by supplemental indenture all of the obligations of the Company under the Notes and this Indenture;

(b) immediately after giving effect to such transaction, no Default or Event of Default shall have occurred and be continuing under this Indenture; and

(c) if the Company is not the Successor Company, the Successor Company shall have delivered to the Trustee an Officer's Certificate and Opinion of Counsel, each stating that such consolidation, merger, sale, conveyance, transfer or lease complies with this Indenture and that such supplemental indenture is authorized or permitted by this Indenture and an Opinion of Counsel stating that the supplemental indenture is the valid and binding obligation of the Successor Company, subject to customary exceptions and qualifications.

Section 11.02. *Successor Corporation to Be Substituted.* In case of any such consolidation, merger, sale, conveyance, transfer or lease and upon the assumption by the Successor Company, by supplemental indenture, executed and delivered to the Trustee and satisfactory in form to the Trustee, of the due and punctual payment of the principal of and accrued and unpaid interest on all of the Notes, the due and punctual delivery and/or payment, as the case may be, of any consideration due upon conversion of the Notes and the due and punctual performance of all of the covenants and conditions of this

Indenture to be performed by the Company, such Successor Company (if not the Company) shall succeed to and, except in the case of a lease of all or substantially all of the consolidated assets of the Company and the Company's Subsidiaries, taken as a whole, shall be substituted for the Company, with the same effect as if it had been named herein as the party of the first part, and the Company shall be discharged from its obligations under the Notes and this Indenture (except in the case of a lease of all or substantially all of the consolidated assets of the Company and the Company's Subsidiaries, taken as a whole). Such Successor Company thereupon may cause to be signed, and may issue either in its own name or in the name of the Company any or all of the Notes issuable hereunder which theretofore shall not have been signed by the Company and delivered to the Trustee; and, upon the order of such Successor Company instead of the Company and subject to all the terms, conditions and limitations in this Indenture prescribed, the Trustee shall authenticate and shall deliver, or cause to be authenticated and delivered, any Notes that previously shall have been signed and delivered by the Officers of the Company to the Trustee for authentication, and any Notes that such Successor Company thereafter shall cause to be signed and delivered to the Trustee for that purpose. All the Notes so issued shall in all respects have the same legal rank and benefit under this Indenture as the Notes theretofore or thereafter issued in accordance with the terms of this Indenture as though all of such Notes had been issued at the date of the execution hereof. In the event of any such consolidation, merger, sale, conveyance or transfer (but not in the case of a lease), upon compliance with this Article 11 the Person named as the "Company" in the first paragraph of this Indenture (or any successor that shall thereafter have become such in the manner prescribed in this Article 11) may be dissolved, wound up and liquidated at any time thereafter and, except in the case of a lease, such Person shall be released from its liabilities as obligor and maker of the Notes and from its obligations under this Indenture and the Notes.

In case of any such consolidation, merger, sale, conveyance, transfer or lease, such changes in phraseology and form (but not in substance) may be made in the Notes thereafter to be issued as may be appropriate.

Section 11.03. *Opinion of Counsel to Be Given to Trustee.* If a supplemental indenture is required pursuant to this Article 11, no such consolidation, merger, sale, conveyance, transfer or lease shall be effective unless the Trustee shall receive an Officer's Certificate and an Opinion of Counsel as conclusive evidence that any such consolidation, merger, sale, conveyance, transfer or lease and any such assumption complies with the provisions of this Article 11.

ARTICLE 12
IMMUNITY OF INCORPORATORS, STOCKHOLDERS, OFFICERS AND DIRECTORS

Section 12.01. *Indenture and Notes Solely Corporate Obligations.* No recourse for the payment of the principal of or accrued and unpaid interest on, or the payment or delivery of consideration due upon conversion of, any Note, nor for any claim based thereon or otherwise in respect thereof, and no recourse under or upon any obligation, covenant or agreement of the Company in this Indenture or in any supplemental indenture

or in any Note, nor because of the creation of any indebtedness represented thereby, shall be had against any incorporator, stockholder, employee, agent, Officer or director or Subsidiary, as such, past, present or future, of the Company or of any successor company, either directly or through the Company or any successor company, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise; it being expressly understood that all such liability is hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issue of the Notes.

ARTICLE 13
[INTENTIONALLY OMITTED]

ARTICLE 14
CONVERSION OF NOTES

Section 14.01. *Conversion Privilege.* (a) Subject to and upon compliance with the provisions of this Article 14, each Holder of a Note shall have the right, at such Holder's option, to convert all or any portion (if the portion to be converted is $1,000 principal amount or an integral multiple thereof) of such Note (i) subject to satisfaction of the conditions described in Section 14.01(b), at any time prior to the close of business on the Business Day immediately preceding June 15, 2027 under the circumstances and during the periods set forth in Section 14.01(b), and (ii) regardless of the conditions described in Section 14.01(b), on or after June 15, 2027 and prior to the close of business on the second Scheduled Trading Day immediately preceding the Maturity Date, in each case, at an initial conversion rate of 3.4941 shares of Common Stock (subject to adjustment as provided in this Article 14, the "**Conversion Rate**") per $1,000 principal amount of Notes (subject to, and in accordance with, the settlement provisions of Section 14.02, the "**Conversion Obligation**").

(b) (i) Prior to the close of business on the Business Day immediately preceding June 15, 2027, a Holder may surrender all or any portion of its Notes for conversion at any time during the five Business Day period immediately after any ten consecutive Trading Day period (the "**Measurement Period**") in which the Trading Price per $1,000 principal amount of Notes, as determined following a request by a Holder of Notes in accordance with this subsection (b)(i), for each Trading Day of the Measurement Period was less than 98% of the product of the Last Reported Sale Price of the Common Stock on each such Trading Day and the Conversion Rate on each such Trading Day (the "**Trading Price Condition**"). The Trading Prices shall be determined by the Bid Solicitation Agent pursuant to this subsection (b)(i) and the definition of Trading Price set forth in this Indenture. The Company shall provide written notice to the Bid Solicitation Agent (if other than the Company) of the three independent nationally recognized securities dealers selected by the Company pursuant to the definition of Trading Price, along with appropriate contact information for each. The Bid Solicitation Agent (if other than the Company) shall have no obligation to solicit the Trading Price per $1,000 principal amount of Notes unless the Company has requested such solicitation, and the Company shall have no obligation to make such request (or, if the Company is acting as

Bid Solicitation Agent, the Company shall have no obligation to determine the Trading Price per $1,000 principal amount of Notes) unless a Holder of at least $5,000,000 aggregate principal amount of Notes provides the Company with reasonable evidence that the Trading Price per $1,000 principal amount of Notes on any Trading Day would be less than 98% of the product of the Last Reported Sale Price of the Common Stock on such Trading Day and the Conversion Rate on such Trading Day, at which time the Company shall instruct the Bid Solicitation Agent (if other than the Company) to solicit, or if the Company is acting as Bid Solicitation Agent, the Company shall solicit, such bids beginning on the next Trading Day and on each successive Trading Day until the Trading Price per $1,000 principal amount of Notes is greater than or equal to 98% of the product of the Last Reported Sale Price of the Common Stock and the Conversion Rate. The Company shall determine the Trading Price per $1,000 amount of Notes in accordance with the bids solicited by the Bid Solicitation Agent. If (x) the Company is not acting as Bid Solicitation Agent, and the Company does not instruct the Bid Solicitation Agent to solicit bids when obligated as provided in the preceding sentence, or if the Company instructs the Bid Solicitation Agent to obtain bids and the Bid Solicitation Agent fails to make such solicitation, or (y) the Company is acting as Bid Solicitation Agent and the Company fails to make such solicitation when obligated as provided in the preceding sentence, then, in either case, the Trading Price per $1,000 principal amount of Notes shall be deemed to be less than 98% of the product of the Last Reported Sale Price of the Common Stock and the Conversion Rate on each Trading Day of such failure. If the Trading Price Condition has been met on any Trading Day, the Company shall so notify the Holders, the Trustee and the Conversion Agent (if other than the Trustee) in writing on or within one Business Day of such Trading Day. If, at any time after the Trading Price Condition has been met, the Trading Price per $1,000 principal amount of Notes is greater than or equal to 98% of the product of the Last Reported Sale Price of the Common Stock and the Conversion Rate for such Trading Day, the Company shall so notify the Holders of the Notes, the Trustee and the Conversion Agent (if other than the Trustee) in writing that the Trading Price Condition is no longer met and thereafter neither the Company nor the Bid Solicitation Agent (if other than the Company) shall be required to solicit bids again until another qualifying request is made as provided above.

(ii) If the Company calls any Note for redemption pursuant to Article 16, then a Holder of the Note called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption may surrender such Note (or a portion thereof) called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption for conversion at any time prior to the close of business on the second Scheduled Trading Day immediately prior to the applicable Redemption Date, even if the Notes are not otherwise convertible at such time. After that time, the right to convert such Note called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption pursuant to this subsection (b)(ii) on account of such Redemption Notice shall expire, unless the Company defaults in the payment of the Redemption Price, in which case a Holder of such Note called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption may convert such Note (or a portion thereof) called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption until the

Redemption Price has been paid or duly provided for. If the Company elects to redeem less than all of the outstanding Notes for redemption pursuant to Article 16, and the Holder of any Note (or any owner of a beneficial interest in any Global Note) is reasonably not able to determine, before the close of business on the 22nd Scheduled Trading Day immediately before the relevant Redemption Date (or, if the Company delivers a Redemption Notice electing Physical Settlement not less than 10 nor more than 45 Scheduled Trading Days prior to the related Redemption Date, then before the close of business on the 9th Scheduled Trading Day immediately before the relevant Redemption Date), whether such Note or beneficial interest, as applicable, is to be redeemed pursuant to such redemption, then such Holder or owner, as applicable, shall be entitled to convert such Note or beneficial interest, as applicable, at any time before the close of business on the second Scheduled Trading Day immediately prior to such Redemption Date, unless the Company defaults in the payment of the Redemption Price, in which case such Holder or owner, as applicable, shall be entitled to convert such Note (or any such beneficial interest in any Global Note), as applicable, until the Redemption Price has been paid or duly provided for, and each such conversion shall be deemed to be of a Note called for redemption (including, without limitation, for purposes of Section 14.03).

(iii) If, prior to the close of business on the Business Day immediately preceding June 15, 2027, the Company elects to:

(A) issue to all or substantially all holders of the Common Stock any rights, options or warrants (other than pursuant to a stockholders rights plan, so long as such rights have not separated from the shares of the Common Stock) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of the Common Stock at a price per share that is less than the average of the Last Reported Sale Prices of the Common Stock for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of such issuance; or

(B) distribute to all or substantially all holders of the Common Stock the Company's assets, securities or rights to purchase securities of the Company (other than pursuant to a stockholders rights plan, so long as such rights have not separated from the shares of the Common Stock), which distribution has a per share value, as reasonably determined by the Company in good faith, exceeding 10% of the Last Reported Sale Price of the Common Stock on the Trading Day preceding the date of announcement for such distribution,

then, in either case, the Company shall notify all Holders of the Notes, the Trustee and the Conversion Agent (if other than the Trustee) (such notification, the "**Certain Distributions Notification**") (x) at least 25 Scheduled Trading Days prior to or (y) if in the Certain Distributions Notification the Company elects Physical Settlement in respect

of any conversions with Conversion Dates that occur after delivery to the Holders of the Certain Distributions Notification until the Certain Distributions Conversion Period End Date, at least 10 Scheduled Trading Days prior to, in either case, the Ex-Dividend Date for such issuance or distribution. Once the Company has given such notice, a Holder may surrender all or any portion of its Notes for conversion at any time until the earlier of (1) the close of business on the Business Day immediately preceding the Ex-Dividend Date for such issuance or distribution and (2) the Company's announcement that such issuance or distribution will not take place (such earlier date and time, the "**Certain Distributions Conversion Period End Date**").

Holders may not convert their Notes pursuant to this Section 14.01(b)(iii) if they participate (other than in the case of a share split or share combination), at the same time and upon the same terms as holders of the Common Stock and solely as a result of holding the Notes, in any of the transactions described above without having to convert their Notes as if they held a number of shares of Common Stock equal to the applicable Conversion Rate as of the Record Date for such issuance or distribution, *multiplied by* the principal amount (expressed in thousands) of Notes held by such Holder.

(iv) If a transaction or event that constitutes a Fundamental Change or a Make-Whole Fundamental Change occurs prior to the close of business on the Business Day immediately preceding June 15, 2027, regardless of whether a Holder has the right to require the Company to repurchase the Notes pursuant to Section 15.02, or if the Company is a party to a Share Exchange Event (other than a Share Exchange Event that is solely for the purpose of changing the Company's jurisdiction of organization that (x) does not constitute a Fundamental Change or a Make-Whole Fundamental Change and (y) results in a reclassification, conversion or exchange of outstanding shares of the Common Stock solely into shares of common stock of the surviving entity and such common stock becomes Reference Property for the Notes) that occurs prior to the close of business on the Business Day immediately preceding June 15, 2027 (each such Fundamental Change, Make-Whole Fundamental Change or Share Exchange Event, a "**Corporate Event**"), all or any portion of a Holder's Notes may be surrendered for conversion at any time from or after the effective date of the Corporate Event until the earlier of (x) 35 Trading Days after the effective date of such Corporate Event (or, if the Company gives notice after the effective date of such Corporate Event, until 35 Trading Days after the date the Company gives notice of such Corporate Event) or, if such Corporate Event also constitutes a Fundamental Change (other than an Exempted Fundamental Change), until the close of business on the Business Day immediately preceding the related Fundamental Change Repurchase Date and (y) the second Scheduled Trading Day immediately preceding the Maturity Date. The Company shall notify Holders, the Trustee and the Conversion Agent (if other than the Trustee) as promptly as practicable following the date the Company publicly announces the effective date of such Corporate Event, but in no event later than the second Business Day after the effective date of such Corporate Event.

(v) Prior to the close of business on the Business Day immediately preceding June 15, 2027, a Holder may surrender all or any portion of its Notes for conversion at any time during any calendar quarter commencing after the calendar quarter ending on December 31, 2022 (and only during such calendar quarter), if the Last Reported Sale Price of the Common Stock for at least 20 Trading Days (whether or not consecutive) during the period of 30 consecutive Trading Days ending on, and including, the last Trading Day of the immediately preceding calendar quarter is greater than or equal to 130% of the Conversion Price on each applicable Trading Day.

Section 14.02. *Conversion Procedure; Settlement Upon Conversion*.

(a) Subject to this Section 14.02, Section 14.03(b) and Section 14.07(a), upon conversion of any Note, the Company shall pay or deliver, as the case may be, to the converting Holder, in respect of each $1,000 principal amount of Notes being converted, cash ("**Cash Settlement**"), shares of Common Stock, together with cash, if applicable, in lieu of delivering any fractional share of Common Stock in accordance with subsection (j) of this Section 14.02 ("**Physical Settlement**") or a combination of cash and shares of Common Stock, together with cash, if applicable, in lieu of delivering any fractional share of Common Stock in accordance with subsection (j) of this Section 14.02 ("**Combination Settlement**"), at its election, as set forth in this Section 14.02.

(i) All conversions of Notes for which the relevant Conversion Date occurs on or after June 15, 2027, and all conversions of Notes during a Redemption Period of Notes called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)), shall be settled using the same Settlement Method.

(ii) Except for any conversions of Notes called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)) for which the relevant Conversion Date occurs during the related Redemption Period and any conversions for which the relevant Conversion Date occurs on or after June 15, 2027, the Company shall use the same Settlement Method for all conversions with the same Conversion Date, but the Company shall not have any obligation to use the same Settlement Method with respect to conversions with different Conversion Dates.

(iii) If, in respect of any Conversion Date (or the period described in the fourth immediately succeeding set of parentheses, as the case may be), the Company elects to deliver a written notice (the "**Settlement Notice**") of the relevant Settlement Method in respect of such Conversion Date (or such period, as the case may be), the Company shall deliver such Settlement Notice to the Trustee, the Conversion Agent (if other than the Trustee) and converting Holders no later than the close of business on the Trading Day immediately following the relevant Conversion Date (or, in the case of any conversions of Notes (x) called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)) for which the relevant Conversion Date occurs during the related Redemption

Period, in such Redemption Notice, (y) for which the relevant Conversion Date occurs on or after June 15, 2027, no later than June 15, 2027 or (z) for which the Company has irrevocably elected Physical Settlement pursuant to Section 14.01(b)(iii), in the related Certain Distributions Notification) (in each case, the "**Settlement Method Election Deadline**"). If the Company does not elect a Settlement Method prior to the deadline set forth in the immediately preceding sentence, the Company shall no longer have the right to elect a Settlement Method with respect to any conversion on such Conversion Date or during such period, and the Company shall be deemed to have elected the Default Settlement Method with respect to such conversion. Any Settlement Notice shall specify the relevant Settlement Method and in the case of an election of Combination Settlement, the relevant Settlement Notice shall indicate the Specified Dollar Amount per $1,000 principal amount of Notes. If the Company timely elects Combination Settlement (or is deemed to have elected Combination Settlement) with respect to a conversion but does not timely notify the converting Holder, the Trustee and the Conversion Agent (if other than the Trustee) of the applicable Specified Dollar Amount, then the Specified Dollar Amount for such conversion will be deemed to be $1,000 per $1,000 principal amount of Notes. For the avoidance of doubt, the Company's failure to timely elect a Settlement Method or specify the applicable Specified Dollar Amount shall not constitute a default under this Indenture.

The Company may, by notice to the Holders, the Trustee and the Conversion Agent (if other than the Trustee) prior to June 15, 2027, irrevocably fix the Settlement Method, to any Settlement Method that the Company is then permitted to elect, including Combination Settlement with a Specified Dollar Amount per $1,000 principal amount of Notes of $1,000 or with an ability to continue to set the Specified Dollar Amount per $1,000 principal amount of Notes at or above any specific amount set forth in such election notice. Concurrently with providing notice to all Holders of an election to change the Default Settlement Method or irrevocably fix the Settlement Method, the Company shall promptly either post an announcement on its website or issue a report on Form 8-K (or any successor form) disclosing such Default Settlement Method or irrevocably fixed Settlement Method. If the Company changes the Default Settlement Method or elects to irrevocably fix the Settlement Method, in either case, to Combination Settlement with an ability to continue to set the Specified Dollar Amount per $1,000 principal amount of Notes at or above a specified amount, the Company will, after the date of such change or election, as the case may be, inform Holders converting their Notes of such Specified Dollar Amount no later than the relevant Settlement Method Election Deadline, or, if the Company does not timely notify Holders, such Specified Dollar Amount will be the specific amount set forth in the change or election notice or, if no specific amount was set forth in the change or election notice, such Specified Dollar Amount shall be $1,000 per $1,000 principal amount of Notes. A change in the Default Settlement Method or an irrevocable election shall apply to all Note conversions on Conversion Dates occurring subsequent to delivery of such notice; *provided, however*, that no such change in the Default Settlement Method or irrevocable election shall affect any Settlement Method theretofore elected (or deemed to be elected) with respect to any conversion. For the

avoidance of doubt, such an irrevocable election, if made, shall be effective without the need to amend this Indenture or the Notes, including pursuant to the provisions described in Section 10.01(l). However, the Company may nonetheless choose to execute such an amendment at the Company's option.

(iv) The cash, shares of Common Stock or combination of cash and shares of Common Stock in respect of any conversion of Notes (the "**Settlement Amount**") shall be computed as follows:

(A) if the Company elects (or is deemed to have elected) to satisfy its Conversion Obligation in respect of such conversion by Physical Settlement, the Company shall deliver to the converting Holder in respect of each $1,000 principal amount of Notes being converted a number of shares of Common Stock equal to the Conversion Rate in effect on the Conversion Date (plus cash in lieu of any fractional share of Common Stock issuable upon conversion);

(B) if the Company elects (or is deemed to have elected) to satisfy its Conversion Obligation in respect of such conversion by Cash Settlement, the Company shall pay to the converting Holder in respect of each $1,000 principal amount of Notes being converted cash in an amount equal to the sum of the Daily Conversion Values for each of the 20 consecutive Trading Days during the related Observation Period; and

(C) if the Company elects (or is deemed to have elected) to satisfy its Conversion Obligation in respect of such conversion by Combination Settlement, the Company shall pay or deliver, as the case may be, in respect of each $1,000 principal amount of Notes being converted, a Settlement Amount equal to the sum of the Daily Settlement Amounts for each of the 20 consecutive Trading Days during the related Observation Period (plus cash in lieu of any fractional share of Common Stock issuable upon conversion).

(v) The Daily Settlement Amounts (if applicable) and the Daily Conversion Values (if applicable) shall be determined by the Company promptly following the last day of the Observation Period. Promptly after such determination of the Daily Settlement Amounts or the Daily Conversion Values, as the case may be, and the amount of cash payable in lieu of delivering any fractional share of Common Stock, the Company shall notify the Trustee and the Conversion Agent (if other than the Trustee) in writing of the Daily Settlement Amounts or the Daily Conversion Values, as the case may be, and the amount of cash payable in lieu of delivering fractional shares of Common Stock. The Trustee and the Conversion Agent (if other than the Trustee) shall have no responsibility for any such determination.

(b) Subject to Section 14.02(e), before any Holder of a Note shall be entitled to convert a Note as set forth above, such Holder shall (i) in the case of a Global Note, comply with the procedures of the Depositary in effect at that time and, if required, pay

funds equal to the interest payable on the next Interest Payment Date to which such Holder is not entitled as set forth in Section 14.02(h) and, if required, pay all transfer or similar taxes, if any, pursuant to Section 14.02(e) and (ii) in the case of a Physical Note (1) complete, manually or electronically sign and deliver an irrevocable notice to the Conversion Agent as set forth in the Form of Notice of Conversion (or a facsimile thereof) (a "**Notice of Conversion**") at the office of the Conversion Agent and state in writing therein the principal amount of Notes to be converted and the name or names (with addresses) in which such Holder wishes the certificate or certificates for any shares of Common Stock to be delivered upon settlement of the Conversion Obligation to be registered, (2) surrender such Notes, duly endorsed to the Company or in blank (and accompanied by appropriate endorsement and transfer documents), at the office of the Conversion Agent, (3) if required, furnish appropriate endorsements and transfer documents, (4) if required, pay funds equal to interest payable on the next Interest Payment Date to which such Holder is not entitled as set forth in Section 14.02(h) and (5) if required, pay all transfer or similar taxes, if any, pursuant to Section 14.02(e). The Trustee (and if different, the Conversion Agent) shall notify the Company of any conversion pursuant to this Article 14 on the Conversion Date for such conversion. No Notice of Conversion with respect to any Notes may be surrendered by a Holder thereof if such Holder has also delivered a Fundamental Change Repurchase Notice to the Company in respect of such Notes and has not validly withdrawn such Fundamental Change Repurchase Notice in accordance with Section 15.03.

If more than one Note shall be surrendered for conversion at one time by the same Holder, the Conversion Obligation with respect to such Notes shall be computed on the basis of the aggregate principal amount of the Notes (or specified portions thereof to the extent permitted thereby) so surrendered.

(c) A Note shall be deemed to have been converted immediately prior to the close of business on the date (the "**Conversion Date**") that the Holder has complied with the requirements set forth in subsection (b) above. Except as set forth in Section 14.03(b) and Section 14.07(a), the Company shall pay or deliver, as the case may be, the consideration due in respect of the Conversion Obligation on the second Business Day immediately following the relevant Conversion Date, if the Company elects to satisfy its Conversion Obligation through Physical Settlement (*provided* that, with respect to any Conversion Date following the Regular Record Date immediately preceding the Maturity Date where Physical Settlement applies to the related conversion, the Company will settle any such conversion on the Maturity Date (or, if the Maturity Date is not a Business Day, the next Business Day), and, for purposes of calculating the consideration due upon such conversion, the Conversion Date thereof will be deemed to occur on the second Scheduled Trading Day preceding the Maturity Date), or on the second Business Day immediately following the last Trading Day of the Observation Period, if the Company elects to satisfy its Conversion Obligation through any other Settlement Method. If any shares of Common Stock are due to a converting Holder, the Company shall issue or cause to be issued, and deliver (if applicable) through its common stock transfer agent to the Conversion Agent or to such Holder, or such Holder's nominee or nominees, the full

number of shares of Common Stock to which such Holder shall be entitled, in book-entry format through the Depositary, in satisfaction of the Company's Conversion Obligation.

(d) In case any Note shall be surrendered for partial conversion, the Company shall execute and the Trustee shall authenticate and deliver to or upon the written order of the Holder of the Note so surrendered a new Note or Notes in authorized denominations in an aggregate principal amount equal to the unconverted portion of the surrendered Note, without payment of any service charge by the converting Holder but, if required by the Company or Trustee, with payment of a sum sufficient to cover any documentary, stamp or similar issue or transfer tax or similar governmental charge required by law or that may be imposed in connection therewith as a result of the name of the Holder of the new Notes issued upon such conversion being different from the name of the Holder of the old Notes surrendered for such conversion.

(e) If a Holder submits a Note for conversion, the Company shall pay any documentary, stamp or similar issue or transfer tax due on the issue of any shares of Common Stock upon conversion, unless the tax is due because the Holder requests such shares to be issued in a name other than the Holder's name, in which case the Holder shall pay that tax. The Conversion Agent may refuse to deliver the certificates representing the shares of Common Stock being issued in a name other than the Holder's name until the Trustee receives a sum sufficient to pay any tax that is due by such Holder in accordance with the immediately preceding sentence.

(f) Except as provided in Section 14.04, no adjustment shall be made for dividends on any shares of Common Stock issued upon the conversion of any Note as provided in this Article 14.

(g) Upon the conversion of an interest in a Global Note, the Trustee, or the Custodian at the direction of the Trustee, shall make a notation on such Global Note as to the reduction in the principal amount represented thereby. The Company shall notify the Trustee in writing of any conversion of Notes effected through any Conversion Agent other than the Trustee.

(h) Upon conversion, a Holder shall not receive any separate cash payment for accrued and unpaid interest, if any, except as set forth below. The Company's settlement of the full Conversion Obligation shall be deemed to satisfy in full its obligation to pay the principal amount of the Note and accrued and unpaid interest, if any, to, but not including, the relevant Conversion Date. As a result, accrued and unpaid interest, if any, to, but not including, the relevant Conversion Date shall be deemed to be paid in full rather than cancelled, extinguished or forfeited. Upon a conversion of Notes into a combination of cash and shares of Common Stock, accrued and unpaid interest will be deemed to be paid first out of the cash paid upon such conversion. Notwithstanding the foregoing, if Notes are converted after the close of business on a Regular Record Date but prior to the open of business on the immediately following Interest Payment Date, Holders of such Notes as of the close of business on such Regular Record Date will receive the full amount of interest payable on such Notes (to, but not including, such Interest Payment Date) on such Interest Payment Date notwithstanding the conversion.

However, Notes surrendered for conversion during the period from the close of business on any Regular Record Date to the open of business on the immediately following Interest Payment Date must be accompanied by funds equal to the amount of interest payable on the Notes so converted on the corresponding Interest Payment Date (regardless of whether the converting Holder was the Holder of record on the corresponding Regular Record Date); *provided* that no such payment shall be required (1) for conversions following the close of business on the Regular Record Date immediately preceding the Maturity Date; (2) for Notes called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption, if the Company has specified a Redemption Date that is after a Regular Record Date and on or prior to the second Scheduled Trading Day immediately following the corresponding Interest Payment Date; (3) if the Company has specified a Fundamental Change Repurchase Date that is after a Regular Record Date and on or prior to the Business Day immediately following the corresponding Interest Payment Date; or (4) to the extent of any Defaulted Amounts, if any Defaulted Amounts exists at the time of conversion with respect to such Note. Therefore, for the avoidance of doubt, all Holders of record on the Regular Record Date immediately preceding the Maturity Date, any Redemption Date described in clause (2) above, and any Fundamental Change Repurchase Date described in clause (3) above shall receive the full interest payment due on the Maturity Date or other applicable Interest Payment Date in cash regardless of whether their Notes have been converted, redeemed and/or repurchased, as applicable, following such Regular Record Date.

(i) The Person in whose name the shares of Common Stock shall be issuable upon conversion shall be treated as a stockholder of record as of the close of business on the relevant Conversion Date (if the Company elects to satisfy the related Conversion Obligation by Physical Settlement) or the last Trading Day of the relevant Observation Period (if the Company elects to satisfy the related Conversion Obligation by Combination Settlement), as the case may be. Upon a conversion of Notes, such Person shall no longer be a Holder of such Notes surrendered for conversion.

(j) The Company shall not issue any fractional share of Common Stock upon conversion of the Notes and shall instead pay cash in lieu of delivering any fractional share of Common Stock issuable upon conversion based on the Daily VWAP for the relevant Conversion Date (or, if such Conversion Date is not a Trading Day, the immediately preceding Trading Day), in the case of Physical Settlement or based on the Daily VWAP for the last Trading Day of the relevant Observation Period, in the case of Combination Settlement. For each Note surrendered for conversion, if the Company has elected Combination Settlement, the full number of shares that shall be issued upon conversion thereof shall be computed on the basis of the aggregate Daily Settlement Amounts for the relevant Observation Period and any fractional shares remaining after such computation shall be paid in cash.

Section 14.03. *Increased Conversion Rate Applicable to Certain Notes Surrendered in Connection with Make-Whole Fundamental Changes or Redemption Notice*. (a) If (x) the Effective Date of a Make-Whole Fundamental Change occurs prior to the Maturity Date or (y) the Company gives a Redemption Notice with respect to any

or all of the Notes in accordance with Section 16.02 and, in each case, a Holder elects to convert its Notes in connection with such Make-Whole Fundamental Change or Redemption Notice, as the case may be, the Company shall, under the circumstances described below, increase the Conversion Rate for the Notes so surrendered for conversion by a number of additional shares of Common Stock (the "**Additional Shares**"), as described below. A conversion of Notes shall be deemed for these purposes to be "in connection with" such Make-Whole Fundamental Change if the relevant Conversion Date occurs during the period from, and including, the Effective Date of the Make-Whole Fundamental Change up to, and including, the close of business on the Business Day immediately prior to the related Fundamental Change Repurchase Date (or, in the case of an Exempted Fundamental Change or a Make-Whole Fundamental Change that would have been a Fundamental Change but for the proviso in clause (b) of the definition thereof, the 35th Trading Day immediately following the Effective Date of such Make-Whole Fundamental Change) (such period, the "**Make-Whole Fundamental Change Period**"). A conversion of Notes shall be deemed for these purposes to be "in connection with" a Redemption Notice if such conversion is of Notes called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)) and the relevant Conversion Date occurs during the related Redemption Period. For the avoidance of doubt, the Company shall increase the Conversion Rate in connection with a Redemption Notice only with respect to conversions of Notes called for redemption (or deemed called for redemption pursuant to Section 14.01(b)(ii)), and not of Notes not called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption. Accordingly, if the Company elects to redeem less than all of the outstanding Notes as described under Article 16, Holders of the Notes not called (or deemed called pursuant to Section 14.01(b)(ii)) for redemption shall not be entitled to an increased Conversion Rate for conversions of such Notes on account of the Redemption Notice during the related Redemption Period if such Notes are otherwise convertible, except in the limited circumstances set forth under Section 14.01(b)(ii).

(b) Upon surrender of Notes for conversion in connection with a Make-Whole Fundamental Change or Redemption Notice, the Company shall, at its option, satisfy the related Conversion Obligation by Physical Settlement, Cash Settlement or Combination Settlement in accordance with Section 14.02; *provided*, *however*, that if, at the effective time of a Make-Whole Fundamental Change described in clause (b) of the definition of Fundamental Change, the Reference Property following such Make-Whole Fundamental Change is composed entirely of cash, for any conversion of Notes following the Effective Date of such Make-Whole Fundamental Change, the Conversion Obligation shall be calculated based solely on the Stock Price for the transaction and shall be deemed to be an amount of cash per $1,000 principal amount of converted Notes equal to the Conversion Rate (including any adjustment for Additional Shares), *multiplied by* such Stock Price. In such event, the Conversion Obligation shall be paid to Holders in cash on the second Business Day following the Conversion Date. The Company shall notify the Holders of Notes, the Trustee and the Conversion Agent (if other than the Trustee) in writing of the Effective Date of any Make-Whole Fundamental Change no later than five Business Days after such Effective Date.

(c) The number of Additional Shares, if any, by which the Conversion Rate shall be increased shall be determined by reference to the table below, based on the date on which the Make-Whole Fundamental Change occurs or becomes effective or the date of the Redemption Notice, as the case may be, (in each case, the "**Effective Date**") and the price paid (or deemed to be paid) per share of the Common Stock in the Make-Whole Fundamental Change or with respect to the Redemption Notice, as the case may be (in each case, the "**Stock Price**"). If the holders of the Common Stock receive in exchange for their Common Stock only cash in a Make-Whole Fundamental Change described in clause (b) of the definition of Fundamental Change, the Stock Price shall be the cash amount paid per share. Otherwise, the Stock Price shall be the average of the Last Reported Sale Prices of the Common Stock over the five consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the Effective Date of the Make-Whole Fundamental Change or the date of the Redemption Notice, as the case may be. In the event that a conversion in connection with a Redemption Notice would also be deemed to be in connection with a Make-Whole Fundamental Change, a Holder of the Notes to be converted shall be entitled to a single increase to the Conversion Rate with respect to the first to occur of the date of the applicable Redemption Notice or the Effective Date of the applicable Make-Whole Fundamental Change, and the later event shall be deemed not to have occurred for purposes of such conversion. The Board of Directors shall make appropriate adjustments to the Stock Price, in its good faith determination, to account for any adjustment to the Conversion Rate that becomes effective, or any event requiring an adjustment to the Conversion Rate where the Ex-Dividend Date, Effective Date (as such term is used in Section 14.04) or Expiration Date of the event occurs during such five consecutive Trading Day period.

(d) The Stock Prices set forth in the column headings of the table below shall be adjusted as of any date on which the Conversion Rate of the Notes is otherwise adjusted. The adjusted Stock Prices shall equal the Stock Prices applicable immediately prior to such adjustment, *multiplied by* a fraction, the numerator of which is the Conversion Rate immediately prior to such adjustment giving rise to the Stock Price adjustment and the denominator of which is the Conversion Rate as so adjusted. The number of Additional Shares set forth in the table below shall be adjusted in the same manner and at the same time as the Conversion Rate as set forth in Section 14.04.

(e) The following table sets forth the number of Additional Shares of Common Stock by which the Conversion Rate shall be increased per $1,000 principal amount of Notes pursuant to this Section 14.03 for each Stock Price and Effective Date set forth below:

	Stock Price												
Effective Date	**$212.00**	**$245.00**	**$286.20**	**$330.00**	**$372.06**	**$420.00**	**$470.00**	**$550.00**	**$660.00**	**$800.00**	**$970.00**	**$1,170.00**	**$1,400.00**
September 15, 2022	1.2228	0.9176	0.6620	0.4819	0.3633	0.2687	0.1996	0.1274	0.0708	0.0337	0.0125	0.0024	0.0000
September 15, 2023	1.2228	0.9176	0.6565	0.4675	0.3452	0.2494	0.1809	0.1112	0.0586	0.0258	0.0082	0.0006	0.0000
September 15, 2024	1.2228	0.9176	0.6304	0.4339	0.3099	0.2157	0.1506	0.0871	0.0421	0.0161	0.0037	0.0000	0.0000
September 15, 2025	1.2228	0.8764	0.5678	0.3673	0.2471	0.1606	0.1046	0.0541	0.0222	0.0062	0.0004	0.0000	0.0000
September 15, 2026	1.2228	0.7796	0.4447	0.2478	0.1441	0.0798	0.0443	0.0179	0.0048	0.0003	0.0000	0.0000	0.0000
September 15, 2027	1.2228	0.5875	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

The exact Stock Price and Effective Date may not be set forth in the table above, in which case:

(i) if the Stock Price is between two Stock Prices in the table above or the Effective Date is between two Effective Dates in the table above, the number of Additional Shares shall be determined by a straight-line interpolation between the number of Additional Shares set forth for the higher and lower Stock Prices and the earlier and later Effective Dates, as applicable, based on a 365- or 366-day year, as applicable;

(ii) if the Stock Price is greater than $1,400.00 per share (subject to adjustment in the same manner as the Stock Prices set forth in the column headings of the table above pursuant to subsection (d) above), no Additional Shares shall be added to the Conversion Rate; and

(iii) if the Stock Price is less than $212.00 per share (subject to adjustment in the same manner as the Stock Prices set forth in the column headings of the table above pursuant to subsection (d) above), no Additional Shares shall be added to the Conversion Rate.

Notwithstanding the foregoing, in no event shall the Conversion Rate per $1,000 principal amount of Notes exceed 4.7169 shares of Common Stock, subject to adjustment in the same manner as the Conversion Rate pursuant to Section 14.04.

(f) Nothing in this Section 14.03 shall prevent an adjustment to the Conversion Rate pursuant to Section 14.04 in respect of a Make-Whole Fundamental Change.

Section 14.04. *Adjustment of Conversion Rate.* The Conversion Rate shall be adjusted from time to time by the Company if any of the following events occurs, except that the Company shall not make any adjustments to the Conversion Rate if Holders of the Notes participate (other than in the case of (x) a share split or share combination or (y) a tender or exchange offer), at the same time and upon the same terms as holders of the Common Stock and solely as a result of holding the Notes, in any of the transactions described in this Section 14.04, without having to convert their Notes, as if they held a number of shares of Common Stock equal to the Conversion Rate, *multiplied by* the principal amount (expressed in thousands) of Notes held by such Holder.

(a) If the Company exclusively issues shares of Common Stock as a dividend or distribution on shares of the Common Stock, or if the Company effects a share split or

share combination in respect of the Common Stock, the Conversion Rate shall be adjusted based on the following formula:

$$CR' = CR_0 \times \frac{OS'}{OS_0}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the open of business on the Ex-Dividend Date of such dividend or distribution, or immediately prior to the open of business on the Effective Date of such share split or share combination, as applicable;

CR' = the Conversion Rate in effect immediately after the open of business on such Ex-Dividend Date or Effective Date, as applicable;

OS_0 = the number of shares of Common Stock outstanding immediately prior to the open of business on such Ex-Dividend Date or Effective Date, as applicable, before giving effect to such dividend, distribution, share split or share combination; and

OS' = the number of shares of Common Stock outstanding immediately after giving effect to such dividend, distribution, share split or share combination.

Any adjustment made under this Section 14.04(a) shall become effective immediately after the open of business on the Ex-Dividend Date for such dividend or distribution, or immediately after the open of business on the Effective Date for such share split or share combination, as applicable. If any dividend or distribution of the type described in this Section 14.04(a) is declared but not so paid or made, the Conversion Rate shall be immediately readjusted, effective as of the date the Board of Directors determines not to pay such dividend or distribution, to the Conversion Rate that would then be in effect if such dividend or distribution had not been declared.

(b) If the Company issues to all or substantially all holders of the Common Stock any rights, options or warrants (other than pursuant to a stockholders rights plan) entitling them, for a period of not more than 60 calendar days after the announcement date of such issuance, to subscribe for or purchase shares of the Common Stock at a price per share that is less than the average of the Last Reported Sale Prices of the Common Stock for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of such issuance, the Conversion Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{OS_0 + X}{OS_0 + Y}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such issuance;

CR' = the Conversion Rate in effect immediately after the open of business on such Ex-Dividend Date;

OS_0 = the number of shares of Common Stock outstanding immediately prior to the open of business on such Ex-Dividend Date;

X = the total number of shares of Common Stock issuable pursuant to such rights, options or warrants; and

Y = the number of shares of Common Stock equal to the aggregate price payable to exercise such rights, options or warrants, *divided by* the average of the Last Reported Sale Prices of the Common Stock over the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement of the issuance of such rights, options or warrants.

Any increase made under this Section 14.04(b) shall be made successively whenever any such rights, options or warrants are issued and shall become effective immediately after the open of business on the Ex-Dividend Date for such issuance. To the extent that shares of the Common Stock are not delivered after the expiration of such rights, options or warrants, the Conversion Rate shall be decreased to the Conversion Rate that would then be in effect had the increase with respect to the issuance of such rights, options or warrants been made on the basis of delivery of only the number of shares of Common Stock actually delivered. If such rights, options or warrants are not so issued, the Conversion Rate shall be decreased to the Conversion Rate that would then be in effect if such Ex-Dividend Date for such issuance had not occurred.

For purposes of this Section 14.04(b) and for the purpose of Section 14.01(b)(iii)(A), in determining whether any rights, options or warrants entitle the holders of Common Stock to subscribe for or purchase shares of the Common Stock at a price per share that is less than such average of the Last Reported Sale Prices of the Common Stock for the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date of announcement for such issuance, and in determining the aggregate offering price of such shares of Common Stock, there shall be taken into account any consideration received by the Company for such rights, options or warrants and any amount payable on exercise or conversion thereof, the value of such consideration, if other than cash, to be determined by the Company in good faith.

(c) If the Company distributes shares of its Capital Stock, evidences of its indebtedness, other assets or property of the Company or rights, options or warrants to acquire its Capital Stock or other securities, to all or substantially all holders of the Common Stock, excluding (i) dividends, distributions or issuances (including share splits) as to which an adjustment was effected (or would be effected, disregarding the 1% Provision) pursuant to Section 14.04(a) or Section 14.04(b), (ii) except as otherwise

described in Section 14.11, rights issued pursuant to any stockholders rights plan of the Company then in effect, (iii) dividends or distributions paid exclusively in cash as to which the provisions set forth in Section 14.04(d) shall apply, (iv) dividends or distributions of Reference Property in exchange for or upon conversion of the Common Stock in a Share Exchange Event, (v) Spin-Offs as to which the provisions set forth below in this Section 14.04(c) shall apply (any of such shares of Capital Stock, evidences of indebtedness, other assets or property or rights, options or warrants to acquire Capital Stock or other securities, the "**Distributed Property**") and (vi) tender offers and exchange offers as to which an adjustment is effected (or would be effected, disregarding the 1% Provision) set forth below in this Section 14.04(e), then the Conversion Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{SP_0}{SP_0 - FMV}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such distribution;

CR' = the Conversion Rate in effect immediately after the open of business on such Ex-Dividend Date;

SP_0 = the average of the Last Reported Sale Prices of the Common Stock over the 10 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the Ex-Dividend Date for such distribution; and

FMV = the fair market value (as determined by the Company in good faith) of the Distributed Property with respect to each outstanding share of the Common Stock on the Ex-Dividend Date for such distribution.

Any increase made under the portion of this Section 14.04(c) above shall become effective immediately after the open of business on the Ex-Dividend Date for such distribution. If such distribution is not so paid or made, the Conversion Rate shall be decreased to the Conversion Rate that would then be in effect if such distribution had not been declared. Notwithstanding the foregoing, if "FMV" (as defined above) is equal to or greater than "SP_0" (as defined above), in lieu of the foregoing increase, each Holder of a Note shall receive, in respect of each $1,000 principal amount thereof, at the same time and upon the same terms as holders of the Common Stock receive the Distributed Property, the amount and kind of Distributed Property such Holder would have received if such Holder owned a number of shares of Common Stock equal to the Conversion Rate in effect on the Ex-Dividend Date for the distribution. If the Company determines the "FMV" (as defined above) of any distribution for purposes of this Section 14.04(c) by reference to the actual or when-issued trading market for any securities, it shall in doing so consider the prices in such market over the same period used in computing the Last Reported Sale Prices of the Common Stock over the 10 consecutive Trading Day period

ending on, and including, the Trading Day immediately preceding the Ex-Dividend Date for such distribution.

With respect to an adjustment pursuant to this Section 14.04(c) where there has been a payment of a dividend or other distribution on the Common Stock of shares of Capital Stock of any class or series, or similar equity interest, of or relating to a Subsidiary or other business unit of the Company, that are, or, when issued, will be, listed or admitted for trading on a U.S. national securities exchange (a "**Spin-Off**"), the Conversion Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{FMV_0 + MP_0}{MP_0}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the end of the Valuation Period;

CR' = the Conversion Rate in effect immediately after the end of the Valuation Period;

FMV_0 = the average of the Last Reported Sale Prices of the Capital Stock or similar equity interest distributed to holders of the Common Stock applicable to one share of the Common Stock (determined by reference to the definition of Last Reported Sale Price as set forth in Section 1.01 as if references therein to Common Stock were to such Capital Stock or similar equity interest) over the first 10 consecutive Trading Day period after, and including, the Ex-Dividend Date of the Spin-Off (the "**Valuation Period**"); and

MP_0 = the average of the Last Reported Sale Prices of the Common Stock over the Valuation Period.

The increase to the Conversion Rate under the preceding paragraph shall occur at the close of business on the last Trading Day of the Valuation Period; *provided* that (x) in respect of any conversion of Notes for which Physical Settlement is applicable, if the relevant Conversion Date occurs during the Valuation Period, references to "10" in the preceding paragraph shall be deemed to be replaced with such lesser number of Trading Days as have elapsed from, and including, the Ex-Dividend Date of such Spin-Off to, and including, the Conversion Date in determining the Conversion Rate and (y) in respect of any conversion of Notes for which Cash Settlement or Combination Settlement is applicable, for any Trading Day that falls within the relevant Observation Period for such conversion and within the Valuation Period, references to "10" in the preceding paragraph shall be deemed to be replaced with such lesser number of Trading Days as have elapsed from, and including, the Ex-Dividend Date for the Spin-Off to, and including, such Trading Day in determining the Conversion Rate as of such Trading Day of such Observation Period. If any dividend or distribution that constitutes a Spin-Off is declared but not so paid or made, the Conversion Rate shall be immediately decreased,

effective as of the date the Board of Directors determines not to pay or make such dividend or distribution, to the Conversion Rate that would then be in effect if such dividend or distribution had not been declared or announced.

For purposes of this Section 14.04(c) (and subject in all respect to Section 14.11), rights, options or warrants distributed by the Company to all holders of the Common Stock entitling them to subscribe for or purchase shares of the Company's Capital Stock, including Common Stock (either initially or under certain circumstances), which rights, options or warrants, until the occurrence of a specified event or events ("**Trigger Event**"): (i) are deemed to be transferred with such shares of the Common Stock; (ii) are not exercisable; and (iii) are also issued in respect of future issuances of the Common Stock, shall be deemed not to have been distributed for purposes of this Section 14.04(c) (and no adjustment to the Conversion Rate under this Section 14.04(c) will be required) until the occurrence of the earliest Trigger Event, whereupon such rights, options or warrants shall be deemed to have been distributed and an appropriate adjustment (if any is required) to the Conversion Rate shall be made under this Section 14.04(c). If any such right, option or warrant, including any such existing rights, options or warrants distributed prior to the date of this Indenture, are subject to events, upon the occurrence of which such rights, options or warrants become exercisable to purchase different securities, evidences of indebtedness or other assets, then the date of the occurrence of any and each such event shall be deemed to be the date of distribution and Ex-Dividend Date with respect to new rights, options or warrants with such rights (in which case the existing rights, options or warrants shall be deemed to terminate and expire on such date without exercise by any of the holders thereof). In addition, in the event of any distribution (or deemed distribution) of rights, options or warrants, or any Trigger Event or other event (of the type described in the immediately preceding sentence) with respect thereto that was counted for purposes of calculating a distribution amount for which an adjustment to the Conversion Rate under this Section 14.04(c) was made, (1) in the case of any such rights, options or warrants that shall all have been redeemed or purchased without exercise by any holders thereof, upon such final redemption or purchase (x) the Conversion Rate shall be readjusted as if such rights, options or warrants had not been issued and (y) the Conversion Rate shall then again be readjusted to give effect to such distribution, deemed distribution or Trigger Event, as the case may be, as though it were a cash distribution, equal to the per share redemption or purchase price received by a holder or holders of Common Stock with respect to such rights, options or warrants (assuming such holder had retained such rights, options or warrants), made to all holders of Common Stock as of the date of such redemption or purchase, and (2) in the case of such rights, options or warrants that shall have expired or been terminated without exercise by any holders thereof, the Conversion Rate shall be readjusted as if such rights, options and warrants had not been issued.

For purposes of Section 14.04(a), Section 14.04(b) and this Section 14.04(c), if any dividend or distribution to which this Section 14.04(c) is applicable also includes one or both of:

(A) a dividend or distribution of shares of Common Stock to which Section 14.04(a) is applicable (the "**Clause A Distribution**"); or

(B) a dividend or distribution of rights, options or warrants to which Section 14.04(b) is applicable (the "**Clause B Distribution**"),

then, in either case, (1) such dividend or distribution, other than the Clause A Distribution and the Clause B Distribution, shall be deemed to be a dividend or distribution to which this Section 14.04(c) is applicable (the "**Clause C Distribution**") and any Conversion Rate adjustment required by this Section 14.04(c) with respect to such Clause C Distribution shall then be made, and (2) the Clause A Distribution and Clause B Distribution shall be deemed to immediately follow the Clause C Distribution and any Conversion Rate adjustment required by Section 14.04(a) and Section 14.04(b) with respect thereto shall then be made, except that, if determined by the Company (I) the "Ex-Dividend Date" of the Clause A Distribution and the Clause B Distribution shall be deemed to be the Ex-Dividend Date of the Clause C Distribution and (II) any shares of Common Stock included in the Clause A Distribution or Clause B Distribution shall be deemed not to be "outstanding immediately prior to the open of business on such Ex-Dividend Date or Effective Date" within the meaning of Section 14.04(a) or "outstanding immediately prior to the open of business on such Ex-Dividend Date" within the meaning of Section 14.04(b).

(d) If the Company pays or makes any cash dividend or distribution to all or substantially all holders of the Common Stock, the Conversion Rate shall be adjusted based on the following formula:

$$CR' = CR_0 \times \frac{SP_0}{SP_0 - C}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the open of business on the Ex-Dividend Date for such dividend or distribution;

CR' = the Conversion Rate in effect immediately after the open of business on the Ex-Dividend Date for such dividend or distribution;

SP_0 = the Last Reported Sale Price of the Common Stock on the Trading Day immediately preceding the Ex-Dividend Date for such dividend or distribution; and

C = the amount in cash per share the Company dividends or distributes to all or substantially all holders of the Common Stock.

Any increase pursuant to this Section 14.04(d) shall become effective immediately after the open of business on the Ex-Dividend Date for such dividend or distribution. If such dividend or distribution is not so paid, the Conversion Rate shall be decreased, effective as of the date the Board of Directors determines not to make or pay such dividend or distribution, to be the Conversion Rate that would then be in effect if such dividend or distribution had not been declared. Notwithstanding the foregoing, if "C" (as defined

above) is equal to or greater than "SP_0" (as defined above), in lieu of the foregoing increase, each Holder of a Note shall receive, for each $1,000 principal amount of Notes it holds, at the same time and upon the same terms as holders of shares of the Common Stock, the amount of cash that such Holder would have received if such Holder owned a number of shares of Common Stock equal to the Conversion Rate in effect on the Ex-Dividend Date for such cash dividend or distribution.

(e) If the Company or any of its Subsidiaries make a payment in respect of a tender or exchange offer for the Common Stock that is subject to the then-applicable tender offer rules under the Exchange Act (other than an odd lot tender offer), to the extent that the cash and value of any other consideration included in the payment per share of the Common Stock exceeds the average of the Last Reported Sale Prices of the Common Stock over the 10 consecutive Trading Day period commencing on, and including, the Trading Day next succeeding the last date on which tenders or exchanges may be made pursuant to such tender or exchange offer, the Conversion Rate shall be increased based on the following formula:

$$CR' = CR_0 \times \frac{AC + (SP' \times OS')}{OS_0 \times SP'}$$

where,

CR_0 = the Conversion Rate in effect immediately prior to the close of business on the 10th Trading Day immediately following, and including, the Trading Day next succeeding the date such tender or exchange offer expires (the date such tender offer or exchange offer expires, the "**Expiration Date**");

CR' = the Conversion Rate in effect immediately after the close of business on the 10th Trading Day immediately following, and including, the Trading Day next succeeding the Expiration Date;

AC = the aggregate value of all cash and any other consideration (as determined by the Company in good faith) paid or payable for shares of Common Stock purchased in such tender or exchange offer;

OS_0 = the number of shares of Common Stock outstanding immediately prior to the Expiration Date (prior to giving effect to the purchase of all shares of Common Stock accepted for purchase or exchange in such tender or exchange offer);

OS' = the number of shares of Common Stock outstanding immediately after the Expiration Date (after giving effect to the purchase of all shares of Common Stock accepted for purchase or exchange in such tender or exchange offer); and

SP' = the average of the Last Reported Sale Prices of the Common Stock over the 10 consecutive Trading Day period commencing on, and including, the Trading Day next succeeding the Expiration Date.

The increase to the Conversion Rate under this Section 14.04(e) shall occur at the close of business on the 10th Trading Day immediately following, and including, the Trading Day next succeeding the date such tender or exchange offer expires; *provided* that (x) in respect of any conversion of Notes for which Physical Settlement is applicable, if the relevant Conversion Date occurs during the 10 Trading Days immediately following, and including, the Trading Day next succeeding the Expiration Date of any tender or exchange offer, references to "10" or "10th" in the preceding paragraph shall be deemed replaced with such lesser number of Trading Days as have elapsed from, and including, the Trading Day next succeeding the Expiration Date of such tender or exchange offer to, and including, the Conversion Date in determining the Conversion Rate and (y) in respect of any conversion of Notes for which Cash Settlement or Combination Settlement is applicable, for any Trading Day that falls within the relevant Observation Period for such conversion and within the 10 Trading Days immediately following, and including, the Trading Day next succeeding the Expiration Date of any tender or exchange offer, references to "10" or "10th" in the preceding paragraph shall be deemed replaced with such lesser number of Trading Days as have elapsed from, and including, the Trading Day next succeeding the Expiration Date of such tender or exchange offer to, and including, such Trading Day in determining the Conversion Rate as of such Trading Day.

In the event that the Company or one of its Subsidiaries is obligated to purchase shares of Common Stock pursuant to any such tender offer or exchange offer, but the Company is, or such Subsidiary is, permanently prevented by applicable law from consummating any such purchases, or all such purchases are rescinded, then the Conversion Rate shall be decreased to be the Conversion Rate that would then be in effect if such tender offer or exchange offer had not been made or had been made only in respect of the purchases that have been consummated.

(f) Notwithstanding this Section 14.04 or any other provision of this Indenture or the Notes, if a Conversion Rate adjustment becomes effective on any Ex-Dividend Date, and a Holder that has converted its Notes on or after such Ex-Dividend Date and on or prior to the related Record Date would be treated as the record holder of the shares of Common Stock as of the related Conversion Date as described under Section 14.02(i) based on an adjusted Conversion Rate for such Ex-Dividend Date, then, notwithstanding the Conversion Rate adjustment provisions in this Section 14.04, the Conversion Rate adjustment relating to such Ex-Dividend Date shall not be made for such converting Holder. Instead, such Holder shall be treated as if such Holder were the record owner of the shares of Common Stock on an unadjusted basis and participate in the related dividend, distribution or other event giving rise to such adjustment.

(g) Except as stated herein, the Company shall not adjust the Conversion Rate for the issuance of shares of the Common Stock or any securities convertible into or

exchangeable for shares of the Common Stock or the right to purchase shares of the Common Stock or such convertible or exchangeable securities.

(h) In addition to those adjustments required by clauses (a), (b), (c), (d) and (e) of this Section 14.04, and to the extent permitted by applicable law and subject to the applicable rules of The Nasdaq Global Select Market, the Company from time to time may increase the Conversion Rate by any amount for a period of at least 20 Business Days if the Board of Directors determines that such increase would be in the Company's best interest. In addition, to the extent permitted by applicable law and subject to the applicable rules of The Nasdaq Global Select Market, the Company may (but is not required to) increase the Conversion Rate to avoid or diminish any income tax to holders of Common Stock or rights to purchase Common Stock in connection with a dividend or distribution of shares of Common Stock (or rights to acquire shares of Common Stock) or similar event. Whenever the Conversion Rate is increased pursuant to either of the preceding two sentences, the Company shall deliver to the Holder of each Note a notice of the increase at least 15 days prior to the date the increased Conversion Rate takes effect, and such notice shall state the increased Conversion Rate and the period during which it will be in effect.

(i) Except as stated in this Indenture, the Company shall not adjust the Conversion Rate for the issuance of shares of Common Stock or any securities convertible into or exchangeable for shares of Common Stock or the right to purchase shares of Common Stock or such convertible or exchangeable securities. For illustrative purposes only and without limiting the generality of the preceding sentence, the Conversion Rate shall not be adjusted:

(i) upon the issuance of shares of Common Stock at a price below the Conversion Price or otherwise, other than any such issuance described in Section 14.04(a), Section 14.04(b), Section 14.04(c) or Section 14.04(e);

(ii) upon the issuance of any shares of Common Stock pursuant to any present or future plan providing for the reinvestment of dividends or interest payable on the Company's securities and the investment of additional optional amounts in shares of Common Stock under any plan;

(iii) upon the issuance of any shares of Common Stock or options or rights to purchase those shares pursuant to any present or future employee, director or consultant benefit plan or program of or assumed by the Company or any of the Company's Subsidiaries;

(iv) upon the issuance of any shares of the Common Stock pursuant to any option, warrant, right or exercisable, exchangeable or convertible security not described in clause (iii) of this subsection and outstanding as of the date the Notes were first issued;

(v) upon the repurchase of any shares of Common Stock pursuant to an open market share repurchase program or other buy-back transaction, including

structured or derivative transactions, that is not a tender or exchange offer described in Section 14.04(e);

(vi) solely for a change in the par value (or lack of par value) of the Common Stock; or

(vii) for accrued and unpaid interest, if any.

(j) All calculations and other determinations under this Article 14 shall be made by the Company and shall be made to the nearest one-ten thousandth (1/10,000th) of a share.

(k) If an adjustment to the Conversion Rate otherwise required by the provisions of this Section 14.04 would result in a change of less than 1% to the Conversion Rate, then, notwithstanding the foregoing, the Company may, at its election, defer and carry forward such adjustment, except that all such deferred adjustments must be given effect immediately upon the occurrence of any of the following:

(i) when all such deferred adjustments would result in an aggregate change of at least 1% to the Conversion Rate;

(ii) on the Conversion Date for any Notes (in the case of Physical Settlement);

(iii) on each Trading Day of any Observation Period related to any conversion of Notes (in the case of Cash Settlement or Combination Settlement);

(iv) on any date on which the Company delivers a Redemption Notice;

(v) on the effective date of any Fundamental Change and/or the Effective Date of any Make-Whole Fundamental Change; and

(vi) on June 15, 2027.

The provisions of this Section 14.04(k) are referred to herein as the "**1% Provision**."

(l) Whenever the Conversion Rate is adjusted as herein provided, the Company shall promptly file with the Trustee (and the Conversion Agent if not the Trustee) an Officer's Certificate setting forth the Conversion Rate after such adjustment and setting forth a brief statement of the facts requiring such adjustment. Unless and until a Responsible Officer of the Trustee shall have received such Officer's Certificate, the Trustee shall not be deemed to have knowledge of any adjustment of the Conversion Rate and may assume without inquiry that the last Conversion Rate of which it has knowledge is still in effect. Promptly after delivery of such certificate, the Company shall prepare a written notice of such adjustment of the Conversion Rate setting forth the adjusted Conversion Rate and the date on which each adjustment becomes effective and shall deliver such notice of such adjustment of the Conversion Rate to each Holder (with

a copy to the Trustee). Failure to deliver such notice shall not affect the legality or validity of any such adjustment.

(m) For purposes of this Section 14.04, the number of shares of Common Stock at any time outstanding shall not include shares of Common Stock held in the treasury of the Company so long as the Company does not pay any dividend or make any distribution on shares of Common Stock held in the treasury of the Company, but shall include shares of Common Stock issuable in respect of scrip certificates issued in lieu of fractions of shares of Common Stock.

Section 14.05. *Adjustments of Prices.* Whenever any provision of this Indenture requires the Company to calculate the Last Reported Sale Prices, the Daily VWAPs, the Daily Conversion Values or the Daily Settlement Amounts over a span of multiple days (including an Observation Period and the period for determining the Stock Price for purposes of a Make-Whole Fundamental Change or Redemption Notice), the Company shall make appropriate adjustments in good faith (without duplication in respect of any adjustment made pursuant to Section 14.04) to each to account for any adjustment to the Conversion Rate that becomes effective, or any event requiring an adjustment to the Conversion Rate where the Ex-Dividend Date, Effective Date or Expiration Date, as the case may be, of the event occurs, at any time during the period when the Last Reported Sale Prices, the Daily VWAPs, the Daily Conversion Values or the Daily Settlement Amounts are to be calculated.

Section 14.06. *Shares to Be Fully Paid.* The Company shall reserve, free from preemptive rights, out of its authorized but unissued shares or shares held in treasury, sufficient shares of Common Stock to provide for conversion of the Notes from time to time as such Notes are presented for conversion (assuming delivery of the maximum number of Additional Shares pursuant to Section 14.03 and that at the time of computation of such number of shares, all such Notes would be converted by a single Holder and that Physical Settlement were applicable).

Section 14.07. *Effect of Recapitalizations, Reclassifications and Changes of the Common Stock*.

(a) In the case of:

(i) any recapitalization, reclassification or change of the Common Stock (other than changes in par value or resulting from a subdivision or combination),

(ii) any consolidation, merger or combination involving the Company,

(iii) any sale, lease or other transfer to a third party of all or substantially all of the consolidated assets of the Company and the Company's Subsidiaries, taken as a whole, or

(iv) any statutory share exchange,

in each case, as a result of which the Common Stock would be converted into, or exchanged for, stock, other securities, other property or assets (including cash or any combination thereof) (any such event, a "**Share Exchange Event**"), then at and after the effective time of such Share Exchange Event, the right to convert each $1,000 principal amount of Notes shall be changed into a right to convert such principal amount of Notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) that a holder of a number of shares of Common Stock equal to the Conversion Rate immediately prior to such Share Exchange Event would have owned or been entitled to receive (the "**Reference Property**," with each "**unit of Reference Property**" meaning the kind and amount of Reference Property that a holder of one share of Common Stock is entitled to receive) upon such Share Exchange Event and, prior to or at the effective time of such Share Exchange Event, the Company or the successor or acquiring company, as the case may be, shall execute with the Trustee a supplemental indenture permitted under Section 10.01(g) providing for such change in the right to convert each $1,000 principal amount of Notes; *provided*, *however*, that at and after the effective time of the Share Exchange Event (A) the Company or the successor or acquiring company, as the case may be, shall continue to have the right to determine the form of consideration to be paid or delivered, as the case may be, upon conversion of Notes in accordance with Section 14.02 and (B) (I) any amount payable in cash upon conversion of the Notes in accordance with Section 14.02 shall continue to be payable in cash, (II) any shares of Common Stock that the Company would have been required to deliver upon conversion of the Notes in accordance with Section 14.02 shall instead be deliverable in the amount and type of Reference Property that a holder of that number of shares of Common Stock would have been entitled to receive in such Share Exchange Event and (III) the Daily VWAP shall be calculated based on the value of a unit of Reference Property.

If the Share Exchange Event causes the Common Stock to be converted into, or exchanged for, the right to receive more than a single type of consideration (determined based in part upon any form of stockholder election), then (i) the Reference Property into which the Notes will be convertible shall be deemed to be the weighted average of the types and amounts of consideration actually received by the holders of Common Stock, and (ii) the unit of Reference Property for purposes of the immediately preceding paragraph shall refer to the consideration referred to in clause (i) attributable to one share of Common Stock. If the holders of the Common Stock receive only cash in such Share Exchange Event, then for all conversions for which the relevant Conversion Date occurs after the effective date of such Share Exchange Event (A) the consideration due upon conversion of each $1,000 principal amount of Notes shall be solely cash in an amount equal to the Conversion Rate in effect on the Conversion Date (as may be increased by any Additional Shares pursuant to Section 14.03), *multiplied by* the price paid per share of Common Stock in such Share Exchange Event and (B) the Company shall satisfy the Conversion Obligation by paying such cash amount to converting Holders on the second Business Day immediately following the relevant Conversion Date. The Company shall notify Holders, the Trustee and the Conversion Agent (if other than the Trustee) of such weighted average as soon as reasonably practicable after such determination is made.

If the Reference Property in respect of any Share Exchange Event includes, in whole or in part, shares of common equity, such supplemental indenture described in the second immediately preceding paragraph shall provide for anti-dilution and other adjustments that shall be as nearly equivalent as is possible to the adjustments provided for in this Article 14 with respect to the portion of the Reference Property consisting of such common equity. If, in the case of any Share Exchange Event, the Reference Property includes shares of stock, securities or other property or assets (other than cash and/or cash equivalents) of a Person other than the successor or purchasing company, as the case may be, in such Share Exchange Event, then such supplemental indenture shall also be executed by such other Person, if such other Person is an affiliate of the Company or the successor or acquiring company, and shall contain such additional provisions to protect the interests of the Holders of the Notes as the Company in good faith reasonably considers necessary by reason of the foregoing, including the provisions providing for the purchase rights set forth in Article 15.

(b) When the Company executes a supplemental indenture pursuant to subsection (a) of this Section 14.07, the Company shall promptly file with the Trustee an Officer's Certificate briefly stating the reasons therefor, the kind or amount of cash, securities or property or asset that will comprise a unit of Reference Property after any such Share Exchange Event, any adjustment to be made with respect thereto and that all conditions precedent have been complied with, and shall promptly deliver notice thereof to all Holders. The Company shall cause notice of the execution of such supplemental indenture to be delivered to each Holder within 20 days after execution thereof. Failure to deliver such notice shall not affect the legality or validity of such supplemental indenture.

(c) The Company shall not become a party to any Share Exchange Event unless its terms are consistent with this Section 14.07. None of the foregoing provisions shall affect the right of a holder of Notes to convert its Notes into cash, shares of Common Stock or a combination of cash and shares of Common Stock, as applicable, as set forth in Section 14.01 and Section 14.02 prior to the effective date of such Share Exchange Event.

(d) The above provisions of this Section shall similarly apply to successive Share Exchange Events.

Section 14.08. *Certain Covenants.* (a) Subject to Sections 14.02(d) and 14.02(e), the Company covenants that all shares of Common Stock issued upon conversion of Notes will be fully paid and non-assessable by the Company and free from all taxes, liens and charges with respect to the issue thereof.

(b) The Company covenants that, if any shares of Common Stock to be provided for the purpose of conversion of Notes hereunder require registration with or approval of any governmental authority under any federal or state law before such shares of Common Stock may be validly issued upon conversion, the Company will, to the extent then permitted by the rules and interpretations of the Commission, secure such registration or approval, as the case may be.

(c) The Company further covenants that if at any time the Common Stock shall be listed on any national securities exchange or automated quotation system the Company will list and use its commercially reasonable efforts to keep listed, so long as the Common Stock shall be so listed on such exchange or automated quotation system, any Common Stock issuable upon conversion of the Notes.

Section 14.09. *Responsibility of Trustee.* The Trustee and any other Conversion Agent shall not at any time be under any duty or responsibility to any Holder to determine the Conversion Rate (or any adjustment thereto) or whether any facts exist that may require any adjustment (including any increase) of the Conversion Rate, or with respect to the nature or extent or calculation of any such adjustment when made, or with respect to the method employed, or herein or in any supplemental indenture provided to be employed, in making the same. The Trustee and any other Conversion Agent shall not be accountable with respect to the validity or value (or the kind or amount) of any shares of Common Stock, or of any securities, property or cash that may at any time be issued or delivered upon the conversion of any Note; and the Trustee and any other Conversion Agent make no representations with respect thereto. Neither the Trustee nor any Conversion Agent shall be responsible for any failure of the Company to issue, transfer or deliver any shares of Common Stock or stock certificates or other securities or property or cash upon the surrender of any Note for the purpose of conversion or to comply with any of the duties, responsibilities or covenants of the Company contained in this Article. Without limiting the generality of the foregoing, neither the Trustee nor any Conversion Agent shall be under any responsibility to determine the correctness of any provisions contained in any supplemental indenture entered into pursuant to Section 14.07 relating either to the kind or amount of shares of stock or securities or property (including cash) receivable by Holders upon the conversion of their Notes after any event referred to in such Section 14.07 or to any adjustment to be made with respect thereto, but, subject to the provisions of Section 7.01, may accept (without any independent investigation) as conclusive evidence of the correctness of any such provisions, and shall be protected in conclusively relying upon, the Officer's Certificate (which the Company shall be obligated to file with the Trustee prior to the execution of any such supplemental indenture) with respect thereto. Neither the Trustee nor the Conversion Agent shall be responsible for determining whether any event contemplated by Section 14.01(b) has occurred that makes the Notes eligible for conversion or no longer eligible therefor. The Trustee and the Conversion Agent may conclusively rely upon any notice with respect to the commencement or termination of such conversion rights, and the Company agrees to deliver such notices to the Trustee and the Conversion Agent immediately after the occurrence of any such event or at such other times as shall be provided for in Section 14.01(b). Neither the Trustee nor any agent acting under this Indenture (other than the Company, if acting in such capacity) shall have any obligation to make any calculation or determine whether the Notes may be surrendered for conversion pursuant to this Indenture, or to notify the Company or the Depositary or any Holders if the Notes have become convertible pursuant to the terms of this Indenture.

Section 14.10. *Notice to Holders Prior to Certain Actions*. In case of any:

(a) action by the Company or one of its Subsidiaries that would require an adjustment in the Conversion Rate pursuant to Section 14.04 or Section 14.11;

(b) Share Exchange Event; or

(c) voluntary or involuntary dissolution, liquidation or winding-up of the Company;

then, in each case (unless notice of such event is otherwise required pursuant to another provision of this Indenture) and to the extent applicable, the Company shall cause to be delivered to the Trustee and the Conversion Agent (if other than the Trustee) and to be delivered to each Holder, a notice stating the date on which a record is to be taken for the purpose of such action by the Company or one of its Subsidiaries or, if a record is not to be taken, the date as of which the holders of Common Stock of record are to be determined for the purposes of such action by the Company or one of its Subsidiaries no later than the earlier of the date notice of such date is required to be provided under Rule 10b-17 of the Exchange Act, other applicable Commission rule or applicable rules of the principal U.S. national or regional securities exchange on which the Common Stock is then listed or admitted for trading and such date is publicly announced by the Company. Failure to give such notice, or any defect therein, shall not affect the legality or validity of such action by the Company or one of its Subsidiaries, Share Exchange Event, dissolution, liquidation or winding-up.

Section 14.11. *Stockholder Rights Plans.* If the Company has a stockholder rights plan in effect upon conversion of the Notes, each share of Common Stock, if any, issued upon such conversion shall be entitled to receive the appropriate number of rights, if any, under such stockholder rights plan and the certificates representing the Common Stock issued upon such conversion shall bear such legends, if any, in each case as may be provided by the terms of any such stockholder rights plan, as the same may be amended from time to time. However, if, prior to any conversion of Notes, the rights have separated from the shares of Common Stock in accordance with the provisions of the applicable stockholder rights plan, the Conversion Rate shall be adjusted at the time of separation as if the Company distributed to all or substantially all holders of the Common Stock Distributed Property as provided in Section 14.04(c), subject to readjustment in the event of the expiration, termination or redemption of such rights.

Section 14.12. *Exchange in Lieu of Conversion.* When a Holder surrenders its Notes for conversion, the Company may, at its election (an "**Exchange Election**"), cause the Notes to be delivered, on or prior to the close of business on the Trading Day following the Conversion Date, to a financial institution designated by the Company for exchange in lieu of conversion. In order to accept any Notes surrendered for conversion, the designated financial institution must agree to timely deliver, in exchange for such Notes, the cash, shares of Common Stock or combination thereof due upon conversion as described in Section 14.02. If the Company makes an Exchange Election, the Company shall, by the close of business on the Trading Day following the relevant Conversion Date, notify the Holder surrendering its Notes for conversion, the Trustee and the Conversion Agent (if other than the Trustee) in writing that it has made the Exchange

Election, and the Company shall notify the designated financial institution of the Settlement Method it has elected with respect to such conversion and the relevant deadline for payment and/or delivery of cash, shares of Common Stock or a combination thereof due upon conversion.

The Company and the Conversion Agent shall cooperate to cause such Notes to be delivered to the designated financial institution and the Conversion Agent shall be entitled to conclusively rely on the Company's instruction in connection with effecting any Exchange Election and shall have no liability for such Exchange Election outside of its control.

Any Notes exchanged by the designated financial institution shall remain outstanding, notwithstanding the surrender of such Notes and will be subject to the Applicable Procedures. If the designated financial institution agrees to accept any Notes for exchange but does not timely pay and/or deliver the required cash, shares of Common Stock or a combination thereof due upon conversion, or if such designated financial institution does not accept the Notes for exchange, the Company shall notify the Trustee, the Conversion Agent (if other than the Trustee) and the Holder surrendering its Notes for conversion in writing and shall pay and/or deliver the required cash, shares of Common Stock or a combination thereof due upon conversion to the converting Holder at the time and in the manner required under this Indenture as if the Company had not made an Exchange Election.

The Company's designation of a financial institution to which the Notes may be submitted for exchange does not require that financial institution to accept any Notes (unless the financial institution has separately made an agreement with the Company). The Company may, but shall not be obligated to, enter into a separate agreement with any designated financial institution that would compensate it for any such transaction.

ARTICLE 15
REPURCHASE OF NOTES AT OPTION OF HOLDERS

Section 15.01. [Intentionally Omitted].

Section 15.02. *Repurchase at Option of Holders Upon a Fundamental Change.* (a) If a Fundamental Change (other than an Exempted Fundamental Change) occurs at any time, each Holder shall have the right, at such Holder's option, to require the Company to repurchase for cash all of such Holder's Notes, or any portion of the principal amount thereof that is equal to $1,000 or an integral multiple of $1,000, on the date (the "**Fundamental Change Repurchase Date**") specified by the Company that is not less than 20 Business Days or more than 35 Business Days following the date of the Fundamental Change Company Notice at a repurchase price equal to 100% of the principal amount thereof, *plus* accrued and unpaid interest thereon to, but excluding, the Fundamental Change Repurchase Date (the "**Fundamental Change Repurchase Price**"), unless the Fundamental Change Repurchase Date falls after a Regular Record Date but on or prior to the Interest Payment Date to which such Regular Record Date relates, in which case the Company shall instead pay the full amount of accrued and

unpaid interest (to, but not including, such Interest Payment Date) to Holders of record as of such Regular Record Date, and the Fundamental Change Repurchase Price shall be equal to 100% of the principal amount of Notes to be repurchased pursuant to this Article 15. The Fundamental Change Repurchase Date shall be subject to postponement in order to allow the Company to comply with applicable law.

(b) Repurchases of Notes under this Section 15.02 shall be made, at the option of the Holder thereof, upon:

(i) delivery to the Paying Agent or the tender agent appointed to facilitate the repurchase by a Holder of a duly completed notice (the "**Fundamental Change Repurchase Notice**") in the form set forth in Attachment 2 to the Form of Note attached hereto as Exhibit A, if the Notes are Physical Notes, or in compliance with the Applicable Procedures for surrendering interests in Global Notes, if the Notes are Global Notes, in each case on or before the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date; and

(ii) delivery of the Notes, if the Notes are Physical Notes, to the Paying Agent at any time after delivery of the Fundamental Change Repurchase Notice (together with all necessary endorsements for transfer) at the office of the Paying Agent, or book-entry transfer of the Notes, if the Notes are Global Notes, in compliance with the procedures of the Depositary, in each case such delivery being a condition to receipt by the Holder of the Fundamental Change Repurchase Price therefor.

The Fundamental Change Repurchase Notice in respect of any Notes to be repurchased shall state:

(i) in the case of Physical Notes, the certificate numbers of the Notes to be delivered for repurchase;

(ii) the portion of the principal amount of Notes to be repurchased, which must be $1,000 or an integral multiple thereof; and

(iii) that the Notes are to be repurchased by the Company pursuant to the applicable provisions of the Notes and this Indenture;

provided, *however*, that if the Notes are Global Notes, the Fundamental Change Repurchase Notice must comply with the Applicable Procedures.

Notwithstanding anything herein to the contrary, any Holder delivering to the Paying Agent or tender agent the Fundamental Change Repurchase Notice contemplated by this Section 15.02 shall have the right to withdraw, in whole or in part, such Fundamental Change Repurchase Notice at any time prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date by delivery of a written notice of withdrawal to the Paying Agent or tender agent in accordance with Section 15.03.

The Paying Agent shall promptly notify the Company of the receipt by it of any Fundamental Change Repurchase Notice or written notice of withdrawal thereof.

(c) On or before the 20th Business Day after the occurrence of the effective date of a Fundamental Change, the Company shall provide to all Holders of Notes, the Trustee, the Conversion Agent (if other than the Trustee) and the Paying Agent (in the case of a Paying Agent other than the Trustee) a notice (the "**Fundamental Change Company Notice**") of the occurrence of the effective date of the Fundamental Change and of the repurchase right at the option of the Holders arising as a result thereof. In the case of Physical Notes, such notice shall be by first class mail or, in the case of Global Notes, such notice shall be delivered in accordance with the Applicable Procedures of the Depositary. Each Fundamental Change Company Notice shall specify:

(i) the events causing the Fundamental Change;

(ii) the effective date of the Fundamental Change;

(iii) the last date on which a Holder may exercise the repurchase right pursuant to this Article 15;

(iv) the Fundamental Change Repurchase Price;

(v) the Fundamental Change Repurchase Date;

(vi) the name and address of the Paying Agent and the Conversion Agent, if applicable;

(vii) if applicable, the Conversion Rate and any adjustments to the Conversion Rate as a result of the related Make-Whole Fundamental Change and/or the 1% Provision;

(viii) that the Notes with respect to which a Fundamental Change Repurchase Notice has been delivered by a Holder may be converted only if the Holder withdraws the Fundamental Change Repurchase Notice in accordance with the terms of this Indenture; and

(ix) the procedures that Holders must follow to require the Company to repurchase their Notes.

No failure of the Company to give the foregoing notices and no defect therein shall limit the Holders' repurchase rights or affect the validity of the proceedings for the repurchase of the Notes pursuant to this Section 15.02.

At the Company's written request, given at least five days prior to the date the Fundamental Change Company Notice is to be sent, the Paying Agent shall give such notice in the Company's name and at the Company's expense; *provided*, *however*, that, in all cases, the text of such Fundamental Change Company Notice shall be prepared by the Company.

(d) Notwithstanding the foregoing, no Notes may be repurchased by the Company on any date at the option of the Holders in connection with a Fundamental Change if the principal amount of the Notes has been accelerated, and such acceleration has not been rescinded, on or prior to such date (except in the case of an acceleration resulting from a Default by the Company in the payment of the Fundamental Change Repurchase Price with respect to such Notes). The Paying Agent will promptly return to the respective Holders thereof any Physical Notes held by it during the acceleration of the Notes (except in the case of an acceleration resulting from a Default by the Company in the payment of the Fundamental Change Repurchase Price with respect to such Notes), or any instructions for book-entry transfer of the Notes in compliance with the Applicable Procedures shall be deemed to have been cancelled, and, upon such return or cancellation, as the case may be, the Fundamental Change Repurchase Notice with respect thereto shall be deemed to have been withdrawn.

(e) Notwithstanding anything to the contrary in this Indenture, the Company shall not be required to repurchase, or to make an offer to repurchase, the Notes upon a Fundamental Change if a third party makes such an offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by the Company as set forth in this Article 15, and such third party purchases all Notes properly surrendered and not validly withdrawn under its offer in the same manner, at the same time and otherwise in compliance with the requirements for an offer made by the Company as set forth in this Article 15.

(f) Notwithstanding anything to the contrary in this Article 15, the Company shall not be required to send a Fundamental Change Company Notice, or offer to repurchase or repurchase Notes in connection with a Fundamental Change occurring pursuant to clause (b)(A) or (b)(B) (or pursuant to clause (a) or (d) that also constitutes a Fundamental Change occurring pursuant to clause (b)(A) or (b)(B)) of the definition thereof, if:

(i) such Fundamental Change constitutes a Share Exchange Event for which the Reference Property consists entirely of cash in U.S. dollars;

(ii) immediately after such Fundamental Change, the Notes become convertible (pursuant to the provisions described in Section 14.07 and, if applicable, Section 14.03) into consideration that consists solely of U.S. dollars in an amount per $1,000 principal amount of Notes that equals or exceeds the Fundamental Change Repurchase Price per $1,000 principal amount of the Notes (calculated assuming that the same includes the maximum amount of accrued but unpaid interest payable as part of the Fundamental Change Repurchase Price for such Fundamental Change); and

(iii) the Company timely sends notice of such Fundamental Change pursuant to Section 14.01(b)(iv).

(g) For purposes of this Article 15, the Paying Agent may be any agent, depositary, tender agent, paying agent or other agent appointed by the Company to accomplish the purposes set forth herein.

Section 15.03. *Withdrawal of Fundamental Change Repurchase Notice.* (a) A Fundamental Change Repurchase Notice may be withdrawn (in whole or in part) by means of a written notice of withdrawal delivered to the office of the Paying Agent in accordance with this Section 15.03 at any time prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date, specifying:

(i) the principal amount of the Notes with respect to which such notice of withdrawal is being submitted, which must be $1,000 or an integral multiple thereof,

(ii) if Physical Notes have been issued, the certificate number of the Note in respect of which such notice of withdrawal is being submitted, and

(iii) the principal amount, if any, of such Note that remains subject to the original Fundamental Change Repurchase Notice, which portion must be in principal amounts of $1,000 or an integral multiple of $1,000;

provided, *however*, that if the Notes are Global Notes, the notice of withdrawal must comply with appropriate procedures of the Depositary.

Section 15.04. *Deposit of Fundamental Change Repurchase Price.* (a) The Company will deposit with the Paying Agent, or if the Company is acting as its own Paying Agent, set aside, segregate and hold in trust as provided in Section 4.04) on or prior to 11:00 a.m., New York City time, on the Fundamental Change Repurchase Date (subject to extension in order to allow the Company to comply with applicable law) an amount of money sufficient to repurchase all of the Notes to be repurchased at the appropriate Fundamental Change Repurchase Price. Subject to receipt of funds and/or Notes by the Paying Agent, payment for Notes surrendered for repurchase (and not withdrawn prior to the close of business on the Business Day immediately preceding the Fundamental Change Repurchase Date) will be made on the later of (i) the Fundamental Change Repurchase Date (*provided* the Holder has satisfied the conditions in Section 15.02) and (ii) the time of book-entry transfer or the delivery of such Note to the Paying Agent by the Holder thereof in the manner required by Section 15.02 by mailing checks for the amount payable to the Holders of such Notes entitled thereto as they shall appear in the Note Register; *provided*, *however*, that payments to the Depositary shall be made by wire transfer of immediately available funds to the account of the Depositary or its nominee. The Paying Agent shall, promptly after such payment and upon written demand by the Company, return to the Company any funds in excess of the Fundamental Change Repurchase Price.

(b) If by 11:00 a.m. New York City time, on the Fundamental Change Repurchase Date, the Paying Agent or tender agent holds money sufficient to make

payment on all the Notes or portions thereof that are to be repurchased on such Fundamental Change Repurchase Date, or, if extended in order to allow the Company to comply with applicable law, such later date, then, with respect to the Notes that have been properly surrendered for repurchase and have not been validly withdrawn, (i) such Notes will cease to be outstanding, (ii) interest will cease to accrue on such Notes on the Fundamental Change Repurchase Date or, if extended in order to allow the Company to comply with applicable law, such later date (whether or not book-entry transfer of the Notes has been made or the Notes have been delivered to the Paying Agent) and (iii) all other rights of the Holders of such Notes with respect to the Notes will terminate on the Fundamental Change Repurchase Date or, if extended in order to allow the Company to comply with applicable law, such later date (other than (x) the right to receive the Fundamental Change Repurchase Price and (y) if the Fundamental Change Repurchase Date falls after a Regular Record Date but on or prior to the related Interest Payment Date, the right of the Holder of record on such Regular Record Date to receive the full amount of accrued and unpaid interest, if any, to, but not including, such Interest Payment Date).

(c) Upon surrender of a Physical Note that is to be repurchased in part pursuant to Section 15.02, the Company shall execute and the Trustee shall authenticate and deliver to the Holder a new Physical Note in an authorized denomination equal in principal amount to the unrepurchased portion of the Physical Note surrendered.

Section 15.05. *Covenant to Comply with Applicable Laws Upon Repurchase of Notes*. In connection with any repurchase offer, the Company will, if required:

(a) comply with the tender offer rules under the Exchange Act;

(b) file a Schedule TO or any other required schedule under the Exchange Act; and

(c) otherwise comply in all material respects with all federal and state securities laws in connection with any offer by the Company to repurchase the Notes;

in each case, so as to permit the rights and obligations under this Article 15 to be exercised in the time and in the manner specified in this Article 15 subject to postponement in order to allow the Company to comply with applicable law. To the extent that the provisions of any securities laws or regulations conflict with the provisions of this Indenture relating to the Company's obligations to purchase the Notes upon a Fundamental Change, the Company will comply with the applicable securities laws and regulations and will not be deemed to have breached the Company's obligations under such provisions of this Indenture by virtue of such conflict.

ARTICLE 16
OPTIONAL REDEMPTION

Section 16.01. *Optional Redemption*. No sinking fund is provided for the Notes, which means that the Company is not required to redeem or retire the Notes periodically.

The Notes shall not be redeemable by the Company prior to September 20, 2025. On or after September 20, 2025, the Company may redeem (an "**Optional Redemption**") for cash all or any portion of the Notes (subject to the Partial Redemption Limitation), at the Redemption Price, if the Last Reported Sale Price of the Common Stock has been at least 130% of the Conversion Price then in effect for at least 20 Trading Days (whether or not consecutive), including the Trading Day immediately preceding the date on which the Company provides the Redemption Notice in accordance with Section 16.02, during any 30 consecutive Trading Day period ending on, and including, the Trading Day immediately preceding the date on which the Company provides the Redemption Notice in accordance with Section 16.02.

Section 16.02. *Notice of Optional Redemption; Selection of Notes*. (a) In case the Company exercises its Optional Redemption right to redeem all or, as the case may be, any part of the Notes pursuant to Section 16.01, it shall fix a date for redemption (each, a "**Redemption Date**") and it or, at its written request received by the Trustee not less than five Business Days prior to the date such Redemption Notice is to be sent (or such shorter period of time as may be acceptable to the Trustee), the Trustee, in the name of and at the expense of the Company, shall deliver or cause to be delivered a notice of such Optional Redemption (a "**Redemption Notice**") not less than 25 nor more than 45 Scheduled Trading Days prior to the Redemption Date (*provided* that if, in accordance with the provisions described in Section 14.02, the Company elects to settle all conversions of Notes called for redemption (or deemed called for redemption as described in Section 14.01(b)(ii)) with a Conversion Date that occurs during the related Redemption Period by Physical Settlement, then the Company shall provide not less than 10 nor more than 45 Scheduled Trading Days' notice before the Redemption Date) to the Trustee, the Conversion Agent (if other than the Trustee), the Paying Agent (if other than the Trustee) and each Holder of Notes. The Redemption Date must be a Business Day, and the Company shall not specify a Redemption Date that falls on or after the 21st Scheduled Trading Day immediately preceding the Maturity Date.

(b) The Redemption Notice shall be delivered in accordance with applicable procedures of the Depositary (if the Notes to be redeemed are Global Notes), and, if delivered in the manner herein provided, shall be conclusively presumed to have been duly given, whether or not the Holder receives such notice. In any case, failure to give such Redemption Notice by mail or any defect in the Redemption Notice to the Holder of any Note designated for redemption as a whole or in part shall not affect the validity of the proceedings for the redemption of any other Note.

(c) Each Redemption Notice shall specify:

(i) the Redemption Date;

(ii) the Redemption Price;

(iii) that on the Redemption Date, the Redemption Price will become due and payable upon each Note to be redeemed, and that interest thereon, if any, shall cease to accrue on and after the Redemption Date;

(iv) the place or places where such Notes are to be surrendered for payment of the Redemption Price;

(v) that Holders may surrender their Notes for conversion at any time prior to the close of business on the second Scheduled Trading Day immediately preceding the Redemption Date;

(vi) the procedures a converting Holder must follow to convert its Notes and the Settlement Method and Specified Dollar Amount, if applicable;

(vii) the Conversion Rate and, if applicable, the number of Additional Shares added to the Conversion Rate in accordance with Section 14.03;

(viii) the CUSIP, ISIN or other similar numbers, if any, assigned to such Notes; and

(ix) in case any Note is to be redeemed in part only, the portion of the principal amount thereof to be redeemed and on and after the Redemption Date, upon surrender of such Note, a new Note in principal amount equal to the unredeemed portion thereof shall be issued.

A Redemption Notice shall be irrevocable.

(d) If fewer than all of the outstanding Notes are to be redeemed and the Notes to be redeemed are Global Notes, the Notes to be redeemed will be selected by the Depositary in accordance with the Applicable Procedures. If fewer than all of the outstanding Notes are to be redeemed and the Notes to be redeemed are not Global Notes, the Trustee shall select the Notes or portions thereof to be redeemed (in principal amounts of $1,000 or multiples thereof) by lot, on a *pro rata* basis or by another method in accordance with the Trustee's procedures. If the Company elects to redeem fewer than all of the outstanding Notes, at least $100,000,000 aggregate principal amount of Notes must be outstanding and not subject to redemption as of, and after giving effect to, delivery of the relevant Redemption Notice (such requirement, the "**Partial Redemption Limitation**"). If the Trustee (or the Depositary, with respect to Global Notes) selects any Note for partial redemption and a Holder submits a portion of that Note after such selection, the portion of the Note submitted for conversion shall be deemed (so far as may be possible) to be the portion selected for redemption.

Section 16.03. *Payment of Notes Called for Redemption*. (a) If any Redemption Notice has been given in respect of the Notes in accordance with Section 16.02, the Notes shall become due and payable on the Redemption Date at the place or places stated in the Redemption Notice and at the applicable Redemption Price. On presentation and surrender of the Notes at the place or places stated in the Redemption Notice, the Notes shall be paid and redeemed by the Company at the applicable Redemption Price.

(b) Prior to 10:00 a.m. New York City time on the Redemption Date, the Company shall deposit with the Paying Agent or, if the Company or a Subsidiary of the Company is acting as the Paying Agent, shall segregate and hold in trust as provided

in Section 7.05 an amount of cash (in immediately available funds if deposited on the Redemption Date), sufficient to pay the Redemption Price of all of the Notes to be redeemed on such Redemption Date. Subject to receipt of funds by the Paying Agent, payment for the Notes to be redeemed shall be made on the Redemption Date for such Notes. The Paying Agent shall, promptly after such payment and upon written demand by the Company, return to the Company any funds in excess of the Redemption Price.

Section 16.04. *Restrictions on Redemption*. The Company may not redeem any Notes on any date if the principal amount of the Notes has been accelerated in accordance with the terms of this Indenture, and such acceleration has not been rescinded, on or prior to the Redemption Date (except in the case of an acceleration resulting from a Default by the Company in the payment of the Redemption Price with respect to such Notes).

ARTICLE 17
MISCELLANEOUS PROVISIONS

Section 17.01. *Provisions Binding on Company's Successors.* All the covenants, stipulations, promises and agreements of the Company contained in this Indenture shall bind its successors and assigns whether so expressed or not.

Section 17.02. *Official Acts by Successor Corporation.* Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or Officer of the Company shall and may be done and performed with like force and effect by the like board, committee or officer of any corporation or other entity that shall at the time be the lawful sole successor of the Company.

Section 17.03. *Addresses for Notices, Etc.* Any notice or demand that by any provision of this Indenture is required or permitted to be given or served by the Trustee or by the Holders on the Company shall be deemed to have been sufficiently given or made, for all purposes if given or served by being deposited postage prepaid by overnight courier or sent electronically in PDF format or via registered or certified mail in a post office letter box addressed (until another address is filed by the Company with the Trustee) to Alnylam Pharmaceuticals, Inc., 675 West Kendall Street, Henri A. Termeer Square, Cambridge, Massachusetts 02142, Attention: Jeff Poulton, Email: jpoulton@alnylam.com, with a copy sent to Goodwin Procter LLP, 100 Northern Avenue, Boston, MA 02210, Attention: James Barri. Any notice, direction, request or demand hereunder to or upon the Trustee shall be deemed to have been sufficiently given or made or filed with, for all purposes, if it is in writing and actually received by the Trustee (including electronically or in PDF format or if given or served by being deposited postage prepaid by registered or certified mail in a post office letter box addressed to the Corporate Trust Office. In no event shall the Trustee or the Conversion Agent be obligated to monitor any website maintained by the Company or any press releases issued by the Company.

The Trustee, by notice to the Company, may designate additional or different addresses for subsequent notices or communications.

Any notice or communication delivered or to be delivered to a Holder of Physical Notes shall be mailed to it by first class mail, postage prepaid, at its address as it appears on the Note Register and shall be sufficiently given to it if so mailed within the time prescribed. Any notice or communication delivered or to be delivered to a Holder of Global Notes shall be delivered in accordance with the Applicable Procedures of the Depositary and shall be sufficiently given to it if so delivered within the time prescribed.

Failure to mail or deliver a notice or communication to a Holder or any defect in it shall not affect its sufficiency with respect to other Holders. If a notice or communication is mailed or delivered, as the case may be, in the manner provided above, it is duly given, whether or not the addressee receives it.

In case by reason of the suspension of regular mail service or by reason of any other cause it shall be impracticable to give such notice to Holders by mail, then such notification as shall be made with the approval of the Trustee shall constitute a sufficient notification for every purpose hereunder.

Section 17.04. *Governing Law; Jurisdiction.* THIS INDENTURE AND EACH NOTE, AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS INDENTURE AND EACH NOTE, SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK (WITHOUT REGARD TO THE CONFLICTS OF LAWS PROVISIONS THEREOF).

The Company irrevocably consents and agrees, for the benefit of the Holders from time to time of the Notes and the Trustee, that any legal action, suit or proceeding against it with respect to obligations, liabilities or any other matter arising out of or in connection with this Indenture or the Notes may be brought in the courts of the State of New York or the courts of the United States of America located in the Borough of Manhattan, New York City, New York and, until amounts due and to become due in respect of the Notes have been paid, hereby irrevocably consents and submits to the non-exclusive jurisdiction of each such court *in personam*, generally and unconditionally with respect to any action, suit or proceeding for itself in respect of its properties, assets and revenues.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection which it may now or hereafter have to the laying of venue of any of the aforesaid actions, suits or proceedings arising out of or in connection with this Indenture brought in the courts of the State of New York or the courts of the United States of America located in the Borough of Manhattan, New York City, New York and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

Section 17.05. *Evidence of Compliance with Conditions Precedent; Certificates and Opinions of Counsel to Trustee.* Upon any application or demand by the Company to the Trustee to take any action under any of the provisions of this Indenture, the Company shall, if requested by the Trustee, furnish to the Trustee an Officer’s Certificate and an

Opinion of Counsel, in form and substance reasonably satisfactory to the Trustee, stating that such action is permitted by the terms of this Indenture and that all conditions precedent to such action have been complied with.

Each Officer's Certificate and Opinion of Counsel provided for, by or on behalf of the Company in this Indenture and delivered to the Trustee with respect to compliance with this Indenture (other than the Officer's Certificates provided for in Section 4.08) shall include (a) a statement that the person signing such certificate is familiar with the requested action and this Indenture; (b) a brief statement as to the nature and scope of the examination or investigation upon which the statement contained in such certificate is based; (c) a statement that, in the judgment of such person, he or she has made such examination or investigation as is necessary to enable him or her to express an informed judgment as to whether or not such action is permitted by this Indenture; and (d) a statement as to whether or not, in the judgment of such person, such action is permitted by this Indenture and that all conditions precedent to such action have been complied with.

Section 17.06. *Legal Holidays.* In any case where any Interest Payment Date, any Redemption Date, any Fundamental Change Repurchase Date or the Maturity Date is not a Business Day or is not a Valid Payment Date, then any action to be taken on such date need not be taken on such date, but may be taken on the next succeeding Business Day that is a Valid Payment Date with the same force and effect as if taken on such date, and no interest shall accrue on any such payment in respect of the delay.

Section 17.07. *No Security Interest Created.* Nothing in this Indenture or in the Notes, expressed or implied, shall be construed to constitute a security interest under the Uniform Commercial Code or similar legislation, as now or hereafter enacted and in effect, in any jurisdiction.

Section 17.08. *Benefits of Indenture.* Nothing in this Indenture or in the Notes, expressed or implied, shall give to any Person, other than the Holders, the parties hereto, any Paying Agent, any Conversion Agent, any Bid Solicitation Agent, any Custodian, any authenticating agent, any Note Registrar and their successors hereunder, any benefit or any legal or equitable right, remedy or claim under this Indenture.

Section 17.09. *Table of Contents, Headings, Etc.* The table of contents and the titles and headings of the articles and sections of this Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

Section 17.10. *Authenticating Agent.* The Trustee may appoint an authenticating agent that shall be authorized to act on its behalf and subject to its direction in the authentication and delivery of Notes in connection with the original issuance thereof and transfers and exchanges of Notes hereunder, including under Section 2.04, Section 2.05, Section 2.06, Section 2.07, Section 10.04 and Section 15.04 as fully to all intents and purposes as though the authenticating agent had been expressly authorized by this Indenture and those Sections to authenticate and deliver Notes. For all purposes of this

Indenture, the authentication and delivery of Notes by the authenticating agent shall be deemed to be authentication and delivery of such Notes "by the Trustee" and a certificate of authentication executed on behalf of the Trustee by an authenticating agent shall be deemed to satisfy any requirement hereunder or in the Notes for the Trustee's certificate of authentication. Such authenticating agent shall at all times be a Person eligible to serve as trustee hereunder pursuant to Section 7.08.

Any corporation or other entity into which any authenticating agent may be merged or converted or with which it may be consolidated, or any corporation or other entity resulting from any merger, consolidation or conversion to which any authenticating agent shall be a party, or any corporation or other entity succeeding to the corporate trust business of any authenticating agent, shall be the successor of the authenticating agent hereunder, if such successor corporation or other entity is otherwise eligible under this Section 17.10, without the execution or filing of any paper or any further act on the part of the parties hereto or the authenticating agent or such successor corporation or other entity.

Any authenticating agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time terminate the agency of any authenticating agent by giving written notice of termination to such authenticating agent and to the Company. Upon receiving such a notice of resignation or upon such a termination, or in case at any time any authenticating agent shall cease to be eligible under this Section, the Trustee may appoint a successor authenticating agent (which may be the Trustee), shall give written notice of such appointment to the Company and shall deliver notice of such appointment to all Holders.

The Company agrees to pay to the authenticating agent from time to time reasonable compensation for its services although the Company may terminate the authenticating agent, if it determines such agent's fees to be unreasonable.

The provisions of Section 7.02, Section 7.03, Section 7.04, Section 8.03 and this Section 17.10 shall be applicable to any authenticating agent.

If an authenticating agent is appointed pursuant to this Section 17.10, the Notes may have endorsed thereon, in addition to the Trustee's certificate of authentication, an alternative certificate of authentication in the following form:

_____,
as Authenticating Agent, certifies that this is one of the Notes described
in the within-named Indenture.

By: _____
Authorized Signatory

Section 17.11. *Execution in Counterparts.* This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument. The exchange of copies of this Indenture and of signature pages by facsimile or PDF or other electronic transmission

shall constitute effective execution and delivery of this Indenture as to the parties hereto and may be used in lieu of the original Indenture for all purposes. Signatures of the parties hereto transmitted by facsimile or PDF or other electronic means shall be deemed to be their original signatures for all purposes.

Section 17.12. *Severability; Entire Agreement.* In the event any provision of this Indenture or in the Notes shall be invalid, illegal or unenforceable, then (to the extent permitted by law) the validity, legality or enforceability of the remaining provisions shall not in any way be affected or impaired. This Indenture and the exhibits hereto set forth the entire agreement and understanding of the parties related to the transactions contemplated hereby and supersedes all prior agreements and understandings, oral or written.

Section 17.13. *Waiver of Jury Trial.* EACH OF THE COMPANY, THE HOLDERS AND THE TRUSTEE HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS INDENTURE, THE NOTES OR THE TRANSACTIONS CONTEMPLATED HEREBY.

Section 17.14. *Force Majeure.* In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including, without limitation, strikes, work stoppages, accidents, acts of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, pandemics, epidemics, and interruptions, loss or malfunctions of utilities, communications or computer (software and hardware) services or the unavailability of the Federal Reserve Bank wire or telex or other wire or communication facility; it being understood that the Trustee shall use reasonable efforts that are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances.

Section 17.15. *Calculations*. The Company shall be responsible for making all calculations called for hereunder or under the Notes. These calculations include, but are not limited to, determinations of the Last Reported Sale Prices of the Common Stock, the Daily VWAPs, the Daily Conversion Values, the Daily Settlement Amounts, accrued interest payable on the Notes and the Conversion Rate of the Notes. The Company shall make all these calculations in good faith and, absent manifest error, the Company's calculations shall be final and binding on Holders of Notes. The Company shall provide a schedule of its calculations to each of the Trustee and the Conversion Agent, and each of the Trustee and Conversion Agent is entitled to rely conclusively upon the accuracy of the Company's calculations without independent verification. The Trustee will forward the Company's calculations to any Holder of Notes upon the written request of that Holder at the sole cost and expense of the Company. Neither the Trustee nor the Conversion Agent will have any responsibility to make calculations under this Indenture, nor will either of them have any responsibility to monitor the Company's stock or trading price, determine whether the conditions to convertibility of the Notes have been met or

determine whether the circumstances requiring changes to the Conversion Rate have occurred.

Section 17.16. *USA PATRIOT Act.* The parties hereto acknowledge that in accordance with Section 326 of the USA PATRIOT Act, the Trustee, like all financial institutions and in order to help fight the funding of terrorism and money laundering, is required to obtain, verify, and record information that identifies each person or legal entity that establishes a relationship or opens an account with the Trustee. The parties to this Indenture agree that they will provide the Trustee with such information as it may request in order for the Trustee to satisfy the requirements of the USA PATRIOT Act.

Section 17.17. *Tax Withholding.* Any applicable withholding taxes (including backup withholding) may be withheld from interest and payments upon conversion, repurchase or maturity of the Notes, or if any withholding taxes (including backup withholding) are paid on behalf of a Holder or beneficial owner of Notes, those withholding taxes may be withheld from payments of cash or Common Stock, if any, payable on the Notes (or any payments on the Common Stock) or sales proceeds received by or other funds or assets of the Holder or beneficial owner. Further, in order to comply with applicable tax laws, rules and regulations, the Company and the Trustee agree to cooperate with each other and, if permitted by law and not subject to confidentiality obligations, share information each has in its possession (upon the reasonable request of the other) about any beneficial owner of Notes, to facilitate the determination of whether such party has tax related obligations in respect of any such beneficial owner of Notes arising under this Indenture pursuant to any such applicable tax laws, rules or regulations, and each agrees that Trustee may make any withholding or deduction from payments under the Indenture to the extent necessary to comply with such applicable laws, rules or regulations as described in the immediately preceding sentence.

Section 17.18. *Electronic Signatures*. The words "execution," "signed," "signature," and words of similar import in this Indenture and the Notes shall be deemed to include electronic or digital signatures or the keeping of records in electronic form, each of which shall be of the same effect, validity, and enforceability as manually executed signatures or a paper-based recordkeeping system, as the case may be, to the extent and as provided for under applicable law, including the Electronic Signatures in Global and National Commerce Act of 2000 (15 U.S.C. §§7001-7006), the Electronic Signatures and Records Act of 1999 (N.Y. State Tech. §§ 301-309), or any other similar state laws based on the Uniform Electronic Transactions Act; *provided* that, notwithstanding anything herein to the contrary, the Trustee is not under any obligation to agree to accept electronic signatures in any form or in any format unless expressly agreed to by the Trustee pursuant to procedures approved by the Trustee.

Section 17.19. *Electronic Means*. The Trustee shall have the right to accept and act upon instructions, including funds transfer instructions ("**Instructions**") given pursuant to this Indenture and delivered using Electronic Means (as hereinafter defined); provided, however, that the Company shall provide to the Trustee an incumbency certificate listing officers with the authority to provide such Instructions ("**Authorized**

Officers") and containing specimen signatures of such Authorized Officers, which incumbency certificate shall be amended by the Company whenever a person is to be added or deleted from the listing. If the Company elects to give the Trustee Instructions using Electronic Means and the Trustee in its discretion elects to act upon such Instructions, the Trustee's understanding of such Instructions shall be deemed controlling. The Company understands and agrees that the Trustee cannot determine the identity of the actual sender of such Instructions and that the Trustee shall conclusively presume that directions that purport to have been sent by an Authorized Officer listed on the incumbency certificate provided to the Trustee have been sent by such Authorized Officer. The Company shall be responsible for ensuring that only Authorized Officers transmit such Instructions to the Trustee and that the Company and all Authorized Officers are solely responsible to safeguard the use and confidentiality of applicable user and authorization codes, passwords and/or authentication keys upon receipt by the Company. The Trustee shall not be liable for any losses, costs or expenses arising directly or indirectly from the Trustee's reliance upon and compliance with such Instructions notwithstanding such directions conflict or are inconsistent with a subsequent written instruction. The Company agrees: (i) to assume all risks arising out of the use of Electronic Means to submit Instructions to the Trustee, including without limitation the risk of the Trustee acting on unauthorized Instructions, and the risk of interception and misuse by third parties; (ii) that it is fully informed of the protections and risks associated with the various methods of transmitting Instructions to the Trustee and that there may be more secure methods of transmitting Instructions than the method(s) selected by the Company; (iii) that the security procedures (if any) to be followed in connection with its transmission of Instructions provide to it a commercially reasonable degree of protection in light of its particular needs and circumstances; and (iv) to notify the Trustee immediately upon learning of any compromise or unauthorized use of the security procedures. "**Electronic Means**" shall mean the following communications methods: e-mail, facsimile transmission, secure electronic transmission containing applicable authorization codes, passwords and/or authentication keys issued by the Trustee, or another method or system specified by the Trustee as available for use in connection with its services hereunder.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed as of the date first written above.

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ Jeffrey V. Poulton
Name: Jeffrey V. Poulton
Title: Executive Vice President, Chief Financial Officer

THE BANK OF NEW YORK MELLON, as Trustee

By: /s/ Latoya S. Elvin
Name: Latoya S Elvin
Title: Vice President

EXHIBIT A

[FORM OF FACE OF NOTE]

[INCLUDE FOLLOWING LEGEND IF A GLOBAL NOTE]

[UNLESS THIS CERTIFICATE IS PRESENTED BY AN AUTHORIZED REPRESENTATIVE OF THE DEPOSITORY TRUST COMPANY, A NEW YORK CORPORATION ("DTC"), TO THE COMPANY OR ITS AGENT FOR REGISTRATION OF TRANSFER, EXCHANGE, OR PAYMENT, AND ANY CERTIFICATE ISSUED IS REGISTERED IN THE NAME OF CEDE & CO. OR IN SUCH OTHER NAME AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC (AND ANY PAYMENT HEREUNDER IS MADE TO CEDE & CO. OR TO SUCH OTHER ENTITY AS IS REQUESTED BY AN AUTHORIZED REPRESENTATIVE OF DTC), ANY TRANSFER, PLEDGE, OR OTHER USE HEREOF FOR VALUE OR OTHERWISE BY OR TO ANY PERSON IS WRONGFUL INASMUCH AS THE REGISTERED OWNER HEREOF, CEDE & CO., HAS AN INTEREST HEREIN.]

[INCLUDE FOLLOWING LEGEND IF A RESTRICTED SECURITY]

[THIS SECURITY AND THE COMMON STOCK, IF ANY, ISSUABLE UPON CONVERSION OF THIS SECURITY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT IN ACCORDANCE WITH THE FOLLOWING SENTENCE. BY ITS ACQUISITION HEREOF OR OF A BENEFICIAL INTEREST HEREIN, THE ACQUIRER:

(1) REPRESENTS THAT IT AND ANY ACCOUNT FOR WHICH IT IS ACTING IS A "QUALIFIED INSTITUTIONAL BUYER" (WITHIN THE MEANING OF RULE 144A UNDER THE SECURITIES ACT) AND THAT IT EXERCISES SOLE INVESTMENT DISCRETION WITH RESPECT TO EACH SUCH ACCOUNT, AND

(2) AGREES FOR THE BENEFIT OF ALNYLAM PHARMACEUTICALS, INC. (THE "COMPANY") THAT IT WILL NOT OFFER, SELL, PLEDGE OR OTHERWISE TRANSFER THIS SECURITY OR ANY BENEFICIAL INTEREST HEREIN PRIOR TO THE DATE THAT IS THE LATER OF (X) ONE YEAR AFTER THE LAST ORIGINAL ISSUE DATE HEREOF OR SUCH SHORTER PERIOD OF TIME AS PERMITTED BY RULE 144 UNDER THE SECURITIES ACT OR ANY SUCCESSOR PROVISION THERETO AND (Y) SUCH LATER DATE, IF ANY, AS MAY BE REQUIRED BY APPLICABLE LAW, EXCEPT:

(A) TO THE COMPANY OR ANY SUBSIDIARY THEREOF, OR

(B) PURSUANT TO A REGISTRATION STATEMENT THAT HAS BECOME EFFECTIVE UNDER THE SECURITIES ACT AND IS EFFECTIVE AT THE TIME OF SUCH TRANSFER, OR

(C) TO A PERSON THAT YOU REASONABLY BELIEVE TO BE A QUALIFIED INSTITUTIONAL BUYER IN COMPLIANCE WITH RULE 144A UNDER THE SECURITIES ACT, OR

(D) PURSUANT TO AN EXEMPTION FROM REGISTRATION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT OR ANY OTHER AVAILABLE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

PRIOR TO THE REGISTRATION OF ANY TRANSFER IN ACCORDANCE WITH CLAUSE (2)(D) ABOVE, THE COMPANY RESERVES THE RIGHT TO REQUIRE THE DELIVERY OF SUCH LEGAL OPINIONS, CERTIFICATIONS OR OTHER EVIDENCE AS MAY REASONABLY BE REQUIRED IN ORDER TO DETERMINE THAT THE PROPOSED TRANSFER IS BEING MADE IN COMPLIANCE WITH THE SECURITIES ACT AND APPLICABLE STATE SECURITIES LAWS. NO REPRESENTATION IS MADE AS TO THE AVAILABILITY OF ANY EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT.

NO AFFILIATE (AS DEFINED IN RULE 144 UNDER THE SECURITIES ACT) OF THE COMPANY OR PERSON THAT HAS BEEN AN AFFILIATE (AS DEFINED IN RULE 144 UNDER THE SECURITIES ACT) OF THE COMPANY DURING THE IMMEDIATELY PRECEDING THREE MONTHS MAY PURCHASE, OTHERWISE ACQUIRE OR HOLD THIS SECURITY OR A BENEFICIAL INTEREST HEREIN.][1]

[1]The Restrictive Legend shall be deemed removed from the face of this Note without further action by the Company, Trustee or the Holders of this Note at such time and in the manner provided under Section 2.05 of the Indenture.

Alnylam Pharmaceuticals, Inc.

1.00% Convertible Senior Note due 2027

No. [_____] [Initially][2] $[_____]

CUSIP No. 02043Q AA5[3]

Alnylam Pharmaceuticals, Inc., a corporation duly organized and validly existing under the laws of the State of Delaware (the "**Company**," which term includes any successor corporation or other entity under the Indenture referred to on the reverse hereof), for value received hereby promises to pay to [CEDE & CO.][4] [_____][5], or registered assigns, the principal sum [as set forth in the "Schedule of Exchanges of Notes" attached hereto][6] [of $[_____]][7], which amount, taken together with the principal amounts of all other outstanding Notes, shall not, unless permitted by the Indenture, exceed $1,035,000,000 in aggregate at any time, in accordance with the rules and procedures of the Depositary, on September 15, 2027, and interest thereon as set forth below.

This Note shall bear interest at the rate of 1.00% per year from September 15, 2022, or from, and including, the most recent date on which interest had been paid or duly provided for to, but excluding, the next scheduled Interest Payment Date until September 15, 2027. Accrued interest on the Notes shall be computed on the basis of a 360-day year composed of twelve 30-day months and, for partial months, on the basis of the number of days actually elapsed in a 30-day month. Interest is payable semi-annually in arrears on each March 15 and September 15, commencing on March 15, 2023, to Holders of record at the close of business on the preceding March 1 and September 1 (whether or not such day is a Business Day), respectively. Additional Interest will be payable as set forth in Section 4.06(d), Section 4.06(e) and Section 6.03 of the within-mentioned Indenture, and any reference to interest on, or in respect of, any Note therein shall be deemed to include Additional Interest if, in such context, Additional Interest is, was or would be payable pursuant to any of such Section 4.06(d), Section 4.06(e) or Section 6.03, and any express mention of the payment of Additional Interest in any provision therein shall not be construed as excluding Additional Interest in those provisions thereof where such express mention is not made.

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[2]Include if a global note.

[3]At such time as the Company notifies the Trustee that the Restrictive Legend is to be removed in accordance with the Indenture, the CUSIP number for this Note shall be deemed to be 02043Q AB3.

[4]Include if a global note.

[5]Include if a physical note.

[6]Include if a global note.

[7]Include if a physical note.

Any Defaulted Amounts shall accrue interest per annum at the rate borne by the Notes, subject to the enforceability thereof under applicable law, from, and including, the relevant payment date to, but excluding, the date on which such Defaulted Amounts shall have been paid by the Company, at its election, in accordance with Section 2.03(c) of the Indenture.

The Company shall pay the principal of and interest on this Note, if and so long as such Note is a Global Note, by wire transfer of immediately available funds to the Depositary or its nominee, as the case may be, as the registered Holder of such Note. As provided in and subject to the provisions of the Indenture, the Company shall pay the principal of any Notes (other than Notes that are Global Notes) at the office or agency designated by the Company for that purpose. The Company has initially designated the Trustee as its Paying Agent and Note Registrar in respect of the Notes and the Corporate Trust Office as a place where Notes may be presented for payment or for registration of transfer and exchange.

Reference is made to the further provisions of this Note set forth on the reverse hereof, including, without limitation, provisions giving the Holder of this Note the right to convert this Note into cash, shares of Common Stock or a combination of cash and shares of Common Stock, as applicable, on the terms and subject to the limitations set forth in the Indenture. Such further provisions shall for all purposes have the same effect as though fully set forth at this place.

This Note, and any claim, controversy or dispute arising under or related to this Note, shall be construed in accordance with and governed by the laws of the State of New York (without regard to the conflicts of laws provisions thereof).

In the case of any conflict between this Note and the Indenture, the provisions of the Indenture shall control and govern.

This Note shall not be valid or become obligatory for any purpose until the certificate of authentication hereon shall have been signed manually, electronically or by facsimile by the Trustee or a duly authorized authenticating agent under the Indenture.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the Company has caused this Note to be duly executed.

ALNYLAM PHARMACEUTICALS, INC.

By: _____
Name:
Title:

Dated:

TRUSTEE'S CERTIFICATE OF AUTHENTICATION

THE BANK OF NEW YORK MELLON
as Trustee, certifies that this is one of the Notes described in the within-named Indenture.

By:_____
Authorized Signatory

[FORM OF REVERSE OF NOTE]

Alnylam Pharmaceuticals, Inc.
1.00% Convertible Senior Note due 2027

This Note is one of a duly authorized issue of Notes of the Company, designated as its 1.00% Convertible Senior Notes due 2027 (the "**Notes**"), limited to the aggregate principal amount of $1,035,000,000, all issued or to be issued under and pursuant to an Indenture dated as of September 15, 2022 (the "**Indenture**"), between the Company and The Bank of New York Mellon, as trustee (the "**Trustee**"), to which Indenture and all indentures supplemental thereto reference is hereby made for a description of the rights, limitations of rights, obligations, duties and immunities thereunder of the Trustee, the Company and the Holders of the Notes. Additional Notes may be issued in an unlimited aggregate principal amount, subject to certain conditions specified in the Indenture. Capitalized terms used in this Note and not defined in this Note shall have the respective meanings set forth in the Indenture.

In case certain Events of Default shall have occurred and be continuing, the principal of, and interest on, all Notes may be declared, by either the Trustee or Holders of at least 25% in aggregate principal amount of Notes then outstanding, and upon said declaration shall become, due and payable, in the manner, with the effect and subject to the conditions and certain exceptions set forth in the Indenture.

Subject to the terms and conditions of the Indenture, the Company will make all payments and deliveries in respect of the Fundamental Change Repurchase Price on the Fundamental Change Repurchase Date, the Redemption Price on any Redemption Date and the principal amount on the Maturity Date, as the case may be, to the Holder who surrenders a Note to a Paying Agent to collect such payments in respect of the Note. The Company will pay cash amounts in money of the United States of America that at the time of payment is legal tender for payment of public and private debts.

The Indenture contains provisions permitting the Company and the Trustee in certain circumstances, without the consent of the Holders of the Notes, and in certain other circumstances, with the consent of the Holders of not less than a majority in aggregate principal amount of the Notes at the time outstanding, evidenced as in the Indenture provided, to execute supplemental indentures modifying the terms of the Indenture and the Notes as described therein. It is also provided in the Indenture that, subject to certain exceptions, the Holders of a majority in aggregate principal amount of the Notes at the time outstanding may on behalf of the Holders of all of the Notes waive any past Default or Event of Default under the Indenture and its consequences.

Notwithstanding any other provision of the Indenture or any provision of this Note, each Holder shall have the contractual right to receive payment or delivery, as the case may be, of (x) the principal (including the Redemption Price and the Fundamental Change Repurchase Price, if applicable) of, (y) accrued and unpaid interest, if any, on, and (z) the consideration due upon conversion of, this Note, on or after the respective due dates expressed or provided for in this Note or in the Indenture, and the contractual right

to institute suit for the enforcement of any such payment or delivery, as the case may be, on or after such respective dates, shall not be amended without the consent of each Holder.

The Notes are issuable in registered form without coupons in minimum denominations of $1,000 principal amount and integral multiples in excess thereof. At the office or agency of the Company referred to on the face hereof, and in the manner and subject to the limitations provided in the Indenture, Notes may be exchanged for a like aggregate principal amount of Notes of other authorized denominations, without payment of any service charge but, if required by the Company or Trustee, with payment of a sum sufficient to cover any transfer or similar tax that may be imposed in connection therewith as a result of the name of the Holder of the new Notes issued upon such exchange of Notes being different from the name of the Holder of the old Notes surrendered for such exchange.

The Notes shall be redeemable at the Company's option on or after September 20, 2025 in accordance with the terms and subject to the conditions specified in the Indenture. No sinking fund is provided for the Notes.

Upon the occurrence of a Fundamental Change, the Holder has the right, at such Holder's option, to require the Company to repurchase for cash all of such Holder's Notes or any portion thereof (in principal amounts of $1,000 or integral multiples thereof) on the Fundamental Change Repurchase Date at a price equal to the Fundamental Change Repurchase Price.

Subject to the provisions of the Indenture, the Holder hereof has the right, at its option, during certain periods and upon the occurrence of certain conditions specified in the Indenture, prior to the close of business on the second Scheduled Trading Day immediately preceding the Maturity Date, to convert any Notes or portion thereof that is $1,000 or an integral multiple thereof, into cash, shares of Common Stock or a combination of cash and shares of Common Stock, as applicable, at the Conversion Rate specified in the Indenture, as adjusted from time to time as provided in the Indenture.

ABBREVIATIONS

The following abbreviations, when used in the inscription of the face of this Note, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM = as tenants in common

UNIF GIFT MIN ACT = Uniform Gifts to Minors Act

CUST = Custodian

TEN ENT = as tenants by the entireties

JT TEN = joint tenants with right of survivorship and not as tenants in common

Additional abbreviations may also be used though not in the above list.

SCHEDULE A[8]

SCHEDULE OF EXCHANGES OF NOTES

Alnylam Pharmaceuticals, Inc.
1.00% Convertible Senior Notes due 2027

The initial principal amount of this Global Note is [_____] DOLLARS ($[_____]). The following increases or decreases in this Global Note have been made:

Date of exchange	Amount of decrease in principal amount of this Global Note	Amount of increase in principal amount of this Global Note	Principal amount of this Global Note following such decrease or increase	Signature of authorized signatory of Trustee or Custodian

[8]Include if a global note.

ATTACHMENT 1

[FORM OF NOTICE OF CONVERSION]

To: The Bank of New York Mellon
240 Greenwich Street, 7th Floor
New York, New York 10286
Attention: Corporate Trust Administration

The undersigned registered owner of this Note hereby exercises the option to convert this Note, or the portion hereof (that is $1,000 principal amount or an integral multiple thereof) below designated, into cash, shares of Common Stock or a combination of cash and shares of Common Stock, at the Company's election, in accordance with the terms of the Indenture referred to in this Note, and directs that any cash payable and any shares of Common Stock issuable and deliverable upon such conversion, together with any cash for any fractional share, and any Notes representing any unconverted principal amount hereof, be issued and delivered to the registered Holder hereof unless a different name has been indicated below. If any shares of Common Stock or any portion of this Note not converted are to be issued in the name of a Person other than the undersigned, the undersigned will pay all documentary, stamp or similar issue or transfer taxes, if any in accordance with Section 14.02(d) and Section 14.02(e) of the Indenture. Any amount required to be paid to the undersigned on account of interest accompanies this Note. Capitalized terms used herein but not defined shall have the meanings ascribed to such terms in the Indenture.

Dated: _____ _____

_____
Signature(s)

_____
Signature Guarantee

Signature(s) must be guaranteed
by an eligible Guarantor Institution
(banks, stock brokers, savings and
loan associations and credit unions)
with membership in an approved
signature guarantee medallion program
pursuant to Securities and Exchange
Commission Rule 17Ad-15 if shares
of Common Stock are to be issued, or

Notes are to be delivered, other than
to and in the name of the registered holder.

Fill in for registration of shares if
to be issued, and Notes if to
be delivered, other than to and in the
name of the registered holder:

_____
(Name)

_____
(Street Address)

_____
(City, State and Zip Code)
Please print name and address

Principal amount to be converted (if less than all): $_____,000

NOTICE: The above signature(s) of the Holder(s) hereof must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

_____
Social Security or Other Taxpayer
Identification Number

ATTACHMENT 2

[FORM OF FUNDAMENTAL CHANGE REPURCHASE NOTICE]

To: Paying Agent

The undersigned registered owner of this Note hereby acknowledges receipt of a notice from Alnylam Pharmaceuticals, Inc. (the "**Company**") as to the occurrence of a Fundamental Change with respect to the Company and specifying the Fundamental Change Repurchase Date and requests and instructs the Company to pay to the registered holder hereof in accordance with Section 15.02 of the Indenture referred to in this Note (1) the entire principal amount of this Note, or the portion thereof (that is $1,000 principal amount or an integral multiple thereof) below designated, and (2) if such Fundamental Change Repurchase Date does not fall during the period after a Regular Record Date and on or prior to the corresponding Interest Payment Date, accrued and unpaid interest, if any, thereon to, but excluding, such Fundamental Change Repurchase Date. Capitalized terms used herein but not defined shall have the meanings ascribed to such terms in the Indenture.

In the case of Physical Notes, the certificate numbers of the Notes to be repurchased are as set forth below:

Dated: _____

_____
Signature(s)

_____
Social Security or Other Taxpayer
Identification Number

Principal amount to be repaid (if less than all): $_____,000

NOTICE: The above signature(s) of the Holder(s) hereof must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

ATTACHMENT 3

[FORM OF ASSIGNMENT AND TRANSFER]

For value received _____ hereby sell(s), assign(s) and transfer(s) unto _____ (Please insert social security or Taxpayer Identification Number of assignee) the within Note, and hereby irrevocably constitutes and appoints _____ attorney to transfer the said Note on the books of the Company, with full power of substitution in the premises.

In connection with any transfer of the within Note occurring prior to the Resale Restriction Termination Date, as defined in the Indenture governing such Note, the undersigned confirms that such Note is being transferred:

To Alnylam Pharmaceuticals, Inc. or a subsidiary thereof; or

Pursuant to a registration statement that has become or been declared effective under the Securities Act of 1933, as amended; or

Pursuant to and in compliance with Rule 144A under the Securities Act of 1933, as amended; or

Pursuant to and in compliance with Rule 144 under the Securities Act of 1933, as amended, or any other available exemption from the registration requirements of the Securities Act of 1933, as amended.

Dated: _____

_____

_____
Signature(s)

_____
Signature Guarantee

Signature(s) must be guaranteed by an eligible Guarantor Institution (banks, stock brokers, savings and loan associations and credit unions) with membership in an approved signature guarantee medallion program pursuant to Securities and Exchange Commission Rule 17Ad-15 if Notes are to be delivered, other than to and in the name of the registered holder.

NOTICE: The signature on the assignment must correspond with the name as written upon the face of the Note in every particular without alteration or enlargement or any change whatever.

EXHIBIT 31.1

CERTIFICATION

I, Yvonne L. Greenstreet, MBChB, certify that:

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

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

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

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

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

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

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

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

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

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

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

Dated: October 27, 2022

/s/ Yvonne L. Greenstreet, MBChB, MBA

Yvonne L. Greenstreet, MBChB, MBA
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: October 27, 2022

/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, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Yvonne L. Greenstreet, MBChB, Chief Executive Officer of the Company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

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

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

Dated: October 27, 2022

/s/ Yvonne L. Greenstreet, MBChB, MBA

Yvonne L. Greenstreet, MBChB, MBA
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, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jeffrey V. Poulton, Executive Vice President, Chief Financial Officer, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

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

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

Dated: October 27, 2022

/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.