FORM 10-Q

Quarterly report pursuant to sections 13 or 15(d)

Filing Date: **2004-08-12** | Period of Report: **2004-06-30**
SEC Accession No. 0000950135-04-003965

FILER

ALNYLAM PHARMACEUTICALS, INC.
CIK:**1178670**| IRS No.: **770602661**
Type: **10-Q** | Act: **34** | File No.: **000-50743** | Film No.: **04970835**
SIC: **2834** Pharmaceutical preparations

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

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

For the quarterly period ended June 30, 2004

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 000-50743

ALNYLAM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	77-0602661
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
300 Third Street, Cambridge, MA	02142
(Address of principal executive offices)	(Zip Code)

Registrant' s telephone number including area code: (617) 551-8200

(Former name, former address, and former fiscal year, if changed since last report)

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

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

As of July 31, 2004, the registrant had 20,045,068 shares of Common Stock, $0.01 par value per share, outstanding.

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ALNYLAM PHARMACEUTICALS, INC.

Consolidated Balance Sheets
($ in thousands, except per share amounts)
(Unaudited)

	June 30, 2004	December 31, 2003
Assets		
Current assets		
Cash and cash equivalents	$ 31,891	$ 23,193
Marketable securities	14,207	–
Restricted cash	–	373
Collaboration receivable	3,000	–
Prepaid expenses and other current assets	1,413	623
Total current assets	50,511	24,189
Property and equipment, net	11,436	4,756
Intangible assets, net	3,642	3,878
Restricted cash	2,313	2,313
Deferred financing costs	571	47
Total assets	$ 68,473	$ 35,183
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities		
Accounts payable	$ 1,810	$ 1,510
Accrued liabilities	5,443	1,443
Current portion of note payable	–	558
Deferred revenue	1,451	333
Total current liabilities	8,704	3,844
Deferred revenue	3,389	1,556
Note payable, net of current portion	5,705	1,301
Total liabilities	17,798	6,701
Commitments and contingencies		
Redeemable convertible preferred stock	–	55,189
Stockholders' equity (deficit)		
Common stock, $0.01 par value, 125,000,000 shares authorized as of June 30, 2004 and $0.0001 par value, 32,000,000 shares authorized as of December 31, 2003; 20,127,962 shares and 2,251,482 shares issued and 20,045,068 shares and 2,251,482 shares outstanding as of June 30, 2004 and December 31, 2003, respectively	200	–
Additional paid-in capital	107,526	7,416
Deferred compensation	(6,125)	(4,681)
Accumulated other comprehensive (loss) income	(37)	76
Accumulated deficit	(50,889)	(29,518)
Total stockholders' equity (deficit)	50,675	(26,707)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 68,473	$ 35,183

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

ALNYLAM PHARMACEUTICALS, INC.

Consolidated Statements of Operations
($ in thousands, except per share amounts)
(Unaudited)

	Three Months Ended,		Six Months Ended,	
	June 30, 2004	June 30, 2003	June 30, 2004	June 30, 2003
Revenue from research collaborators	$ 131	$ –	$ 265	$ –
Costs and expenses				
Research and development[(1)]	4,159	1,784	14,594	3,051
General and administrative[(1)]	2,947	1,480	5,978	2,388
Total operating costs and expenses	7,106	3,264	20,572	5,439
Loss from operations	(6,975)	(3,264)	(20,307)	(5,439)
Other income (expense)				
Interest income	74	56	111	88
Interest expense	(97)	(35)	(305)	(42)
Other income (expense)	42	(1)	(37)	(1)
Total other income (expense)	19	20	(231)	45
Net loss	(6,956)	(3,244)	(20,538)	(5,394)
Accretion of redeemable convertible preferred stock	(751)	(435)	(2,713)	(870)
Net loss attributable to common stockholders	$ (7,707)	$ (3,679)	$ (23,251)	$ (6,264)
Comprehensive income (loss)				
Net loss	$ (6,956)	$ (3,244)	$ (20,538)	$ (5,394)
Foreign currency translation adjustments	(106)	–	(113)	–
Comprehensive loss	$ (7,062)	$ (3,244)	$ (20,651)	$ (5,394)
Net loss per common share				
Net loss per common share (basic and diluted)	$ (1.10)	$ (6.83)	$ (5.39)	$ (12.52)
Weighted average common shares used to compute basic and diluted net loss per common share	6,997,479	538,706	4,315,860	500,341
[(1)]Noncash stock-based compensation (income) expense included in these amounts are as follows:				
Research and development	$ (531)	$ 247	$ 1,193	$ 747
General and administrative	484	58	991	77
Total stock-based compensation	$ (47)	$ 305	$ 2,184	$ 824

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

ALNYLAM PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows
($ in thousands, except per share amounts)
(Unaudited)

	Six Months Ended, June 30, 2004	June 30, 2003
Cash flows from operating activities		
Net loss	$ (20,538)	$ (5,394)
Adjustments to reconcile net loss to net cash flows used in operating activities:		
Depreciation and amortization	965	124
Gain on disposal of property and equipment	(19)	–
Stock-based compensation	2,184	824
Changes in operating assets and liabilities; net of acquisition		
Collaboration receivable	(3,000)	–
Prepaid expenses and other current assets	(786)	(469)
Accounts payable	294	670
Accrued expenses	3,010	787
Deferred revenue	2,948	–
Net cash used in operating activities	(14,942)	(3,458)
Cash flows from investing activities		
Purchases of property and equipment	(6,438)	(1,023)
Proceeds from the sale of equipment	67	–
Purchases of marketable securities	(15,457)	–
Sales of marketable securities	1,250	–
Net cash used in investing activities	(20,578)	(1,023)
Cash flows from financing activities		
Proceeds from the issuance of common stock, net of issuance costs	30,100	7
Proceeds from issuance of Series D convertible preferred stock, net of issuance costs	10,000	–
Proceeds of bank debt	5,705	589
Repayment of bank debt	(1,859)	(79)
Decrease in restricted cash	373	–
Deferred financing costs incurred in connection with the acquisition of Ribopharma	–	(615)
Deferred financing costs incurred in connection with the equipment line of credit	(47)	–
Net cash provided by (used by) financing activities	44,272	(98)
Effect of exchange rate changes on cash	(54)	–
Net increase (decrease) in cash and cash equivalents	8,698	(4,579)
Cash and cash equivalents, beginning of period	23,193	15,477
Cash and cash equivalents, end of period	$ 31,891	$ 10,898
Supplemental disclosure of cash flows		
Cash paid for interest	$ 155	$ 10
Supplemental disclosure of noncash financing activities		
Fair value of warrants issued in connection with equipment line of credit included as deferred financing costs	$ 557	$ –
Accretion of redeemable convertible preferred stock	2,713	870
Conversion of redeemable convertible preferred stock into common stock	67,626	–

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

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements
($ in thousands, except per share amounts)

1. Nature of the Business

Alnylam Pharmaceuticals, Inc. (the "Company" or "Alnylam") commenced operations on June 14, 2002 as a biopharmaceutical company seeking to develop and commercialize new drugs that work through a recently discovered system in cells known as RNA interference, or RNAi. Alnylam is focused on discovering, developing and commercializing RNAi therapeutics by establishing strategic alliances with leading pharmaceutical companies, establishing and maintaining a strong intellectual property position in the RNAi field and generating revenues through licensing agreements. The Company has devoted substantially all of its efforts to business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff, and raising capital. Prior the quarter ended June 30, 2004, the Company operated as a development-stage company. During the quarter ended June 30, 2004, the Company emerged from the development stage because its collaboration research activities became significant with the addition of the second collaboration with Merck. The Company has received payments from Merck and expects these collaborations to be a significant part of the Company' s ongoing business operations.

In June 2004, the Company completed the initial public offering of its common stock. The initial public offering consisted of the sale of 5,000,000 shares of common stock at a price of $6.00 per share. As part of the offering, the Company granted to the underwriters an option to purchase an additional 750,000 shares within 30 days of the initial public offering to cover over-allotments. This option was exercised in full in June 2004. Net proceeds from the initial public offering after deducting underwriters' discounts and expenses were $30,000.

2. Basis of Presentation

The accompanying consolidated financial statements of the Company have been prepared in accordance with accounting principles generally accepted in the United States applicable to interim periods. These statements, however, are condensed and do not include all disclosures required by accounting principles generally accepted in the United States for complete financial statements and should be read in conjunction with the Company' s consolidated financial statements for the year ended December 31, 2003 included in the Company' s Registration Statement on Form S-1, which was declared effective by the Securities and Exchange Commission (the "SEC") on May 27, 2004.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

In the opinion of the Company, the unaudited financial statements contain all adjustments (all of which were considered normal and recurring) necessary to present fairly the Company' s financial position at June 30, 2004 and the results of operations for the three and six months ended June 30, 2004 and 2003 and cash flows for the six months ended June 30, 2004 and 2003. The preparation of the Company' s consolidated financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts and disclosure of certain assets and liabilities at the balance sheet date. Such estimates include the carrying value of property and equipment and intangible assets and the value of certain liabilities. Actual results may differ from such estimates.

These interim results are not necessarily indicative of results to be expected for a full year or subsequent interim periods.

3. Accounting Policies

Except as otherwise disclosed in the financial statements, the accounting policies underlying these quarterly financial statements are those set forth in the consolidated financial statements for the year ended December 31, 2003 included in the Company' s Registration Statement on Form S-1, which was declared effective by the SEC on May 27, 2004.

Segment Information

Management uses consolidated financial information in determining how to allocate resources and assess financial performance. For this reason, the Company has determined that it is principally engaged in one industry segment.

The following table presents total long-lived tangible assets by geographic area as of June 30, 2004 and December 31, 2003:

	June 30, 2004	December 31, 2003
Long-lived tangible assets		
United States	$ 9,117	$ 2,343
Germany	2,319	2,413
Total long-lived tangible assets	$ 11,436	$ 4,756

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

Recent Accounting Pronouncements

In April 2004, the Emerging Issues Task Force ("EITF") issued Statement No. 03-06, "Participating Securities and the Two-Class Method Under Financial Accounting Standards Board ("FASB") Statement No. 128, Earnings Per Share." EITF 03-06 addresses a number of questions regarding the computation of earnings per share by a company that has issued securities other than common stock that contractually entitle the holder to the right to participate in dividends when, and if, declared. The issue also provides further guidance in applying the two-class method of calculating earnings per share, clarifying the definition of a participating security and how to apply the two-class method. EITF 03-06 is effective for fiscal periods beginning after March 31, 2004, which is the Company' s second quarter, and is required to be retroactively applied. There was no impact from the adoption of EITF 03-06 on the Company' s earnings per share as the Company has incurred net operating losses during each period presented in the consolidated financial statements and the effect would be anti-dilutive.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

4. Net Loss Per Common Share

The Company accounts for and discloses net loss per common share in accordance with Statement of Financial Accounting Standards ("SFAS") No. 128, *Earnings Per Share* ("SFAS No. 128"). Basic loss per common share is computed by dividing net loss available to common stockholders by the weighted average number of common shares outstanding. Diluted loss per common share is computed by dividing net loss available to common stockholders by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options and warrants (using the treasury stock method), options that were exercised prior to vesting, unvested restricted stock awards and the weighted average conversion of the preferred stock into shares of common stock (using the if-converted method). The following sets forth the computation of basic and diluted net loss per common share:

	Three Months Ended,		Six Months Ended,	
	June 30, 2004	June 30, 2003	June 30, 2004	June 30, 2003
Basic and diluted net loss per common share				
Net loss attributable to common stockholders	$ (7,707)	$ (3,679)	$ (23,251)	$ (6,264)
Basic and diluted net loss per common share	$ (1.10)	$ (6.83)	$ (5.39)	$ (12.52)
Basic and diluted weighted average number of common shares outstanding	6,997,479	538,706	4,315,860	500,341

The following potentially dilutive, common share equivalents were excluded from the calculation of diluted and pro forma net loss per common share because their effect was anti-dilutive for each of the periods presented:

	Three Months Ended,		Six Months Ended,	
	June 30, 2004	June 30, 2003	June 30, 2004	June 30, 2003
Options	2,051,885	607,360	2,051,885	607,360
Warrants	65,787	13,157	65,787	13,157
Convertible preferred stock	–	4,294,736	–	4,294,736
Unvested restricted stock	524,003	787,500	524,003	787,500
Options that were exercised before vesting	6,737	15,789	121,804	15,789

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

5. Accounting for Stock-Based Compensation

Employee stock awards granted under the Company' s compensation plans are accounted for in accordance with Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* ("APB 25"), and related interpretations. The Company has not adopted the fair value method of accounting for stock-based compensation. All stock-based awards granted to nonemployees are accounted for at their fair value in accordance with SFAS No. 123, as amended, and EITF Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, under which compensation expense is generally recognized over the vesting period of the award.

Under the intrinsic value method, compensation associated with stock-based awards to employees is determined as the difference, if any, between the current fair value of the underlying common stock on the date compensation is measured and the price an employee must pay to exercise the award. The measurement date for employee awards is generally the grant date. Under the fair-value method, compensation associated with stock-based awards to nonemployees is determined based on the estimated fair value of the award itself, measured using an established option pricing model. The measurement date for nonemployee awards is generally the date performance of certain services is complete. Pro forma information regarding net loss and basic and diluted net loss per common share for the three and six months ended June 30, 2004 and 2003 has been determined as if the Company had accounted for its employee stock options under the fair-value method.

Pro forma information for the three and six months ended June 30, 2004 and 2003 is as follows:

	Three Months Ended,		Six Months Ended,	
	June 30, 2004	June 30, 2003	June 30, 2004	June 30, 2003
Net loss attributable to common stockholders				
Net loss, as reported	$ (7,707)	$ (3,679)	$ (23,251)	$ (6,264)
Add employee stock-based compensation (income) expense included in reported net loss	852	61	1,605	82
Deduct stock-based compensation expense determined under fair value method	(898)	(65)	(1,736)	(87)
Net loss − pro forma	$ (7,753)	$ (3,683)	$ (23,382)	$ (6,269)
Net loss per common share (basic and diluted)				
As reported	$ (1.10)	$ (6.83)	$ (5.39)	$ (12.52)
Pro forma	$ (1.11)	$ (6.84)	$ (5.42)	$ (12.53)

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

Since options vest over several years and additional option grants are expected to be made in future years, the pro forma effects of applying the fair value method may be material to reported net income or loss in future years.

6. Intangibles

Intangible assets consist of the following:

	June 30, 2004	December 31, 2003
Core Technology	$ 3,638	$ 3,638
Workforce	437	437
	4,075	4,075
Less − accumulated amortization	(433)	(197)
	$ 3,642	$ 3,878

Amortization expense was $118 and $236 in the three and six months ended June 30, 2004. There was no amortization expense recorded in either the three or six months ended June 30, 2003.

7. Property and Equipment

	Estimated Useful Life (Years)	June 30, 2004	December 31, 2003
Laboratory equipment and software	5	$ 5,407	$ 4,300
Computer equipment	3	511	270
Furniture and fixtures	5	827	431
Leasehold improvements	*	6,066	50
Construction in progress		−	363
		12,811	5,414
Less − accumulated depreciation		(1,375)	(658)
		$ 11,436	$ 4,756

* shorter of asset life or lease term

Depreciation and amortization expense was $401 and $649 and $71 and $114 for the three and six months ended June 30, 2004 and 2003, respectively.

As a part of the lease agreement signed with the landlord, the landlord will reimburse the Company for certain of the costs of the tenant improvements, up to a maximum of $2,978. The Company will record this upon receipt from the landlord.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

8. Notes Payable

Equipment Line of Credit

On March 26, 2004, the Company entered into an agreement with Lighthouse Capital Partners V, L.P. ("Lighthouse") to establish an equipment line of credit for $10,000. The Company has the ability to draw down amounts under the line of credit through June 30, 2005 upon adherence to certain conditions. All borrowings under the line of credit are collateralized by the assets financed. Borrowings bear interest at prime rate plus 3 percent (7.25% at June 30, 2004). The Company will make interest only payments on all draw-downs made during the period from March 26, 2004 through June 30, 2005 at which point all draw-downs under the line of credit will be repaid over 48 months. On the maturity of each equipment advance under the line of credit, the Company is required to pay, in addition to the paid principal and interest, an additional amount of 11.5 percent of the original principal. This amount is being accrued over the applicable borrowing period as additional interest expense. In connection with the agreement, Alnylam issued to Lighthouse and an affiliate warrants to purchase 100,000 shares of Series C redeemable convertible preferred stock at an exercise price of $5.00 per share and a term of seven years, which were converted into warrants to purchase 52,630 shares of our common stock at an exercise price of $9.50 per share upon the closing of our initial public offering. Alnylam recorded the fair value of these warrants of $557 as a deferred financing cost which is being amortized to interest expense over the repayment term of the first advance of 63 months. The fair value of the warrants was calculated using the Black-Scholes option pricing model with the following assumptions: 100% volatility, risk-free interest rate of 3.49%, no dividend yield, and a seven-year term.

In conjunction with entering into the agreement with Lighthouse in March 2004, Alnylam paid off the remaining balance of the loan with Silicon Valley Bank, of $1,859, via an initial draw in the amount of the payoff balance. As a result of the early termination of the Silicon Valley Bank loan, Alnylam paid additional interest of $168.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

As of June 30, 2004, future cash payments under the note payable to Lighthouse are as follows:

Year Ended December 31,		
Remaining 6 months in 2004	$	205
2005		1,027
2006		1,645
2007		1,645
2008		1,645
2009		1,477
		7,644
Less: portion representing interest		1,939
		5,705
Less: current portion		–
Long-term equipment loan	$	5,705

The terms of the Lighthouse agreement include covenants which limit the Company' s ability to sell or transfer certain assets or businesses or to pay dividends or other distributions above specified limits. Through June 30, 2004, the Company has drawn $5,705 under the agreement and $4,295 is available on the line of credit to finance additional equipment. The Company is in compliance with the covenants of the agreement as of June 30, 2004.

9. Equity

Common Stock

As of June 30, 2004, the Company had 125,000,000 shares of common stock authorized, 20,127,962 shares issued and 20,045,068 shares outstanding. As of June 30, 2004, the Company has reserved 65,787 shares for issuance to warrant holders in the event that the warrants to purchase 65,787 shares of common stock are exercised. In addition, the Company has reserved 2,075,673 shares of common stock for future issuance upon the exercise of common stock options. During the six months ended June 30, 2004, the Company repurchased 82,894 shares of unvested common stock from a terminated employee for $0.00019 per share. The Company has recorded this as treasury stock.

On May 7, 2004, the Company effected a reverse 1-for-1.9 split of all outstanding shares of common stock. All common share and per share data presented in the accompanying consolidated financial statements and the notes thereto have been retroactively restated to reflect this event.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

In June 2004, the Company completed the initial public offering of its common stock. The initial public offering consisted of the sale of 5,000,000 shares of common stock at a price of $6.00 per share. As part of the offering, the Company granted to the underwriters an option to purchase an additional 750,000 shares within 30 days of the initial public offering to cover over-allotments. This option was exercised in full in June 2004. Net proceeds from the initial public offering after deducting underwriters' discounts and expenses were $30,000.

Preferred Stock

As of June 30, 2004, the Company had 5,000,000 shares of preferred stock authorized, no shares issued and no shares outstanding.

Restricted Stock to NonEmployees

In connection with restricted stock issued to nonemployees, the Company has recorded deferred compensation which represents the cumulative fair value of the awards. Shares remaining unvested or subject to forfeiture for nonemployees still providing services are subject to a mark-to-market adjustment during each reporting period prior to vesting in full which could result in additional expenses as well as credits to stock-based compensation expense based on the current fair market value of the Company's common stock price.

Stock Option Plans

On May 27, 2004, the effective date of the Company' s Registration Statement on Form S-1 filed with the SEC, the Company' s 2004 Stock Incentive Plan (the "2004 Plan") became effective. The 2004 Plan has 1,578,947 shares available for issuance under the plan plus an additional amount available for issuance equal to the remaining shares available under the 2002 Employee, Director and Consultant Stock Plan and 2003 Employee, Director and Consultant Stock Plan immediately prior to the closing of the Company' s initial public offering. In addition, the 2004 Plan provides for an annual increase in the number of shares available for issuance under the plan equal to the lesser of 2,631,578 shares of common stock, 5% of the Company' s outstanding shares or an amount determined by the board of directors. The 2004 Plan includes a nonemployee director stock option program under which each eligible nonemployee director will be entitled to receive a grant of options to purchase 7,105 shares of common stock upon his or her initial appointment to the board of directors and a subsequent annual grant of an options to purchase 5,263 shares of common stock based on continued services.

The 2004 Employee Stock Purchase Plan (the "2004 ESPP") became effective on May 28, 2004. The 2004 ESPP has 315,789 shares available for issuance under the plan.

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

10. Significant Agreements

Isis Pharmaceuticals, Inc. Collaboration and License Agreement

In March 2004, Alnylam entered into a collaboration and license agreement with Isis Pharmaceuticals, Inc. ("Isis"). Isis granted Alnylam licenses to its current and future patents and patent applications relating to chemistry and to RNA-targeting mechanisms for the research, development and commercialization of double-stranded RNA products. Alnylam has the right to use Isis technologies in its development programs or in collaborations and Isis has agreed not to grant licenses under these patents to any other organization for the discovery, development and commercialization of double-stranded RNA products designed to work through a RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. Alnylam granted Isis non-exclusive licenses to its current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. Alnylam also granted Isis the exclusive or co-exclusive right to develop and commercialize double-stranded RNA products developed using RNAi technology against a limited number of targets. In addition, Alnylam granted Isis non-exclusive rights to research, develop and commercialize single-stranded RNA products.

Under the terms of the agreement, Alnylam agreed to pay Isis an upfront license fee of $5,000, $3,000 of which was paid upon signing of the agreement and the remaining $2,000 of which is due on January 3, 2005. Alnylam has recorded this $5,000 of consideration as license fee expense within research and development costs during the six months ended June 30, 2004 as the technology has not reached technological feasibility and does not have any alternative future use. Alnylam also agreed to make milestone payments (totaling $3,400 payable upon the occurrence of specified development and regulatory events) and royalties to Isis for each product that Alnylam or a collaborator develops utilizing Isis intellectual property. In addition,

ALNYLAM PHARMACEUTICALS, INC.

Notes to Unaudited Interim Consolidated Financial Statements − (Continued)
($ in thousands, except per share amounts)

Alnylam agreed to pay to Isis a percentage of certain fees earned from strategic collaborations it may enter into that include access to the Isis intellectual property. In connection with the Merck ocular collaboration signed in June 2004, which is discussed below, the Company recorded $500 in license fee expense related to payments due to Isis. In conjunction with the agreement, Isis purchased 1,666,667 shares of Series D preferred stock of Alnylam for $10,000, which were converted into 877,193 shares of common stock upon the closing of the Company' s initial public offering in June 2004. Isis also agreed to pay Alnylam a license fee, milestone payments (totaling $3,400 payable upon the occurrence of specified development and regulatory events) and royalties for each product developed by Isis or a collaborator that utilizes its intellectual property. The agreement also gives Alnylam an option to use Isis manufacturing services for RNA-based therapeutics.

In addition, the agreement with Isis gives Alnylam the exclusive right to grant sub-licenses for Isis technology to third parties with whom Alnylam is not collaborating. Alnylam may include these sub-licenses in its InterfeRx licenses and research reagent and services licenses. If a license includes rights to Isis intellectual property, Alnylam will share revenues from that license equally with Isis.

Merck Ocular Collaboration

In June 2004, Alnylam entered into a collaboration and license agreement with Merck. The agreement is a multi-year collaboration to develop and commercialize RNAi therapeutics for ocular diseases. This collaboration, the second strategic alliance between Merck and Alnylam, will focus on age-related macular degeneration ("AMD") and other ocular diseases caused by abnormal growth or leakage of small blood vessels in the eye. Alnylam' s existing program to develop a Direct RNAi™ therapeutic for the treatment of AMD will be incorporated into the new collaboration.

Under the terms of the agreement, Alnylam receives a $2,000 license fee from Merck as well as $1,000 representing reimbursement of prior research and development costs incurred by the Company. These amounts have been deferred and will be recognized as revenue over the estimated period of performance under the collaboration agreement. In addition, the agreement provides for Alnylam to work on two additional mutually agreed ocular targets in addition to its vascular endothelial growth factor ("VEGF") program with Merck. Merck and Alnylam will jointly fund the development of, and share the profits from, any RNAi therapeutics for the United States market that result from the collaboration. Alnylam will also have the option to co-promote these RNAi therapeutics in the United States. Marketing and sales outside of the United States will be conducted by Merck, with Alnylam receiving royalties.

Item 2. Management' s Discussion and Analysis of Financial Condition and Results of Operations

This Quarterly Report on Form 10-Q contains forward-looking statements about our plans, objectives, expectations, and intentions. You can identify these statements by words such as "may," "will," "should," "could," "expects," "plans," "intends," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or similar expressions. You should read statements that contain these words carefully. They discuss our future expectations, contain projections of our future results of operations or our financial condition or state other forward-looking information, and may involve known and unknown risks over which we have no control. You should not place undue reliance on forward-looking statements. We cannot guarantee any future results, levels of activity, performance or achievements. Moreover, we assume no obligation to update forward-looking statements or update the reasons actual results could differ materially from those anticipated in forward-looking statements, except as required by law. The factors discussed in the sections captioned "Management' s Discussion and Analysis of Financial Condition and Results of Operations" and "Certain Factors That May Affect Future Results," in this report identify important factors that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements.

Overview

We are a biopharmaceutical company that is seeking to develop and commercialize new drugs that work through a recently discovered mechanism in cells known as RNA interference, or RNAi. We believe that RNAi therapeutics have the potential to become a major class of drugs with applications in a wide range of therapeutic areas. We have initiated programs to develop RNAi therapeutics that will be administered directly to diseased parts of the body. We are also working to extend our capabilities by investing in RNAi therapeutics that will be administered systemically in order to treat a broad range of diseases. To realize the potential of RNAi therapeutics, we are developing capabilities that we can apply to any specific small interfering RNA, or siRNA, in a systematic way to endow it with drug-like properties. We use the term "product engine" to describe these capabilities because we believe they will enable us to develop many products across a variety of therapeutic areas. We expect that our product engine will enable us to produce RNAi therapeutic candidates that are potent against and specific for a particular target, appropriately stable and able to penetrate cells of target tissues.

We commenced operations in June 2002. To date, our revenue has been derived primarily from our first strategic alliance with Merck. We expect our revenues to continue to be derived primarily from strategic alliances and license fee revenues. Since our inception, we have generated significant losses. As of June 30, 2004, we had an accumulated deficit of $50.9 million. We have funded our operations primarily through the proceeds of $84.9 million from the sale of equity securities, including $30.0 million in net proceeds from the sale of 5.75 million shares of our common stock from our initial public offering, which closed in June 2004. We have yet to submit any drug applications to any regulatory authority. We have focused our efforts since inception primarily on business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff, and raising capital. We are unable to predict when, if ever, we will be able to commence sales of any product. We have not achieved profitability on a quarterly or annual basis and we expect to

incur significant additional losses over the next several years. We expect our net losses to increase primarily due to research and development activities relating to our collaborations, drug development programs and other general corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods. Our sources of potential funding for the next several years are expected to include proceeds from the sale of equity, license and other fees, funded research and development payments, and milestone payments under existing and future collaborative arrangements. Prior the quarter ended June 30, 2004, we operated as a development-stage company. During the quarter ended June 30, 2004, we emerged from the development stage because our collaboration research activities became significant with the addition of the second collaboration with Merck. We have received payments from Merck and expect these collaborations to be a significant part of our ongoing business operations.

Research and Development

Since our inception, we have focused on drug discovery and development programs. Research and development expenses represented approximately 59% and 71% for the three and six months ended June 30, 2004 of our total operating expenses and 55% and 56% for the three and six months ended June 30, 2003. We have not tracked our historical research and development costs or our personnel and personnel-related costs on a project-by-project basis, since the majority of our efforts to date have been focused on the development of capabilities associated with our product engine rather than on specific projects.

We have initiated two programs to identify specific RNAi therapeutics that will be administered directly to diseased parts of the body, which we refer to as Direct RNAi drug candidates and we expect to initiate additional programs as the capabilities of our product engine evolve. Our current programs are focused on age-related macular degeneration, or AMD, and Parkinson' s disease, or PD. In conjunction with Merck, we are currently evaluating several RNAi therapeutics in animal models and expect to begin a clinical trial for an AMD product candidate in the second half of 2005. We entered into a collaboration with the Mayo Foundation for Medical Education and Research and the Mayo Clinic Jacksonville to explore the potential of a PD treatment by initiating testing in animal models. We plan to begin animal model testing by the end of 2004. In June 2004, we entered into a collaboration and license agreement with Merck. The agreement is a new, multi-year collaboration to develop and commercialize RNAi therapeutics for ocular diseases. This collaboration, the second strategic alliance between Merck and Alnylam, will focus on AMD and other ocular diseases caused by abnormal growth or leakage of small blood vessels in the eye. Our existing program to develop a Direct RNAi(™) therapeutic for the treatment of AMD will be incorporated into the new collaboration.

There is a risk that any drug discovery and development program may not produce revenue because of the risks inherent in drug discovery and development. Moreover, there are uncertainties specific to any new field of drug discovery, including RNAi. The successful development of any product candidate we develop is highly uncertain. Due to the numerous risks associated with developing drugs, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts necessary to complete the development of, or the period in which material net cash inflows are expected to commence from, any potential product candidate. These risks include the uncertainty of:

our ability to progress any product candidates into preclinical and clinical trials;

the scope, rate and progress of our preclinical trials and other research and development activities;

the scope, rate of progress and cost of any clinical trials we commence;

clinical trial results;

the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the terms and timing of any collaborative, licensing and other arrangements that we may establish;

the cost and timing of regulatory approvals;

the cost and timing of establishing sales, marketing and distribution capabilities;

the cost of establishing clinical and commercial supplies of any products that we may develop; and

the effect of competing technological and market developments.

Any failure to complete any stage of the development of any potential products in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of the risks and uncertainties associated with completing our projects on schedule, or at all, and the potential consequences of failing to do so, are set forth in “Certain Factors That May Affect Future Results” below.

Acquisition

In July 2003, we acquired Ribopharma AG, now called Alnylam Europe, AG, a RNAi therapeutics company based in Kulmbach, Germany. To effect the acquisition, we paid $1.5 million in cash and transaction costs of $0.4 million and issued common shares with a fair value of $1.9 million. In addition, we assumed $7.1 million in debt, of which $3.0 million was subsequently paid in cash and $4.1 million was settled through the issuance of our Series B redeemable convertible preferred stock. As a result of the acquisition, we expensed $4.6 million in the year ended December 31, 2003 of purchased in-process research and development and allocated $5.8 million to long lived assets representing the value ascribed to the Alnylam Europe work force, core technology and fixed assets acquired in the transaction. The results of Alnylam Europe are included in our consolidated results from the date of acquisition.

Critical Accounting Policies and Estimates

Our significant accounting policies are described in the notes to our consolidated financial statements included in our Registration Statement on Form S-1, which was declared effective by the SEC on May 27, 2004. There have been no changes to these policies and no significant changes to these estimates since December 31, 2003.

Results of Operations

Three and Six Months Ended June 30, 2004 Compared to the Three and Six Months Ended June 30, 2003

Revenue

We do not currently sell any therapeutic products. To date, our revenue has been derived primarily from our first strategic alliance with Merck. We received a $2.0 million license fee from our first agreement with Merck in 2003, which has been deferred and is being recognized as revenue over six years, the estimated period of performance under the collaboration agreement. We did not recognize any revenue in the three and six months ended June 30, 2003. In June 2004, we entered into a collaboration and license agreement with Merck. The agreement is a new, multi-year collaboration to develop and commercialize RNAi therapeutics for ocular diseases. Under the terms of the agreement, we will receive a $2.0 million license fee from Merck as well as $1.0 million representing reimbursement of prior research and development costs we incurred on our age-related macular degeneration, or AMD, program targeting vascular endothelial growth factor, or VEGF. These amounts have been deferred and will be recognized as revenue over the estimated period of performance under the collaboration agreement. For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances. In addition, we have recently established license programs for research reagents and services, which are expected to provide revenues from license fees and from royalties on sales.

Research and Development Expenses

We expense research and development costs as incurred. Research and development expenses were $4.2 million and $14.6 million for the three and six months ended June 30, 2004, as compared to $1.8 million and $3.1 million for the three and six months ended June 30, 2003. The increase for the three and six months ended June 30, 2004 as compared to the three and six months ended June 30, 2003 resulted primarily from the $0.5 million and $5.0 million license fees incurred during the three months ended June 30, 2004 and March 31, 2004, under our agreement with Isis Pharmaceuticals, Inc., or Isis, research and development expenses of $1.3 million and $2.5 million incurred by Alnylam Europe, which we acquired in July 2003, for which there are no comparable amounts in the prior period, and the increase in payroll and related expenses of our research and development team of $0.5 million and $1.3 million. The remainder of the increase is primarily a result of an expansion of our technology development program during 2004 and the increased rent and associated rent charges related to our new headquarters in Cambridge, Massachusetts which we began to occupy in the quarter ended June 30, 2004. Noncash compensation (income) expense charges were ($0.5) million and $1.2 million for the three and six months ended June 30, 2004 as compared to $0.2 million and $0.7 million for the three and six months ended June 30, 2003. Noncash compensation charges can fluctuate significantly based on our stock price and the number of unvested options granted to our nonemployees because of the need to calculate the charge associated with such options at the end of each quarter. We expect to continue to devote substantial and increasing resources to research and development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related expenses, professional fees, and expenses related to general corporate activities. General and administrative expenses were $2.9 million and $6.0 million for the three and six months ended June 30, 2004 as compared to $1.5 million and $2.4 million for the three and six months ended June 30, 2003. The increase in the three and six month periods resulted primarily from an increase of $0.4 million and $0.9 million in noncash stock-based compensation, the acquisition of Alnylam Europe, which resulted in additional expenses of $0.3 million and $0.6 million, for which there are no comparable amounts in the prior period, and an increase in payroll and related expenses of $0.1 million and $0.8 million resulting from the hiring of additional employees and members of the management team. The remainder of the increase resulted primarily from infrastructure building and various costs associated with growth and related increased business activities. We anticipate that these expenses will continue to increase as a result of the expected expansion of our operations, facilities and other activities associated with the planned expansion of our business, together with additional costs associated with operating as a public company.

Interest Income and Expense

We did not generate significant interest income for the three and six months ended June 30, 2004 or 2003. Interest expense was $0.1 million and $0.3 million for the three and six months ended June 30, 2004. We did not have any significant interest expense for the three and six months ended June 30, 2003. The interest expense for the three and six months ended June 30, 2004 is related to our borrowings for equipment purchases under our previous Silicon Valley Bank line of credit, the premium paid to pay off this line of credit in March 2004, as well as the amounts incurred under our new Lighthouse line of credit. We expect that our interest expense will increase as we continue to draw down our equipment loan with Lighthouse.

Accretion of Redeemable Convertible Preferred Stock

Accretion of redeemable convertible preferred stock relates primarily to the 10% annual interest feature on the Series A and Series B redeemable convertible preferred stock as well as the deemed dividend of $0.8 million recorded on the Series D preferred stock issued in March 2004 resulting from a beneficial conversion feature. The accretion and deemed dividend were $0.8 million and $2.7 million for the three and six months ended June 30, 2004, as compared to $0.4 and $0.9 million for the three and six months ended June 30, 2003. The increase resulted from the issuance of Series A and Series B redeemable convertible preferred stock during the third quarter of 2003 and the issuance of the Series D convertible preferred stock in March 2004. Upon the closing of our initial public offering in June 2004, all of our preferred stock was converted into common stock, and therefore, there will not be any further accretion charges recorded after June 2004.

Liquidity and Capital Resources

We commenced operations in June 2002. Since our inception, we have generated significant losses. As of June 30, 2004, we had an accumulated deficit of $50.9 million. We have funded our operations primarily through the proceeds of $84.9 million from the sale of equity securities, including $30.0 million in net proceeds from the sale of 5.75 million shares of our common stock from our initial public offering, which closed in June 2004. As of June 30, 2004, we had cash and cash equivalents and marketable securities of $46.0 million, compared to cash and cash equivalents of $23.2 million as of December 31, 2003. The significant increase in cash and cash equivalents as of June 30, 2004 as compared to December 31, 2003 was primarily related to the $30.0 million of net proceeds that we received as a result of the closing of our initial public offering in June 2004, partially offset by cash used to fund our operations.

We invest in cash equivalents, U.S. Government obligations, high-grade corporate notes and commercial paper. Our investment objectives for our investments, are, primarily, to assure liquidity and preservation of capital, and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value. Fair value is determined based on quoted market prices.

Net cash used in operating activities was $14.9 million for the six months ended June 30, 2004. The use of cash in this period resulted primarily from funding our efforts in business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff and raising capital. In addition, during the six months ended June 30, 2004, we paid $3 million of the $5 million due under the license agreement with Isis, which was signed in March 2004.

Net cash used in investing activities was $20.6 million for the six months ended June 30, 2004. The use of cash in this period resulted primarily from the purchase of research and development equipment and, in the six months ended June 30, 2004, capital expenditures related to the tenant improvements for our new facility in Cambridge, Massachusetts.

Net cash provided by financing activities was $44.3 million for the six months ended June 30, 2004. The net cash provided by financing activities resulted primarily from the sale of convertible preferred stock of $10.0 million for the six months ended June 30, 2004 as well as $30.0 million in net proceeds from the closing of our initial public offering in June 2004.

In March 2004, we entered into a collaboration and license agreement providing for an upfront license payment to Isis of $5.0 million, of which $3.0 million was paid upon the signing of the agreement and the remaining $2.0 million is due in January 2005. We also agreed to make milestone payments (totaling $3.4 million payable upon the occurrence of specified development and regulatory events) and royalties to Isis for each product that we or a collaborator develop utilizing Isis intellectual property. In addition, we agreed to pay to Isis a percentage of some fees from strategic collaborations we enter into that include access to the Isis intellectual property. In connection with the Merck ocular collaboration discussed below, the Company recorded $0.5 million in license fee expense due to Isis, which was recorded in June 2004. In connection with the agreement, in March 2004, Isis purchased 1,666,667 shares of our Series D preferred stock for $10.0 million, which were converted into 877,193 shares of our common stock upon the

closing of our initial public offering in June 2004. Isis also agreed to pay us a license fee, milestone payments (totaling $3.4 million payable upon the occurrence of specified development and regulatory events) and royalties for each product developed by Isis or a collaborator that utilizes our intellectual property.

In June 2004, we entered into a collaboration and license agreement with Merck. The agreement is a new, multi-year collaboration to develop and commercialize RNAi therapeutics for ocular diseases. Under the terms of the agreement, we will receive a $2.0 million license fee from Merck as well as $1.0 million for reimbursement of prior research and development costs we incurred on our AMD program. These amounts have been deferred and will be recognized as revenue over the estimated period of performance under the collaboration agreement. Cash milestone payments to us could collectively total $19.5 million. In addition, the agreement provides for us to work on two additional mutually agreed ocular targets in addition to our VEGF program with Merck. Merck and Alnylam will jointly fund the development of, and share the profits from, any RNAi therapeutics for the United States market that result from the collaboration. We will also have the option to co-promote these RNAi therapeutics in the United States. Marketing and sales outside of the United States will be conducted by Merck and we will receive royalties.

Based on our current operating plan, we believe that the proceeds from our initial public offering, together with our existing resources, will be sufficient to fund our planned operations through at least the end of 2005, during which time we expect to extend the capabilities of our product engine, initiate development of a product for the treatment of wet AMD and continue to prosecute patent applications and otherwise build and maintain our patent portfolio. However, we may require significant additional funds earlier than we currently expect in order to develop and commence clinical trials for any product candidates we identify.

We expect to seek additional funding through collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our

stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. 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 or product candidates that we would otherwise pursue.

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

- our progress in demonstrating that siRNAs can be active as drugs;
- our ability to develop relatively standard procedures for selecting and modifying siRNA drug candidates;
- progress in our research and development programs, as well as the magnitude of these programs;
- the timing, receipt, and amount of milestone and other payments, if any, from present and future collaborators, if any;
- our ability to establish and maintain additional collaborative arrangements;
- the resources, time and costs required to successfully initiate and complete our preclinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property;
- the cost of preparing, filing, prosecuting, maintaining, and enforcing patent claims; and
- the timing, receipt and amount of sales and royalties, if any, from our potential products.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements or relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities.

Contractual Obligations and Commitments

Set forth below is a description of our contractual cash obligations as of June 30, 2004.

Contractual Obligations	Total	Less than One Year	2005 through 2007	2008 through 2009	After 2009
			($ in thousands)		
Operating lease obligations	$ 15,246	$ 1,637	$ 6,092	$ 4,086	$ 3,431
Short and long-term debt	7,644	205	4,317	3,122	–
Consulting agreements	360	144	216	–	–
Total contractual cash obligations	$ 23,250	$ 1,986	$ 10,625	$ 7,208	$ 3,431

We also in-license technology from a number of other sources. Pursuant to these in-license agreements, we will be required to make payments if and when we achieve specified development and regulatory milestones. If we successfully commercialize products that utilize technology licensed under these agreements, we will be required to pay aggregate milestone payments ranging from $0.6 million to $2.4 million per product under each of these agreements.

On March 26, 2004, we entered into an equipment line of credit with Lighthouse to finance equipment purchases of up to $10 million. The borrowings bear interest at 3% over the prime rate of interest plus an additional 11.5% due at the end of the term of each borrowing. We will make interest only payments on all draw-downs through June 30, 2005, at which point all draw-downs under the line of credit will be repaid over 48 months. The borrowings are collateralized by the assets financed. At June 30, 2004, we had an outstanding balance of $5.7 million under this facility. The terms of the Lighthouse agreement include covenants which limit our ability to sell or transfer certain assets or businesses or to pay dividends or other distributions above specified limits.

On March 26, 2004, we entered into an agreement with Perini Building Company, Inc. for the build out of our new facility in Cambridge, Massachusetts. The contract contains a guaranteed maximum price of $5.6 million, $4.4 million of which we had paid as of June 30, 2004 and the remainder of which we expect to pay by September 30, 2004. As part of the lease agreement that we entered into with the landlord of this facility, the landlord will reimburse us for up to approximately $3.0 million of certain of the costs of the tenant improvements which we expect to receive in the quarter ended September 30, 2004.

Recently Issued Accounting Pronouncements

In April 2004, the Emerging Issues Task Force or EITF issued Statement No. 03-06, “Participating Securities and the Two-Class Method Under Financial Accounting Standards Board or FASB Statement No. 128, Earnings Per Share.” EITF 03-06 addresses a number of questions regarding the computation of earnings per share by a company that has issued securities other than common stock that contractually entitle the holder to the right to participate in dividends when, and if, declared. The issue also provides further guidance in applying the two-class method of calculating earnings per share, clarifying the definition of a participating security and how to apply the two-class method. EITF 03-06 is effective for fiscal periods beginning after March 31, 2004, which is our second quarter, and is required to be retroactively applied. There was no impact from the adoption of EITF 03-06 on our earnings per share as we have incurred net operating losses during each period presented in the consolidated financial statements and the effect would be anti-dilutive.

CERTAIN FACTORS THAT MAY AFFECT FUTURE RESULTS

We caution you that the following important factors, among others, in the future could cause our actual results to differ materially from these expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Quarterly Report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Business

Risks Related to Being an Early Stage Company

Because we have a short operating history, there is a limited amount of information about us upon which you can evaluate our business and prospects.

Our operations began in June 2002 and we have only a limited operating history upon which you can evaluate our business and prospects. In addition, as an early stage company, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

execute product development activities using an unproven technology;

build and maintain a strong intellectual property portfolio;

gain acceptance for the development and commercialization of our products;

develop and maintain successful strategic relationships; and

manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, raise capital, expand our business or continue our operations.

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

We have concentrated our efforts and therapeutic product research on RNAi technology, and our future success depends on the successful development of this technology and products based on RNAi technology. Neither we nor any other company has received regulatory approval to market therapeutics utilizing siRNAs. The scientific discoveries that form the basis for our

efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Skepticism as to the feasibility of developing RNAi therapeutics has been expressed in scientific literature. For example, Richard Robinson, in an article titled "RNAi Therapeutics, How Likely, How Soon?" published in *Public Library of Science Biology*, indicates that no clinical trials have been commenced for any RNAi therapeutic, that two similar but more advanced therapies that showed promise in the laboratory have not yet demonstrated equal success in humans, that stability and delivery of siRNAs are obstacles intrinsic to the biochemical nature of RNA and that the human body' s reaction to RNAi therapies is still unknown.

Very few drug candidates based on these discoveries have ever been tested in animals, and none has been tested in humans. siRNAs, the class of molecule we are trying to develop into drugs, do not naturally possess the inherent properties typically required of drugs, such as the ability to be stable in the body long enough to reach the tissues in which their effects are required, nor the ability to enter cells within these tissues in order to exert their effects. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these drug-like properties into siRNAs. We may spend large amounts of money trying to introduce these properties, and never succeed in doing so. In addition, these compounds may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable product. If we do not successfully develop and commercialize drugs based upon our technological approach, we will not become profitable and the value of our common stock will decline.

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

Risks Related to Our Financial Results and Need for Financing

We have a history of losses and may never be profitable.

We have experienced significant operating losses since our inception. As of June 30, 2004, we had an accumulated deficit of $50.9 million. To date, we have not developed any products nor generated any revenues from the sale of products. Further, we do not expect to generate any such revenues in the foreseeable future. We expect our annual operating losses to increase over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We anticipate that the majority of any revenue we generate over the next several years will be from collaborations with pharmaceutical companies, but cannot be certain that we will be able to secure these collaborations or to meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments. To date, our collaboration and license agreements have provided us with minimal revenue. If we are unable to secure revenue from collaborations, we may be unable to continue our efforts to discover, develop and commercialize RNAi therapeutics without raising financing from other sources.

To become and remain profitable, we must succeed in developing and commercializing novel drugs with significant market potential. This will require us to be successful in a range of challenging activities that we have yet to initiate, including preclinical testing and clinical trial stages of development, obtaining regulatory approval for these novel drugs, and manufacturing, marketing and selling them. We may never succeed in these activities, and may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we cannot become and remain profitable, the market price of our common stock could decline. In addition, we may be unable to raise capital, expand our business, diversify our product offerings or continue our operations.

We will require substantial additional funds to complete our research and development activities and if additional funds are not available we may need to critically limit, significantly scale back or cease our operations.

We have used substantial funds to develop our RNAi technologies and will require substantial funds to conduct further research and development, including preclinical testing and clinical trials of any product candidates, and to manufacture and market any products that are approved for commercial sale. Because the successful development of our products is uncertain, we are unable to estimate the actual funds we will require to develop and commercialize them.

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

- our progress in demonstrating that siRNAs can be active as drugs;
- our ability to develop relatively standard procedures for selecting and modifying siRNA drug candidates;
- progress in our research and development programs, as well as the magnitude of these programs;
- the timing, receipt, and amount of milestone and other payments, if any, from present and future collaborators, if any;
- our ability to establish and maintain additional collaborative arrangements;
- the resources, time and costs required to initiate and complete our preclinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property; and
- the timing, receipt and amount of sales and royalties, if any, from our potential products.

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

We will be required to seek additional funding in the future and intend to do so through collaborative arrangements and public or private equity offerings and debt financings. Additional funds may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our then-existing stockholders will result. Debt financing, if available, may involve restrictive covenants that could limit our flexibility in conducting future business activities. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. 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.

Risks Related to Our Dependence on Third Parties

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

We do not have any capability for sales, marketing or distribution and have limited capabilities for drug development. Accordingly, we must enter into alliances with other companies that can provide such capabilities. For example, we may enter into alliances with major pharmaceutical companies to jointly develop specific drug candidates and to jointly commercialize them if they are approved. In such alliances, we would expect our pharmaceutical collaborators to provide substantial capabilities in clinical development, regulatory affairs, marketing and sales. We may not be successful in entering into any such alliances on favorable terms. Even if we do succeed in securing such alliances, we may not be able to maintain them if, for example, development or approval of a drug candidate is delayed or sales of an approved drug are disappointing. Furthermore, any delay in entering into collaboration agreements could delay the development and commercialization of our drug candidates and reduce their competitiveness even if they reach the market. Any such delay related to our collaborations could adversely affect our business.

In addition, we expect that we will need to enter into alliances with other companies to provide substantial additional cash for development and potential commercialization of our drug candidates. We entered into a collaboration agreement with Merck in September 2003, under which Merck may elect to pay a portion of the costs to develop and market certain drug candidates that we may initially develop based on information and materials provided by Merck. Merck is under no obligation to pay any of the development and commercialization costs for any of these drug candidates, and they may elect not to do so. For drug candidates from our Merck collaboration that Merck does not elect to fund, and for drug candidates we may develop outside of this collaboration, we expect to seek additional collaborations with other pharmaceutical companies to fund all or part of the costs of drug development and commercialization. In June 2004, we entered into a second collaboration and license agreement with Merck for ocular disease, including our current VEGF program. The agreement is a new, multi-year collaboration to develop and commercialize RNAi therapeutics for ocular diseases. The agreement provides for us to work with Merck on two additional mutually agreed ocular targets in addition to our

VEGF program. We may not be able to enter into such further collaborations, 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 a particular drug candidate, we may not have sufficient funds to develop this or any other drug candidate internally, or to bring any drug candidates to market. If we do not have sufficient funds to develop and bring our drug candidates to market, we will not be able to generate sales revenues from these drug candidates, and this will substantially harm our business.

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

Our expected dependence on collaborators for capabilities and funding means that our business would be adversely affected if any collaborator terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future collaborations, if any, may not be scientifically or commercially successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. If a collaborator terminates its collaboration with us, for breach or otherwise, it would be difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. In addition, a collaborator could determine that it is in its financial interest 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 their 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 they do for product candidates of their own development.

If any of these occur, the development and commercialization of one or more drug 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.

In addition, we have entered into a research collaboration agreement with the Mayo Foundation for Medical Education and Research and the Mayo Clinic Jacksonville, which we refer to collectively as the Mayo Clinic, in connection with our PD program and we may enter into similar agreements in the future. Either party may terminate this research collaboration agreement upon a breach by the other party. The agreement provides us with an option to acquire an exclusive license to any intellectual property or inventions developed in connection

with the collaboration. However, in order to secure any such license, we and the Mayo Clinic must agree on terms within 90 days of the exercise of the option. We may not be able to enter into any such license on reasonable terms, if at all.

We have no manufacturing experience or resources and we must incur significant costs to develop this expertise or rely on third parties to manufacture our products.

We have no manufacturing experience. In order to develop products, apply for regulatory approvals and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. We expect to rely on others to manufacture the materials we will require for any clinical trials that we initiate. Only a limited number of manufacturers can supply synthetic RNAi, and we have not secured any long-term commercial supply arrangements. The manufacturing process for any products that we may develop is an element of the FDA approval process and we will need to contract with manufacturers who can meet the FDA requirements on an ongoing basis. In addition, if we receive the necessary regulatory approval for any product candidate, we also expect to rely on third parties, including our collaborators, to produce materials required for commercial production. We may experience difficulty in obtaining adequate manufacturing capacity for our needs. If we are unable to obtain or maintain contract manufacturing for these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our products.

To the extent that we enter into manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner and consistent with regulatory requirements. The failure of a third-party manufacturer to perform its obligations as expected could adversely affect our business in a number of ways, including:

- we may not be able to initiate or continue clinical trials of products that are under development;
- we may be delayed in submitting applications for regulatory approvals for our products;
- we may lose the cooperation of our collaborators;
- we may be required to cease distribution or recall some or all batches of our products; and
- ultimately, we may not be able to meet commercial demands for our products.

If a third-party manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different third-party manufacturer, which we may not be able to do on reasonable terms, if at all. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. This would increase our reliance on such

manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our products.

We have no sales, marketing or distribution experience and expect to depend significantly on third parties who may not successfully commercialize our products.

We have no sales, marketing or distribution experience. We expect to rely heavily on third parties to launch and market certain of our product candidates, if approved. We may have limited or no control over the 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.

To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources. For products where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

we may not be able to attract and build a significant marketing or sales force;

the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and

our direct sales and marketing efforts may not be successful.

Risks Related to Managing Our Operations

If we are unable to attract and retain qualified key management and scientists, staff consultants and advisors, our ability to implement our business plan may be adversely affected.

We are highly dependent upon our senior management and scientific staff. The loss of the service of any of the members of our senior management, including Dr. John Maraganore, our President and Chief Executive Officer, may significantly delay or prevent the achievement of product development and other business objectives. Our employment agreements with our key personnel are terminable without notice. We do not carry key man life insurance on any of our key employees.

Although we have generally been successful in our recruiting efforts, we face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our business plan.

We may have difficulty managing our growth and expanding our operations successfully as we seek to evolve from a company primarily involved in discovery and preclinical testing into one that develops and commercializes drugs.

Since we commenced operations in 2002, we have grown rapidly to over 60 full time employees, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. This rapid and substantial growth, and the geographical separation of our sites, has placed a strain on our administrative and operational infrastructure, and we anticipate that our continued growth will have a similar impact. If drug candidates we develop enter and advance through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with other organizations to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various collaborators, suppliers and other organizations. Our ability to manage our operations and growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures in at least two different countries. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

If we are unable to manage the challenges associated with our international operations, the growth of our business could be limited.

In addition to our operations in Cambridge, Massachusetts, we operate an office and laboratory in Kulmbach, Germany. We are subject to a number of risks and challenges that specifically relate to these international operations. Our international operations may not be successful if we are unable to meet and overcome these challenges, which could limit the growth of our business and may have an adverse effect on our business and operating results. These risks include:

fluctuations in foreign currency exchange rates that may increase the U.S. dollar cost of our international operations;

difficulty managing operations in multiple locations, which could adversely affect the progress of our product candidate development program and business prospects;

local regulations that may restrict or impair our ability to conduct biotechnology-based research and development;

foreign protectionist laws and business practices that favor local competition; and

failure of local laws to provide the same degree of protection against infringement of our intellectual property, which could adversely affect our ability to develop product candidates or reduce future product or royalty revenues, if any, from product candidates we may develop.

Risks Related to Our Industry

Risks Related to Development, Clinical Testing and Regulatory Approval of Our Drug Candidates

Any drug candidates we develop may fail in development or be delayed so much that they do not become commercially viable.

Preclinical testing and clinical trials of new drug candidates are lengthy and expensive and the historical failure rate for drug candidates is high. We may not be able to advance any product candidates into clinical trials. Even if we do successfully enter into clinical studies, the results from preclinical testing of a drug candidate may not predict the results that will be obtained in human clinical trials. We, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons. Among other reasons, adverse side effects of a drug candidate on subjects or patients in a clinical trial could result in the FDA or foreign regulatory authorities suspending or terminating the trial and refusing to approve a particular drug candidate for any or all indications of use.

Clinical trials of a new drug candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the drug 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 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. Delays in patient enrollment can result in increased costs and longer development times.

Clinical trials also require the review and oversight of institutional review boards, referred to as IRBs, which approve and continually review clinical investigations and protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or delay the initiation and completion of clinical trials, and the FDA may decide not to consider any data or information derived from a clinical investigation not subject to initial and continuing IRB review and approval in support of a marketing application.

Our drug candidates that we develop may encounter problems during clinical trials that will cause us or regulatory authorities to delay or suspend these trials, or that will delay 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 drug candidate that is affected, or development of any of our other drug candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected drug candidate and for other drug candidates we are developing.

Delays in clinical trials could reduce the commercial viability of our drug candidates. Any of the following could delay our clinical trials:

discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;

problems in engaging IRBs to oversee trials or problems in obtaining IRB approval of

studies;

delays in enrolling patients and volunteers into clinical trials;

high drop-out rates for patients and volunteers in clinical trials;

negative results of clinical trials;

inadequate supply or quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;

serious and unexpected drug-related side effects experienced by participants in our clinical trials; or

unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation.

The FDA approval process may be delayed for any drugs we develop that require the use of specialized drug delivery devices.

Some drug candidates that we develop may need to be administered using specialized drug delivery devices. We believe that any product candidate we develop for PD will need to be administered using such a device. While we expect to rely on drug delivery systems that have been approved by the FDA or other regulatory agencies to deliver drugs like ours to similar physiological sites, we may need to modify the design or labeling of such delivery device for some products we may develop. In such an event, the FDA may regulate the product as a combination product or require additional approvals or clearances for the modified delivery device. Further, to the extent the specialized delivery device is owned by another company, we would need that company' s cooperation to implement the necessary changes to the device, or its labeling, and to obtain any additional approvals or clearances. Obtaining such additional approvals or clearances, and cooperation of such other companies, when necessary, could significantly delay and increase the cost of obtaining marketing approval, which could reduce the commercial viability of our drug candidate.

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

Our drug candidates are subject to extensive governmental regulations relating to development, clinical trials, manufacturing and commercialization. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the United States and in many foreign jurisdictions before a new drug can be sold. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we may develop will obtain the appropriate regulatory approvals necessary for us or our collaborators to begin selling them.

We have no experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and

other approvals is unpredictable but typically exceeds five years following the commencement of clinical trials, depending upon the complexity of the drug candidate. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review.

Because the drugs we are intending to develop may represent a new class of drug, the FDA has not yet established any definitive policies, practices or guidelines in relation to these drugs. While we expect any AMD or PD product candidates we develop will be regulated as a new drug under the Federal Food, Drug, and Cosmetic Act, the FDA could decide to regulate them or other products we may develop as biologics under the Public Health Service Act. The lack of such policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there are approved treatments for both AMD and PD, in order to receive regulatory approval, we will 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.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular drug candidate. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. These limitations may limit the size of the market for the product.

We are also subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process 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 assure approval by regulatory authorities outside the United States.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. and foreign regulations, we could lose our approvals to market drugs and our business would be seriously harmed.

Following any initial regulatory approval of any drugs we may develop, we will also be subject to continuing regulatory review, 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 vigilance required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. The discovery of any previously unknown problems with the product, manufacturer or facility may result in restrictions on the drug or manufacturer or facility, including withdrawal of the drug from the market. We do not have, and currently do not intend to develop, the ability to manufacture material for our clinical trials or on a commercial scale. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including

reliance on the third-party manufacturer for regulatory compliance. Our product promotion and advertising is also subject to regulatory requirements and continuing FDA review.

If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and criminal prosecutions.

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

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

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, efficacy and ease of administration;

the success of our physician education programs;

the availability of government and third-party payor reimbursement;

the pricing of our products, particularly as compared to alternative treatments; and

the availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat.

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

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

warning letters;

recalls or public notification or medical product safety alerts;

restrictions on, or prohibitions against, marketing our products;

restrictions on importation of our products;

suspension of review or refusal to approve pending applications;

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties and fines.

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. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness and the level or method of reimbursement. Increasingly, the third-party payors who reimburse patients, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are challenging the prices charged for medical products. If the price we are able to charge for any products we develop is inadequate in light of our development and other costs, our profitability could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician. Under currently applicable law, drugs that are not usually self-administered may be eligible for coverage by the Medicare 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 standard of medical practice;

they are not excluded as immunizations; and

they have not been determined by the FDA to be less than effective.

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. 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. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, 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 health care programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for new drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed in recent years. These proposals have included prescription drug benefit legislation recently enacted in the United States and healthcare reform legislation recently enacted by certain states. Further federal and state legislative and regulatory developments are possible and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from drug candidates that we may successfully develop.

Another development that may affect the pricing of drugs is Congressional action regarding drug reimportation into the United States. The Medicare Prescription Drug Plan legislation, which became law in December 2003, requires the Secretary of Health and Human Services to promulgate regulations for drug reimportation from Canada into the United States under some circumstances, including when the drugs are sold at a lower price than in the United States. The Secretary retains the discretion not to implement a drug reimportation plan if he finds that the benefits do not outweigh the cost. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, they could decrease the price we receive for any products that we may develop, negatively affecting our anticipated revenues and prospects for profitability.

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, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, or limitations on the indications for which they may be used, or suspension or withdrawal of approval. We currently do not have any product liability insurance, but plan to obtain such insurance at appropriate levels prior to initiating clinical trials and at higher levels prior to marketing any of our drug candidates. Any insurance we obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business.

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

Our research and development involves 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 Germany that are required for our research and development activities. We believe our procedures for storing, handling and disposing these materials in our Cambridge facility comply with the relevant guidelines of the City of Cambridge and the Commonwealth of Massachusetts and the procedures we employ in our German facility comply with the standards mandated by applicable German laws and guidelines. 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 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 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 preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing and marketing pharmaceutical products;
- product candidates that are based on previously tested or accepted technologies;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. We believe a significant number of drugs are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. For instance, we are currently evaluating RNAi therapeutics to suppress VEGF gene activity as a potential drug candidate for the treatment of wet AMD and we are currently evaluating the potential of RNAi therapeutics for the treatment of PD. One drug, Visudyne, is already marketed for the treatment of wet AMD, and numerous drugs are currently marketed for the treatment of PD. In addition, we are aware of a number of experimental drugs for the treatment of wet AMD that, unlike our product candidate, are in advanced stages of clinical development. These experimental drugs include Macugen, which is being developed by Eyetech Pharmaceuticals, Inc. in collaboration with Pfizer, Inc., and Lucentis, which is being developed by Genentech, Inc. in collaboration with Novartis. These drug candidates may be approved for marketing before our product candidate receives approval. Furthermore, our competitors' products may be more effective, or marketed and sold more effectively, than any products we develop.

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

- the safety and effectiveness of our products;
- the timing and scope of regulatory approvals for these products;

the availability and cost of manufacturing, marketing and sales capabilities;

price;

reimbursement coverage; and

patent position.

Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above. 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 drug candidates. 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 drug candidates noncompetitive, obsolete or uneconomical.

We face competition from other companies that are working to develop novel drugs using technology similar to ours. If these companies develop drugs more rapidly than we do or their technologies are more effective, our ability to successfully commercialize drugs will 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 in the field of RNAi, including Sirna Therapeutics, Inc., Acuity Pharmaceuticals, Inc., Nucleonics, Inc., Benitec Ltd. and CytRx Corporation. In addition, we granted a license to Isis under which it may develop RNAi therapeutics against a limited number of targets. Any of these companies may develop its RNAi technology more rapidly and more effectively than us.

We also compete with companies working to develop antisense-based drugs. Like RNAi product candidates, antisense drugs target mRNAs in order to suppress the activity of specific genes. Isis is currently marketing an antisense drug and has several antisense drug candidates in clinical trials, and another company, Genta Inc., has an antisense drug candidate under FDA review. The development of antisense drugs is more advanced than that of RNAi therapeutics and may become the preferred technology for drugs that target mRNAs to silence specific genes.

Risks Related to Patents, Licenses and Trade Secrets

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

Our success depends, in part, on our ability to protect proprietary methods and technologies that we develop under the patent and other intellectual property laws of the United States and other countries, so that we can prevent others from unlawfully using our inventions and proprietary information. However, we may not hold proprietary rights to some patents required

for us to commercialize our proposed products. Because certain U.S. patent applications are confidential until patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date which will not be filed in foreign countries, third parties may have filed patent applications for technology covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over those applications. For this and other reasons, we may be unable to secure desired patent rights, thereby losing desired exclusivity. Further, we may be required to obtain licenses under third-party patents to market our proposed products or conduct our research and development or other activities. If licenses are not available to us on acceptable terms, we will 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 will 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 will 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. The mere issuance of a patent does not guarantee that it is valid or enforceable, so even if we obtain patents, they may not be valid or enforceable against third parties.

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 United States Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. 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 on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.

We license patent rights from third party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will 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 Isis, Hybridon, Carnegie Institution of Washington, Cancer Research Technology Limited, the Massachusetts Institute of Technology, the Whitehead Institute, Garching Innovation GmbH, representing the Max Planck Gesellschaft zur Förderung der Wissenschaften e.V., referred to as the Max Planck organization, and Cold Spring Harbor Laboratory. 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.

One of our key patents, the so-called Kreutzer-Limmer patent, is the subject of an opposition proceeding in the European Patent Office, which could result in the invalidation of this patent.

We believe our so-called Kreutzer-Limmer patent is the only patent granted to date that specifically covers the use of short dsRNAs as therapeutics. A German Utility Model covering RNAi composition was registered in 2003, and a patent covering RNAi compositions and their use was granted by the European Patent Office, or EPO, in 2002 and in South Africa in 2003. Related patent applications are pending in other countries, including the United States. A German Utility Model is a form of patent that is directed only to physical matter, such as medicines, and does not cover methods. The maximum period of protection afforded by the German Utility Model ends in 2010. After the grant by the EPO of the Kreutzer-Limmer patents published under publication number EP 1144623B9, several oppositions to the issuance of the European patent were filed with the EPO, a practice that is allowed under the European Patent Convention. Each of the oppositions raises a number of grounds for the invalidation of the patent, including the use of disclaimer practice. The EPO opposition division in charge of the opposition proceedings may agree with one or more of the grounds and could revoke the patent in whole or restrict the scope of the claims. It may be several years before the outcome of the opposition proceeding is decided by the EPO.

In addition, the Enlarged Board of Appeal at the EPO recently rendered a decision in an unrelated case covering what is known as “disclaimer practice”. With a disclaimer, a patent applicant gives up, or disclaims, part of the originally claimed invention in a patent application in order to overcome prior art and adds a limitation to the claims which may have no basis in the original disclosure. The Enlarged Board determined that disclaimer practice is allowed under the European Patent Convention under a defined set of circumstances. It now has to be determined as part of the opposition proceedings regarding the Kreutzer-Limmer patent whether the use of a disclaimer during the prosecution of this case falls within one of the allowable circumstances. Determination by the EPO opposition division that the use of the disclaimer in this case does not fall under one of the allowed circumstances could result in the invalidation of the Kreutzer-Limmer patent. Even if the EPO opposition division determines that the use of a disclaimer is permissible, the Kreutzer-Limmer patent would remain subject to the other issues raised in the opposition. If the Kreutzer-Limmer patent is invalidated or limited for any reason, other companies will be better able to develop products that compete with ours, which could adversely affect our competitive business position, business prospects and financial condition.

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

RNA interference is a relatively new scientific field that has generated many different patent applications from organizations and individuals seeking to obtain important patents in the field. These applications claim many different methods, compositions and processes relating to the discovery, development and commercialization of RNAi therapeutics. Because the field is so new, very few of these patent applications have been fully processed by government patent offices around the world, and there is a great deal of uncertainty about which patents will issue, when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference proceedings in various patent offices, relating to patent rights in the RNAi field. Others may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes among third parties could lead to the weakening or invalidation of our intellectual property rights.

In addition, there are many issued and pending patents that claim aspects of oligonucleotide chemistry that we may need to apply to our siRNA drug candidates. There are also many issued patents that claim genes or portions of genes that may be relevant for siRNA drugs we wish to develop.

Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we will not be able to market products or perform research and development or other activities covered by these patents.

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

A third party may sue us for infringing its patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of third-party proprietary rights. In addition, a third party may claim that we have improperly obtained or used its confidential or proprietary information. Furthermore, in connection with a license agreement, we have agreed to indemnify the licensor for costs incurred in connection with litigation relating to intellectual property rights. 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 the litigation would divert our management' s efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

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

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

If we fail to comply with our obligations under any licenses or related agreements, we could lose license rights that are necessary for developing and protecting our RNAi technology and any related product candidates that we develop, or we could lose certain exclusive rights to grant sublicenses.

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, royalty, diligence, sublicensing, insurance and other obligations on us. If we breach any of these obligations, 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 and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. In addition, while we cannot currently determine the amount of the royalty obligations we will be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

For two important pending patent applications, owned in part or solely by the Max Planck organization of Germany, our licenses include a condition requiring us to operate a German company comparable to our United States operation until at least December 2007. If we fail to comply with this condition, the owners of the patent applications that are the subject of these licenses would have the right to grant similar licenses to one other company for each pending patent application. We regard these pending patent applications as significant because they relate to important aspects of the structure of siRNA molecules and their use as therapeutics.

We have an agreement with Isis under which we were granted licenses to over 150 patents and patent applications that we believe will be useful to the development of RNAi therapeutics. If, by January 1, 2008, we or a collaborator have not completed the studies required for an investigational new drug application filing or similar foreign filing for at least one product candidate involving these patent rights, Isis would have the right to grant licenses to third parties for these patents and patent applications, thereby making our rights non-exclusive.

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

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of

unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Risks Related to Our Common Stock

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

The market price of our common stock may fluctuate significantly in response to factors that are beyond our control. The stock market in general has recently 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 operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause purchasers of our common stock to incur substantial losses.

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

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. Recently, when the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

If there are substantial sales of our common stock, the price of our common stock could decline.

If our existing stockholders sell a large number of shares of our common stock or the public market perceives that existing stockholders might sell shares of common stock, the market price of our common stock could decline significantly. All of the shares sold in our initial public offering were freely tradable without restriction or further registration under the federal securities laws, unless purchased by our "affiliates" as that term is defined in Rule 144 under the Securities Act. Substantially all of our remaining shares will be eligible for sale pursuant to Rule 144 upon the expiration of 180-day lock-up agreements on November 23, 2004.

The holders of 11,964,908 shares of common stock have rights to require us to file registration statements under the Securities Act or to include their shares in registration statements that we may file in the future for ourselves or other stockholders. If we register their shares of common stock following the expiration of the lock-up agreements, they can sell those shares in the public market. In addition, the holders of warrants to purchase 65,787 shares of our common stock will be entitled to include shares issued upon exercise of the warrants in registration statements that we may file in the future. If we register their shares of common stock issued upon exercise of the warrants, they can sell those shares in the public market.

Insiders have substantial control over Alnylam and could delay or prevent a change in corporate control.

Our directors, executive officers and principal stockholders, together with their affiliates, beneficially own, in the aggregate, approximately 60% of our outstanding common stock as of May 28, 2004. As a result, these stockholders, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

delaying, deferring or preventing a change in control of our company;

impeding a merger, consolidation, takeover or other business combination involving our company; or

discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company.

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

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

a classified board of directors;

a prohibition on actions by our stockholders by written consent;

the ability of our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors;

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.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of

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

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. Our current investment policy is to maintain an investment portfolio consisting mainly of U.S. money market and government-grade securities, directly or through managed funds, with maturities of one year or less. Our cash and cash equivalents are deposited in and primarily invested through highly rated financial institutions in North America, primarily in money market funds, as of June 30, 2004. Our short-term investments consist of U.S. Government obligations, high-grade corporate notes and commercial paper. All of our investments in debt securities are recorded at fair value. Our short-term investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the conservative nature of our short-term investments and investments policies we do not believe that we have a material exposure to interest rate risk. Although are investments are subject to credit risk, our investment policies specify credit quality standards for our investments and limit the amount of credit exposure from any single issue, issuer or type of investment.

If market interest rates were to increase immediately and uniformly by 10% from levels at June 30, 2004, we estimate that the fair value of our investment portfolio would decline by an immaterial amount. While our cash and investment balances have increased upon the recent completion of our initial public offering, we will have the ability to hold our fixed income investments until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Item 4. Controls and Procedures

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on this evaluation, our chief executive officer and chief financial officer concluded that, as of the end of the period covered by this Quarterly Report on Form 10-Q, our disclosure controls and procedures were (1) designed to ensure that material information relating to Alnylam, including our consolidated subsidiaries, is made known to our chief executive officer and chief financial officer by others within those entities, particularly during the period in which this report was being prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC' s rules and forms.

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) identified in connection with the evaluation of our internal control over financial reporting performed during our last fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 2. Changes in Securities, Use of Proceeds and Issuer Purchases of Equity Securities

(c) Recent Sales of Unregistered Securities

During the quarterly period ended June 30, 2004, we granted stock options to purchase an aggregate of 128,641 shares of our common stock under our 2003 Employee, Director and Consultant Stock Plan and 2004 Employee, Director and Consultant Stock Plan at a weighted-average exercise price of $0.99 per share. In addition, during the quarterly period ended June 30, 2004, we issued and sold an aggregate of 11,736 shares of our common stock to employees and a consultant pursuant to exercises of options under our 2002 Employee, Director and Consultant Stock Plan and 2003 Employee, Director and Consultant Stock Plan at a weighted-average exercise price of $0.56 per share.

The issuance of stock options and the common stock issuable upon the exercise of such options as described above were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of common stock described above included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

(d) Initial Public Offering and Use of Proceeds from Sales of Registered Securities

We registered shares of our common stock in connection with our initial public offering under the Securities Act. Our Registration Statement on Form S-1 (Reg. No. 333-113162) in connection with our initial public offering was declared effective by the SEC on May 27, 2004. The offering commenced as of May 27, 2004. The offering did not terminate before any securities were sold. As of the date of the filing of this report, the offering has terminated and 5,000,000 shares of our common stock registered were sold in the initial public offering and an additional 750,000 shares of our common stock registered were sold in connection with the exercise of an over-allotment option by the underwriters. The underwriters of the offering were Banc of America Securities LLC, Citigroup Global Markets Inc., Piper Jaffray & Co. and ThinkEquity Partners LLC.

All 5,750,000 shares of our common stock registered in the offering were sold at the initial public offering price per share of $6.00. The aggregate purchase price of the offering was $34,500,000. The net offering proceeds to us after deducting total expenses were $30,000,000. We incurred total expenses in connection with the offering of $4,519,000, which consisted of direct payments of:

(i) $1,929,000 in legal, accounting and printing fees;

(ii) $2,415,000 in underwriters discounts, fees and commissions; and

(iii) $175,000 in miscellaneous expenses.

No payments for such expenses were made directly or indirectly to (i) any of our directors, officers or their associates, (ii) any person(s) owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

We completed our initial public offering on May 28, 2004. The net offering proceeds have been invested into short-term investment-grade securities and money market accounts.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b).

Item 4. Submission of Matters to Vote of Security Holders

We held our annual meeting of stockholders on April 8, 2004. The following matters were voted upon at the annual meeting:

1. The first matter voted upon was the election of directors for the ensuing year. The nominees for election were Peter Barrett, Ph.D., John E. Berriman, John K. Clarke, John M. Maraganore, Ph.D., Paul R. Schimmel, Ph.D., Phillip A. Sharp, Ph.D., Kevin P. Starr and Christoph H. Westphal, M.D., Ph.D. Each of the nominees was elected. For each of the nominees, the aggregate votes of the holders of shares of our capital stock were as follows:

a. The holders of 3,000,010 shares of our Series A preferred stock voted to elect John K. Clarke and Christoph H. Westphal, M.D., Ph.D. as directors.

b. The holders of 16,379,951 shares of our Series B preferred stock voted to elect Peter Barrett, Ph.D. as a director.

c. The holders of 19,379,961 shares of our Series A preferred stock and Series B preferred stock, voting together as a single class, voted to elect John E. Berriman as a director.

d. The holders of 4,190,407 shares of our common stock voted to elect Paul R. Schimmel, Ph.D. and Phillip A. Sharp, Ph.D. as directors.

e. The holders of 25,056,886 shares of our common stock and preferred stock, voting together as a single class, voted to elect John M. Maraganore, Ph.D. and Kevin P. Starr as directors.

No holders of shares of our capital stock withheld votes from any of the nominees.

2. The second matter voted upon was the reduction of the size of the board of directors, effective upon the closing of our initial public offering, from nine members to eight members. The reduction in the size of board of directors, effective upon the closing of our initial public offering, was approved. Holders of an aggregate of 25,056,886 shares of our common stock and preferred stock voted to decrease, effective upon the closing of our initial public offering, the size of the board of directors from nine members of eight members. No holders of shares of our capital stock voted against, or abstained from voting on, this proposal.

3. The third matter voted upon was the election, effective upon the closing of our initial public offering and subject to (i) stockholder approval of an amendment to our certificate of incorporation establishing a classified board of directors and (ii) the filing of a Certificate of Amendment relating to such amendment with the Secretary of State of the State of Delaware, of the following directors into the following classes:

Class	Name	Expiration of Term
Class I directors	John M. Maraganore, Ph.D. Paul R. Schimmel, Ph.D. Phillip A. Sharp, Ph.D.	2005 Annual Meeting

Class	Name	Expiration of Term
Class II directors	John E. Berriman John K. Clarke Christoph H. Westphal, M.D., Ph.D.	2006 Annual Meeting
Class III directors	Peter Barrett, Ph.D. Kevin P. Starr	2007 Annual Meeting

Holders of an aggregate of 25,056,886 shares of our common stock and preferred stock, voted to elect, effective upon the closing of our initial public offering and subject to (i) stockholder approval of an amendment to our certificate of incorporation establishing a classified board of directors and (ii) filing of a Certificate of Amendment relating to such amendment with the Secretary of State of the State of Delaware, Dr. Maraganore, Dr. Schimmel and Dr. Sharp as Class I directors, Mr. Berriman, Mr. Clarke and Dr. Westphal as Class II directors and Dr. Barrett and Mr. Starr as Class III directors. No holders of shares of our capital stock withheld votes from any of the nominees.

Pursuant to a written consent of stockholders in lieu of a meeting solicited prior to the closing of our initial public offering of common stock, the holders of shares of an aggregate of 25,510,098 shares of our common stock and preferred stock, approved the following matters:

1. An amendment of our 2002 Employee, Director and Consultant Stock Plan (the "2002 Plan"), providing for an increase in the number of shares of common stock available for issuance under the 2002 Plan to 2,862,356 shares (before giving effect to the reverse stock split referred to below).

2. An amendment of our 2003 Employee, Director and Consultant Stock Plan (the "2003 Plan"), providing for an increase in the number of shares of common stock available for issuance under the 2003 Plan to 1,795,144 shares (before giving effect to the reverse stock split referred to below), plus such additional shares as are represented by options and other awards granted under the 2002 Plan that are cancelled or expire without delivery of shares of stock by us, provided, however, that the number of such additional shares shall not exceed 2,862,356 shares (before giving effect to the reverse stock split referred to below).

3. Our 2004 Stock Incentive Plan (the "2004 Stock Incentive Plan") pursuant to which we may grant incentive stock options, non-qualified stock options and restricted stock awards for the purchase of up to an aggregate of 3,000,000 shares of common stock (before giving effect to the reverse stock split referred to below) and such additional shares of common stock as may be automatically added to the 2004 Stock Incentive Plan from time to time in accordance with its terms, subject to the limitations described therein.

4. Our 2004 Employee Stock Purchase Plan pursuant to which we may issue up to an aggregate of 600,000 shares of common stock (before giving effect to the reverse stock split referred to below).

5. Amendments to our Certificate of Incorporation, providing for the following reverse splits of our common stock: (a) a one-for-1.1 reverse split, (b) a one-for-1.2 reverse split, (c) a one-for-1.25 reverse split, (d) a one-for-1.3 reverse split, (d) a one-for-1.4 reverse split, (e) a one-for-1.5 reverse split, (c) a one-for-1.6 reverse split, (d) a one-for-1.7 reverse split, (e) a one-

for-1.75 reverse split, (f) a one-for-1.8 reverse split, (g) a one-for-1.9 reverse split, (h) a one-for-two reverse split; provided, however, that notwithstanding the authorization and approval by the stockholders of such amendments, the board of directors may, at any time prior to the effectiveness of said amendments with the Secretary of State of the State of Delaware, abandon any or all of such amendments without further action by the stockholders.

6. An amendment to our Certificate of Incorporation, providing for (a) an increase in the authorized number of shares of our common stock to 125,000,000, (b) the authorization of 5,000,000 shares of undesignated preferred stock that may be issued from time to time by the board of directors in one or more series, (c) an amendment of the provisions relating to the indemnification of, and limitation on liability of, officers and directors of the Company, (d) upon the closing of our initial public offering, the classification of the board into three classes, (e) upon the closing of our initial public offering, the elimination of the ability of stockholders to take action by written consent or to call a special meeting of stockholders and (f) an amendment of the mandatory conversion provisions with respect to the outstanding preferred stock to provide that upon mandatory conversion of the preferred stock, each series of preferred stock so converted shall be automatically retired and all references to such preferred stock will be deleted from the Certificate of Incorporation.

7. An amendment and restatement, effective upon the closing of our initial public offering, of our Certificate of Incorporation in its entirety, among other things, providing (a) for the elimination of all references to the preferred stock and (b) that the authorized capitalization of the Company shall consist of 125,000,000 shares of common stock and 5,000,000 shares of undesignated preferred stock.

8. An amendment and restatement, effective upon the closing of our initial public offering, of our bylaws in their entirety, among other things, providing (a) for the establishment of procedures relating to the presentation of stockholder proposals at stockholders meetings, (b) for the establishment of procedures relating to the nomination of directors, (c) for the classification of the board into three classes, (d) that the number of directors may only be set by the board and (e) that directors may only be removed by stockholders for cause and upon the vote of the holders of at least 75% of the votes entitled to be cast in any election.

9. An adoption, ratification and confirmation of all actions taken and things done by the incorporators, stockholders, directors and officers of the Company.

Item 6. Exhibits and Reports on Form 8-K

(a) Exhibits:

Exhibit No.	
3.1	Restated Certificate of Incorporation.
10.1†	Collaboration and License Agreement by and between Merck and Co., Inc. and Alnylam Pharmaceuticals, Inc. dated as of June 29, 2004.
31.1	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13a-14(a)/15d-14(a), by Chief Executive Officer.
31.2	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13a-14(a)/15d-14(a), by Chief Financial Officer.
32.1	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Chief Executive Officer.
32.2	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Chief Financial Officer.

† Confidential treatment requested as to certain portions, which portions have been filed separately with the Securities and Exchange Commission.

(b) During the quarter ended June 30, 2004, the Company did not file any Current Reports on Form 8-K.

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.
(Registrant)

Date: August 12, 2004

By: /s/ John M. Maraganore, Ph.D.
John M. Maraganore, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 12, 2004

By: /s/ Barry E. Greene
Barry E. Greene
Chief Operating Officer and Treasurer
(Principal Financial and Accounting Officer)

EXHIBIT 3.1

RESTATED CERTIFICATE OF INCORPORATION

OF

ALNYLAM PHARMACEUTICALS, INC.

(originally incorporated under the name Alnylam Holding Co. on May 8, 2003)

FIRST: The name of the Corporation is Alnylam Pharmaceuticals, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is One Hundred Thirty Million (130,000,000) shares, consisting of (i) One Hundred Twenty-Five Million (125,000,000) shares of Common Stock, par value $.01 per share (the "Common Stock"), and (ii) Five Million (5,000,000) shares of Preferred Stock, par value $.01 per share (the "Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designation of any

series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders

of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law. Different series of Preferred Stock shall not be construed to constitute different classes of shares for the purposes of voting by classes unless expressly provided.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by resolution or resolutions providing for the issuance of the shares thereof, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred

Stock may provide that such series shall be superior or rank equally or be junior to the Preferred Stock of any other series to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the laws of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the Corporation's Bylaws. The

affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present shall be required to adopt, amend, alter or repeal the Corporation's Bylaws. The Corporation's Bylaws also may be adopted, amended, altered or repealed by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors, in addition to any other vote required by this Certificate of Incorporation. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of

the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal.

EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any

threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all

expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation,

(ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advance of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event that the Corporation does not assume the defense pursuant to Section 4 of this Article EIGHTH of any action, suit, proceeding or investigation of which the Corporation receives notice under this Article, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article; and further provided that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6) that (i) Indemnitee did not act in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any

such advancement of expenses shall be made promptly, and in any event within 30 days after receipt by the Corporation of the written request of Indemnitee, unless the Corporation determines within such 30-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors"), whether or not a quorum, (b) by a

committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. The right to indemnification or advancement of expenses as granted by this Article shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. Indemnitee's expenses (including attorneys' fees) reasonably incurred in connection with successfully establishing Indemnitee's right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation.

8. Limitations. Notwithstanding anything to the contrary in this Article, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation. Notwithstanding anything to the contrary in this Article, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall

promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement; provided, however, that nothing contained in this Section 8 shall be construed to require any Indemnitee to seek reimbursement under any insurance policy.

9. Subsequent Amendment. No amendment, termination or repeal of this Article or of the relevant provisions of the General Corporation Law of Delaware or any other applicable laws shall affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee's official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant

indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), judgments, fines or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys' fees), judgments, fines or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of

the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him in any such capacity, or arising out of his status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of Delaware.

13. Savings Clause. If this Article or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees), judgments, fines and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Corporation's Board of Directors.

2. Number of Directors; Election of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the Bylaws of the Corporation.

3. Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes: Class I, Class II and Class III.

4. Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual

meeting following the annual meeting at which such director was elected; provided, that each director initially appointed to Class I shall serve for a term expiring at the Corporation's annual meeting of stockholders held in 2005;

each director initially appointed to Class II shall serve for a term expiring at the Corporation's annual meeting of stockholders held in 2006; and each director initially appointed to Class III shall serve for a term expiring at the Corporation's annual meeting of stockholders held in 2007; provided further, that the term of each director shall continue until the election and qualification of his successor and be subject to his earlier death, resignation or removal.

5. Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

6. Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.

8. Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly created directorships in the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director's earlier death, resignation or removal.

9. Stockholder Nominations and Introduction of Business, Etc. Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the Bylaws of the Corporation.

10. Amendments to Article. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation

or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time by the Board of Directors, the Chairman of the Board or the Chief Executive Officer, but such special meetings may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provision of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the Delaware General Corporation Code, has been executed by its duly authorized officer this 3rd day of June, 2004.

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ John M. Maraganore

John M. Maraganore
President and Chief Executive Officer

EXHIBIT 10.1

EXECUTION COPY

CONFIDENTIAL MATERIALS OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. ASTERISKS DENOTE OMISSIONS.

COLLABORATION AND LICENSE AGREEMENT
BY AND BETWEEN
MERCK & CO., INC.
AND
ALNYLAM PHARMACEUTICALS, INC.

COLLABORATION AND LICENSE AGREEMENT

THIS AGREEMENT, effective as of June 29, 2004 (the "EFFECTIVE DATE"), by and between MERCK & CO., INC., a corporation organized and existing under the laws of New Jersey ("MERCK"), and ALNYLAM Pharmaceuticals, Inc., a corporation organized and existing under the laws of Delaware ("ALNYLAM").

RECITALS:

WHEREAS, ALNYLAM has developed technology useful for the discovery, development, manufacture, characterization, or use of therapeutic products that function through RNA interference ("RNAI"), and is developing capabilities to develop and commercialize such therapeutic products;

WHEREAS, MERCK is engaged in the business of discovering, developing, manufacturing and commercializing human therapeutic products, including therapeutic products for ophthalmic indications;

WHEREAS, MERCK and ALNYLAM desire to enter into a collaboration to research, develop and commercialize RNAi Products (as hereinafter defined) for the treatment of Ocular Microvascular Disease (as hereinafter defined) in humans upon the terms and conditions set forth herein;

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, the Parties hereby agree as follows:

1. DEFINITIONS

Unless specifically set forth to the contrary herein, the following terms, whether used in the singular or plural, shall have the respective meanings set forth below:

1.1 "ADDITIONAL PROGRAM TARGET" means (a) a genomic locus other than VEGF, (b) any portions of such locus, (c) all transcript variants and allelic variants of such locus, (d) any RNA transcribed from within or overlapping such locus and (e) any proteins encoded by any such RNA transcripts; any of which is the target of an Ophthalmic Product that the Parties mutually agree to develop in an Additional Program pursuant to Section 2.4.

1.2 "AFFILIATE" means, with respect to a Party, (i) any corporation or business entity of which fifty percent (50%) or more of the securities or other ownership interests representing the equity, the voting stock or general partnership interest are owned, controlled or held, directly or indirectly, by such Party; (ii) any corporation or business entity, which, directly or indirectly, owns, controls or holds fifty percent (50%) (or the maximum ownership interest permitted by law) or more of the securities or other ownership

interests representing the equity, the voting stock or, if applicable, the general partnership interest, of such Party; or (iii) any corporation or business entity, fifty percent (50%) or more of the securities or other ownership interests representing the equity of which is directly or indirectly owned, controlled or held by the same corporation, business entity or security holders, or holders of ownership interests, that

own, control or hold fifty percent (50%) or more of the securities or other ownership interests representing the equity or the voting stock of such Party.

1.3 "ALNYLAM COLLABORATION IP" means (a) any improvement, discovery or Know-How, patentable or otherwise, first identified, discovered or developed solely by employees of ALNYLAM or its Affiliates or other persons not employed by MERCK acting on behalf of ALNYLAM, under the Ophthalmic Collaboration, and (b) any Patent Rights in the Territory which claim, cover or relate to such improvements, discoveries or Know-How and are Controlled by ALNYLAM at any time during the Agreement Term. ALNYLAM Collaboration IP excludes ALNYLAM's interest in Joint Collaboration IP.

1.4 "ALNYLAM IN-LICENSE" means an agreement between ALNYLAM and a Third Party pursuant to which ALNYLAM has rights and obligations with respect to, or which otherwise Cover, an Ophthalmic Product and which is necessary to Develop, Commercialize and/or Manufacture Ophthalmic Products in the Field in the Territory, including without limitation the Existing ALNYLAM In-Licenses.

1.5 "ALNYLAM KNOW-HOW" means Know-How that is either (a) Controlled by ALNYLAM on the Effective Date, or (b) comes within ALNYLAM's Control during the Agreement Term (other than ALNYLAM's rights in Joint Collaboration IP and ALNYLAM Collaboration IP).

1.6 "ALNYLAM PATENT RIGHTS" means Patent Rights that (a) claim (i) ALNYLAM Know-How, or (ii) the identification, characterization, optimization, construction, expression, use or production of an Ophthalmic Product to a Program Target, and which ALNYLAM reasonably determines to be useful or necessary to Develop, Commercialize and/or Manufacture Ophthalmic Products in the Field in the Territory, and (b) are Controlled by ALNYLAM at any time during the Agreement Term. As of the Effective Date, ALNYLAM Patent Rights include without limitation those listed on Schedule 1.6. ALNYLAM Patent Rights shall not include Patent Rights included in ALNYLAM Collaboration IP.

1.7 "ALNYLAM TECHNOLOGY" means, collectively, ALNYLAM Know-How, ALNYLAM Patent Rights, ALNYLAM Collaboration IP and ALNYLAM's interest in Joint Collaboration IP.

1.8 "BROAD RNAI TECHNOLOGY" means RNAi Technology arising from or necessary for the performance of the Program Workplan which [**].

1.9 "BROAD RNAI TECHNOLOGY COLLABORATION IP" means Joint Collaboration IP that constitutes Broad RNAi Technology.

1.10 "CALENDAR QUARTER" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31.

1.11 "CALENDAR YEAR" means each successive period of twelve (12) months commencing on January 1 and ending on December 31.

1.12 "CLINICAL STUDY" means a Phase I Study, Phase II Study, Phase III Study or Post-Approval Study, as applicable.

1.13 "COMBINATION PRODUCT" means an Ophthalmic Product combined with any other clinically active therapeutic, prophylactic or diagnostic ingredient. All references to Ophthalmic Product in this Agreement shall be deemed to include Combination Product, to the extent applicable.

1.14 "COMMERCIALIZATION" or "COMMERCIALIZE" means any and all activities directed to marketing, promoting, distributing, importing and selling a product, including the conduct of Post-Approval Studies, and activities directed to obtaining pricing and reimbursement approvals, as applicable.

1.15 "COMMERCIALIZATION EXPENSES" means, with respect to each Profit-Sharing Product, the following costs and expenses to the extent incurred by the Parties and/or their Related Parties in the Commercialization and Manufacturing of such Profit-Sharing Product in or for the United States:

(a) Cost of Goods Sold;

(b) Manufacturing Development Expenses incurred after the First Commercial Sale of such Profit-Sharing Product in the United States;

(c) Distribution Expenses;

(d) Sales and Marketing Expenses;

(e) Losses arising out of Third Party product liability claims as set forth in Section 10.5.3(c)(iii); and

(f) payments to Third Parties under In-Licenses of Necessary Third Party IP pursuant to Section 8.3.6.1(b).

1.16 "COMMERCIALIZATION PLAN" means the multi-year business plan and annual profit plan relating to each Profit-Sharing Product that is mutually agreed between the Parties pursuant to Section 5.4.

1.17 "COMMERCIALLY REASONABLE EFFORTS" means the carrying out of obligations in a diligent and sustained manner using such effort and employing such resources as would normally be exerted or employed by a similarly situated biopharmaceutical company for a product of similar market potential at a similar stage of its product life.

1.18 "COMPLETION OF PHASE I" means, with respect to an Ophthalmic Product, the completion of data analysis for those Phase I Studies of such Ophthalmic Product that the Parties prospectively identify in the applicable Program Workplan as the studies the data from which would provide a sufficient basis to Initiate a Phase II Study.

1.19 "COMPLETION OF PHASE II" means, with respect to an Ophthalmic Product, the completion of data analysis for those Phase II Studies of such Ophthalmic Product that the Parties prospectively identify in the applicable Program Workplan as the studies the data from which would provide a sufficient basis to Initiate a Phase III Study.

1.20 "CONTROL", "CONTROLS" OR "CONTROLLED BY" means, with respect to any (a) material, know-how or other information or (b) intellectual property right, the possession of (whether by ownership or license, other than pursuant to this Agreement), or the ability of a Party or its Affiliates to grant access to, or a license or sublicense of, such item or right as provided for herein without violating the terms of any agreement or other arrangement with any Third Party existing at the time such Party would be required hereunder to grant the other Party such access or license or sublicense.

1.21 "COST OF GOODS SOLD" means, with respect to an Ophthalmic Product, the reasonable internal and external costs of a Party incurred in Manufacturing such Ophthalmic Product (including[**]to the extent that such costs are reasonably allocated to the Manufacture of such Ophthalmic Product, and [**]), including: (a) to the extent that such Ophthalmic Product is sourced from a Party, fully allocated cost of Manufacture of such Ophthalmic Product, consisting of [**] (such reasonable allocation shall [**] to be provided for such Ophthalmic Product, but excluding [**]), all calculated in accordance with generally accepted accounting principles in the United States consistently applied by the applicable Party, [**], and (b) to the extent that such Ophthalmic Product is sourced from a Third Party manufacturer, the actual price paid by a Party to the Third Party for the Manufacture, supply and packaging of such Ophthalmic Product plus any additional reasonable costs incurred by the Party relating to managing the Third Party relationship. Cost of Goods Sold shall not include royalties paid to Third Parties. [**] the Cost of Goods Sold charged by the Manufacturing Party for such Ophthalmic Product [**] that a Third Party manufacturer, or an alternative Third Party manufacturer, [**] such Ophthalmic Product [**] Cost of Goods Sold, then the Parties [**] the non-Manufacturing Party's [**] and the non-Manufacturing Party shall [**] by the JSC or JCC, as the case may be. The non-Manufacturing Party's [**] the Cost of Goods [**] shall be [**]; provided, however, that the non-Manufacturing Party may [**] in the event that the Manufacturing Party [**] Cost of Goods Sold for an Ophthalmic Product that is [**]for the equivalent period. If the JSC or JCC [**] shall provide the non-Manufacturing Party [**].

1.22 "CO-PROMOTION" means the joint promotion of an Ophthalmic Product by both Parties and/or their respective Affiliates under the same product trademark(s). "CO-PROMOTE" when used as a verb shall mean to engage in such Co-Promotion.

1.23 "COUNTRY SALES" means the Net Sales of a Royalty-Bearing Product in a Calendar Year by a Party or its Related Parties in a particular country, converted into United States dollars as set forth in Section 8.5.

1.24 "COVER," "COVERING" OR "COVERS" means, with respect to an Ophthalmic Product, that in the absence of a license granted under a Valid Claim, the Development, Manufacture

or Commercialization of the Ophthalmic Product would or is reasonably likely to infringe such Valid Claim.

1.25 "DETAIL" OR "DETAILING" means a product presentation in a face-to-face meeting in an individual or group practice setting between a professional sales representative and a targeted prescriber in which one or more key benefits of the Profit-Sharing Product are verbally presented in a balanced manner.

1.26 "DEVELOPMENT," "DEVELOPING" or "DEVELOP" means the research and

development activities related to the generation, characterization, optimization, construction, expression, use and production of Ophthalmic Products directed to any Program Target, any other research and development activities related to the clinical testing and qualification of Ophthalmic Products for clinical testing, and such other tests, studies and activities as may be required or recommended from time to time by the JSC or any Regulatory Authority to obtain Regulatory Approval of an Ophthalmic Product, including toxicology studies, statistical analysis and report writing, pre-clinical testing, clinical studies and regulatory affairs, product approval and registration activities.

1.27 "DEVELOPMENT EXPENSES" means, with respect to each Program Workplan, the internal and external costs and expenses incurred by the Parties and/or their Related Parties in the Development of Ophthalmic Products, in accordance with such Program Workplan and the related budget for Development Expenses, including without limitation:

(a) all costs as set forth in the applicable Program Workplan that are incurred in connection with the generation, characterization and optimization of Ophthalmic Products directed to the Program Target, and the subsequent pre-clinical and clinical Development of such Ophthalmic Products;

(b) all Development-related out-of-pocket costs and expenses as set forth in the applicable Program Workplan that are incurred, including without limitation payments to investigators, contract research organizations (CROs), other Third Party Development service providers and other contract labor services relating to Development activities, institutional study expenses, investigator meeting expenses, central laboratory expenses, data management, statistical designs and studies, and document preparation;

(c) fees incurred in connection with filings relating to Regulatory Approvals;

(d) Cost of Goods Sold of Ophthalmic Product used in Development activities, the costs and expenses incurred to purchase and/or package comparator or combination drugs or devices, and costs and expenses of disposal of clinical supplies;

(e) Manufacturing Development Expenses incurred with respect to an Ophthalmic Product prior to the First Commercial Sale of such Ophthalmic Product in the United States;

(f) the costs of internal scientific, medical, technical or managerial personnel engaged in such efforts, which costs shall be determined based on the FTE Costs, unless another basis is otherwise agreed by the Parties in writing;

(g) payments to Third Parties [**]pursuant to [**]

(h) Losses arising out of Third Party product liability claims as set forth in Section 10.5.3(c)(ii);

(i) Patent Expenses as set forth in Section 11.3.7 and costs of infringement suits as set forth in Section 11.4.4; and

(j) any other costs explicitly included in the budgets included in the Program Workplan.

1.28 "DEVELOPMENT MATERIALS" means animal models, cell lines, tissue samples, genes, plasmids, siRNAs, constructs, vectors, receptors and other proteins, peptides, and other biological materials related to Ophthalmic Products or Program Targets that in each case are used in or that may be necessary or useful to conduct the Programs.

1.29 "DISTRIBUTION EXPENSES" means, with respect to a Profit-Sharing Product, the expenses incurred by MERCK and its Related Parties in the distribution of such Profit-Sharing Product in the United States, calculated as [**]. The Parties will agree upon [**].

1.30 "EXISTING ALNYLAM IN-LICENSES" means the Third Party agreements listed on Schedule 1.30, as such schedule may be amended pursuant to Sections 2.15 or 7.5.

1.31 "FDA" means the United States Food and Drug Administration and any successor governmental authority having substantially the same function.

1.32 "FIELD" shall mean the treatment, prophylaxis and diagnosis of Ocular Microvascular Disease in humans with RNAi Products.

1.33 "FIRST COMMERCIAL SALE" means, with respect to any Ophthalmic Product, the first sale for end use or consumption of such Ophthalmic Product in a country after all required Regulatory Approvals have been granted by the Regulatory Authority of such country. For the avoidance of doubt, sales for clinical study purposes or compassionate, named patient or similar use, shall not constitute a First Commercial Sale.

1.34 "FTE" means a full time equivalent person year (based on consistently applied practices of the applicable party) of scientific, medical, technical, quality control, quality assurance, or managerial work performed by or on behalf of a Party on or directly related to the Ophthalmic Collaboration.

1.35 "FTE COSTS" means the amount determined by multiplying the number of FTEs allocated by a Party during the relevant time period, subject to any limitations set forth in the applicable Program Workplan or otherwise established by the JSC, times the FTE Rate. "FTE RATE" means initially $[**] per FTE, which amount shall be increased or

decreased on an annual basis as mutually agreed by the Parties, but in no event more than [**] percent ([**]%) per Calendar Year.

1.36 "HEALTH SCIENCE ASSOCIATE" means an individual employed by a Party who is responsible for providing scientific and medical information to healthcare professionals regarding an Ophthalmic Product. Health Science Associates do not engage in Detailing or other promotional efforts.

1.37 "IND" means an Investigational New Drug application, Clinical Study Application, Clinical Trial Exemption, or similar application or submission for approval to conduct human clinical investigations filed with or submitted to a Regulatory Authority in conformance with the requirements of such Regulatory Authority.

1.38 "IND-ENABLING GLP TOXICOLOGY STUDIES" means genotoxicity, acute toxicology, safety pharmacology, and sub-chronic toxicology studies in species that satisfy applicable regulatory requirements using applicable good laboratory practices which meet the standard necessary for submission as part of an IND filing with a Regulatory Authority.

1.39 "INFORMATION" means any and all information and data, including without limitation all ALNYLAM Technology and MERCK Technology, and all other scientific, pre-clinical, clinical, regulatory, manufacturing, marketing, financial and commercial information or data, whether communicated in writing or orally or by any other method, which is provided by one Party to the other Party in connection with this Agreement.

1.40 "INITIATE", "INITIATED" or "INITIATION" means, with respect to a Clinical Study, the administration of the first dose to a subject in such Clinical Study.

1.41 "IN-LICENSES" means collectively, the ALNYLAM In-Licenses and the MERCK In-Licenses.

1.42 "JOINT COLLABORATION IP" means, collectively, (a) any improvement, discovery or Know-How, patentable or otherwise, first identified, discovered or developed jointly by the Parties or their Affiliates or others acting on behalf of MERCK and ALNYLAM under the Ophthalmic Collaboration, and (b) any Patent Rights in the Territory which claim, cover or relate to such improvements, discoveries or Know-How.

1.43 "JOINT STEERING COMMITTEE" or "JSC" means the joint steering committee as more fully described in Section 3.1.

1.44 "KNOW-HOW" means, with respect to each Ophthalmic Product, all biological materials and other tangible materials, inventions, practices, methods, protocols, formulas, knowledge, know-how, trade secrets, processes, assays, skills, experience, techniques and results of experimentation and testing, including without limitation pharmacological, toxicological and pre-clinical and clinical test data and analytical and quality control data, patentable or otherwise, which relates to the identification, characterization, optimization, construction, expression, use or production of an

Ophthalmic Product and which is reasonably useful or necessary to Develop, Manufacture or Commercialize such Ophthalmic Product in the Territory in the Field.

1.45 "MANUFACTURING" or "MANUFACTURE" means, as applicable, all activities associated with the production, manufacture, processing, filling, finishing, packaging, labeling, shipping, and storage of Ophthalmic Products, including process and formulation development, process validation, stability testing, manufacturing scale-up, pre-clinical, clinical and commercial manufacture and analytical development, product characterization, quality assurance and quality control, whether such activities are conducted by (i) ALNYLAM, its Affiliates or a Third Party contractor of ALNYLAM, or (ii) MERCK, its Affiliates or a Third Party contractor of MERCK.

1.46 "MANUFACTURING DEVELOPMENT EXPENSES" means, with respect to an Ophthalmic Product, to the extent not included in Development Expenses or Cost of Goods Sold, the [**]. Manufacturing Development Expenses shall be determined by a Party in accordance with generally accepted accounting principles in the United States consistently applied by such Party.

1.47 "MERCK COLLABORATION IP" means (a) any improvement, discovery or Know-How, patentable or otherwise, first identified, discovered or developed solely by employees of MERCK or its Affiliates or other persons not employed by ALNYLAM acting on behalf of MERCK, under the Ophthalmic Collaboration, and (b) any Patent Rights in the Territory

which claim, cover or relate to such improvements, discoveries or Know-How and are Controlled by MERCK at any time during the Agreement Term. MERCK Collaboration IP excludes MERCK's interest in Joint Collaboration IP.

1.48 "MERCK IN-LICENSE" means an agreement between MERCK and a Third Party pursuant to which MERCK has rights and obligations with respect to, or which otherwise Cover, an Ophthalmic Product and is necessary to Develop, Commercialize and/or Manufacture Ophthalmic Products in the Field in the Territory.

1.49 "MERCK KNOW-HOW" means Know-How that is either (a) Controlled by MERCK on the Effective Date, or (b) comes within MERCK's Control during the Agreement Term (other than MERCK's rights in Joint Collaboration IP and MERCK Collaboration IP).

1.50 "MERCK PATENT RIGHTS" means Patent Rights that (a) claim (i) MERCK Know-How, or (ii) the identification, characterization, optimization, construction, expression, use or production of an Ophthalmic Product to a Program Target, and which MERCK reasonably determines to be useful or necessary to Develop, Commercialize and/or Manufacture Ophthalmic Products in the Field in the Territory, and (b) are Controlled by MERCK at any time during the Agreement Term. MERCK Patent Rights shall not include Patent Rights included in MERCK Collaboration IP.

1.51 "MERCK TECHNOLOGY" means, collectively, MERCK Know-How, MERCK Patent Rights, MERCK Collaboration IP and MERCK's interest in Joint Collaboration IP.

1.52 "NDA" means a New Drug Application, Biologics License Application, Worldwide Marketing Application, Marketing Authorization Application, Section 510(k) filing or

similar application or submission filed with a Regulatory Authority in a country or group of countries to obtain marketing approval for a biological, pharmaceutical or other therapeutic, prophylactic or diagnostic product in that country or in that group of countries.

1.53 "NDA FILING" means, with respect to an Ophthalmic Product, the acceptance by a Regulatory Authority of an NDA for such Ophthalmic Product for filing.

1.54 "NECESSARY THIRD PARTY IP" means, with respect to any country in the Territory, on a country-by-country basis, Know-How or Patent Rights in such country owned or controlled by a Third Party that Cover an Ophthalmic Product.

1.55 "NET SALES" means, with respect to an Ophthalmic Product, the aggregate gross invoice prices of all units of such Ophthalmic Product sold by MERCK or its Related Parties or by ALNYLAM or its Related Parties to Third Parties (other than a Sublicensee of a Party) after deducting, if not previously deducted, from the amount invoiced or received:

(a) trade and quantity discounts actually given other than early pay cash discounts;

(b) returns, rebates, chargebacks and other allowances actually given;

(c) retroactive price reductions that are actually granted; and

(d) a fixed amount equal to [**] to cover bad debt, sales or excise taxes, early payment cash discounts, transportation and insurance, custom duties, and other governmental charges.

With respect to sales of Combination Products, Net Sales shall be calculated on the basis of the gross invoice price of the Ophthalmic Product(s) containing the same composition and concentration of RNAi Product sold without other clinically active ingredients.

In the event that the Ophthalmic Product is sold only as a Combination Product and not sold without other clinically active ingredients, the Parties shall negotiate in good faith another basis on which to calculate Net Sales with respect to the Combination Product that fairly reflects the value of the Ophthalmic Product relative to the other clinically active ingredients in the Combination Product, but in no event shall such calculation result in the gross invoice price on which Net Sales are based being [**]of the gross invoice price of such Combination Product.

A percentage of the deductions set forth in paragraphs (a) through (d) above equal to the ratio of the Net Sales for the Ophthalmic Product to the Net Sales of the entire Combination Product will be applied in calculating Net Sales for a Combination Product.

1.56 "OCULAR MICROVASCULAR DISEASE" means age-related macular degeneration and [**], including without limitation [**], including without limitation [**]; but specifically excluding [**], such as (by way of example only) [**].

1.57 "OPHTHALMIC COLLABORATION" means the collaboration of the Parties in the Development, Manufacture and Commercialization of Profit-Sharing Products, and shall include, without limitation, the Pre-Clinical Development Collaboration.

1.58 "OPHTHALMIC PRODUCT" means an RNAi Product which is directed at a Program Target, that is (a) contributed by a Party to a Program in the Ophthalmic Collaboration, including without limitation, the Ophthalmic Product(s) identified on Schedule 2.3, or (b) discovered, derived or developed by a Party or any person or entity acting on behalf of a Party, including Affiliates, consultants and scientific advisors thereof, in the course of the Ophthalmic Collaboration, including, without limitation, any Combination Product, Profit-Sharing Product and/or Royalty-Bearing Product.

1.59 "OPT-OUT RIGHTS" means, collectively, Target Opt-Out Rights and Product Opt-Out Rights.

1.60 "PARTY" means MERCK and/or ALNYLAM.

1.61 "PATENT RIGHTS" means all patents (including all reissues, extensions, substitutions, confirmations, re-registrations, re-examinations, invalidations, supplementary protection certificates and patents of addition) and patent applications (including all provisional applications, continuations, continuations-in-part and divisions).

1.62 "PHASE I STUDY" means a clinical study of an Ophthalmic Product in human volunteers or patients the purpose of which is preliminary determination of safety and tolerability of a dosing regime and for which there are no primary endpoints (as understood by the FDA or other Regulatory Authorities) in the protocol relating to efficacy.

1.63 "PHASE II STUDY" means (a) a dose exploration, dose response,

duration of effect, kinetics, dynamic relationship or preliminary efficacy and safety study of an Ophthalmic Product in the target patient population or (b) a controlled dose ranging clinical trial to evaluate further the efficacy and safety of an Ophthalmic Product in the target patient population and to define the optimal dosing regimen.

1.64 "PHASE III STUDY" means a controlled pivotal clinical study of an Ophthalmic Product that is prospectively designed to demonstrate statistically whether such Ophthalmic Product is effective and safe for use in a particular indication in a manner sufficient to obtain Regulatory Approval to market such Ophthalmic Product.

1.65 "POST-APPROVAL STUDY" means a clinical study Initiated in a country after receipt of Regulatory Approval for the Ophthalmic Product in such country.

1.66 "PRE-CLINICAL DEVELOPMENT COLLABORATION" means the Development activities undertaken by the Parties to (a) generate, characterize and optimize Ophthalmic Products directed to Program Targets and (b) support the filing of an IND for

Ophthalmic Products, including without limitation, non-clinical studies and Manufacturing development activities.

1.67 "PRODUCT TRADEMARKS" means the trademark(s), service mark(s), accompanying logos, trade dress and/or indicia of origin used in connection with the distribution, marketing, promotion and sale of Ophthalmic Products in the Territory. For purposes of clarity, the term Product Trademark(s) shall not include, without limitation, the corporate names and logos of either Party, and shall include any internet domain names incorporating such Product Trademarks.

1.68 "PROGRAM" means the VEGF Program or an Additional Program.

1.69 "PROGRAM TARGET" means VEGF or an Additional Program Target.

1.70 "PROGRAM WORKPLAN" means the detailed written workplan for each Program that is mutually agreed between the Parties pursuant to Sections 2.2 and 2.4 of this Agreement.

1.71 "REGULATORY APPROVAL" means any and all approvals (including pricing and reimbursement approvals), licenses, registrations or authorizations of any Regulatory Authority, necessary for the Development, Commercialization and Manufacture of an Ophthalmic Product, including the acceptance or non-rejection of INDs and the approval of NDAs.

1.72 "REGULATORY AUTHORITY" means any applicable government regulatory authority involved in granting approvals for the Development, Manufacturing, Commercialization, reimbursement and/or pricing of an Ophthalmic Product in the Territory, including without limitation the FDA.

1.73 "RELATED PARTY" means a Party's Affiliates and permitted Sublicensees, which term does not include wholesale distributors of the Party or its Affiliates who purchase Ophthalmic Products from such Party or its Affiliates in an arm's length transaction and who have no other obligation, including without limitation a reporting obligation, to such Party or its Affiliates. For purposes of clarity, such wholesale distributors do not include those distributors whose obligations to such Party or Affiliate include responsibility for sales and/or marketing efforts in a country or

sharing of costs and expenses with respect to sales and/or marketing on behalf of a Party or its Affiliates, which distributors shall be deemed to be permitted Sublicensees for purposes of this definition.

1.74 "RNAI PRODUCT" means a therapeutic, prophylactic or diagnostic product containing, comprised of or based on siRNAs or siRNA derivatives or other moieties effective in gene function modulation and designed to modulate the function of particular genes or gene products through RNA interference.

1.75 "RNAI TECHNOLOGY" means any and all Know-How, whether or not patentable, that is useful for the identification, characterization, optimization, construction, expression, discovery, development, production, manufacture, or use of RNAi Products.

1.76 "ROYALTY PAYOR" means, in relation to a Royalty-Bearing Product, the Party obligated to pay royalties to the other Party under the terms and conditions of this Agreement.

1.77 "ROYALTY RECIPIENT" means, in relation to a Royalty-Bearing Product, the Party entitled to receive royalties from the other Party under the terms and conditions of this Agreement.

1.78 "SALES AND MARKETING EXPENSES" means, with respect to a Profit-Sharing Product, the internal and external costs and expenses incurred by the Parties and their Related Parties in connection with the pre-launch market development, and the promotion, marketing, selling and product support of such Profit-Sharing Product in the United States, in accordance with the Commercialization Plan for such Profit-Sharing Product and the related budget for Sales and Marketing Expenses, including without limitation:

(a) promotional and training materials for the sales representatives;

(b) patient support program costs;

(c) disease management programs specifically developed for such Profit-Sharing Product;

(d) outcomes and pharmacoeconomic studies and Post-Approval Studies for Profit-Sharing Product;

(e) costs incurred in conducting joint meetings relating to Commercialization of such Profit-Sharing Product (excluding JCC meetings) prior to the date of First Commercial Sale of such Profit-Sharing Product in the United States (including lodging expenses and travel expenses associated with such a meeting);

(f) costs associated with Detailing to physicians;

(g) costs associated with market development activities and other similar pre-launch activities;

(h) Cost of Goods Sold of samples of such Profit-Sharing Product distributed in accordance with the Commercialization Plan;

(i) the costs of internal scientific, medical, technical, quality assurance, quality control or managerial personnel engaged in Commercialization efforts (including without limitation Health Science Associates fielded by the Parties), which costs shall be determined based on the FTE Costs, unless another basis is

otherwise agreed by the Parties in writing;

(j) other out-of-pocket costs and expenses related to promotion, marketing, selling and product support of such Profit-Sharing Product, including without limitation costs and expenses associated with symposia, seminars, media advertising, market research and direct mailing, that are incurred in accordance with the applicable Commercialization Plan and the related budget; and

(k) any other costs explicitly included in the budget for the Commercialization Plan.

1.79 "SMALL INTERFERING RNA" or "SIRNA" means a double-stranded ribonucleic acid (RNA) composition designed to act primarily through an RNA interference mechanism that consists of either (a) two separate oligomers of native or chemically modified RNA that are hybridized to one another along a substantial portion of their lengths, or (b) a single oligomer of native or chemically modified RNA that is hybridized to itself by self-complementary base-pairing along a substantial portion of its length to form a hairpin.

1.80 "SUBLICENSEE" means a Third Party to whom a Party grants a sublicense under any ALNYLAM Technology, MERCK Technology or Joint Collaboration IP, as the case may be, to Develop, Manufacture or Commercialize an Ophthalmic Product in the Field in the Territory subject to Section 7.2.5 or otherwise grants rights to distribute, promote or sell an Ophthalmic Product.

1.81 "TERRITORY" means all of the countries in the world, and their territories and possessions.

1.82 "THIRD PARTY" means an entity other than a Party and its Affiliates.

1.83 "UNITED STATES" means the United States of America and its territories, possessions and commonwealths.

1.84 "VALID CLAIM" means a claim of: (a) an issued and unexpired Patent Right, which claim has not been revoked or held unenforceable, unpatentable or invalid by a decision of a court or other governmental agency of competent jurisdiction, which is not appealable or has not been appealed within the time allowed for appeal, and which has not been abandoned, disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise, or (b) a patent application for a patent included within the Patent Rights that has [**] from the earliest date on which such patent application claims priority and which claim has not been cancelled, withdrawn or abandoned or finally rejected by an administrative agency action from which no appeal can be taken.

1.85 "VEGF" means (a) the genomic locus encoding vascular endothelial growth factor (LocusLink ID# 7422, Unigene ID# Hs.73793, OMIM ID# 192240), [**]

1.86 "VEGF PRODUCT" means an Ophthalmic Product developed in the VEGF Program.

1.87 "VEGF PROGRAM" means the Program to research and develop Ophthalmic Product(s) whose target is VEGF, as more fully described in Section 2.2 of this Agreement. The VEGF Program is not an Additional Program.

1.88 "WORLDWIDE SALES" means aggregate worldwide Net Sales of a Royalty-Bearing Product in a Calendar Year by a Party or its Related Parties.

ADDITIONAL DEFINITIONS. The following terms have the meanings set forth in the corresponding Sections of this Agreement:

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2. DEVELOPMENT COLLABORATION

2.1 OVERVIEW. The Parties shall collaborate in carrying out the Ophthalmic Collaboration with the objective of Developing Ophthalmic Products in the Field. The Parties anticipate that there will be [**] Programs in the Ophthalmic Collaboration, each focused on Developing Ophthalmic Products directed to different Program Targets. The Development of each Ophthalmic Product shall be governed by the applicable Program Workplan and the Parties agree to conduct all their Development activities relating to the Ophthalmic Products in accordance with the applicable Program Workplan.

2.2 INITIAL DEVELOPMENT PROGRAM. The first Program in the Ophthalmic Collaboration will be the VEGF Program. The activities to be undertaken in the course of the VEGF Program are set forth in the Program Workplan attached hereto as Schedule 2.2, which may be amended from time to time upon the mutual written agreement of authorized representatives of the Parties. The focus of the Program Workplan for the VEGF Program will be on the further characterization, optimization and development of Ophthalmic Products directed to VEGF as candidates for Clinical Studies, and as appropriate, the conduct of these studies.

2.3 INITIAL CONTRIBUTION OF OPHTHALMIC PRODUCTS. On the Effective Date, ALNYLAM shall contribute to the VEGF Program any Ophthalmic Products that are directed to VEGF that have been generated by ALNYLAM and its Affiliates prior to the Effective Date, including without limitation those identified on Schedule 2.3.

2.4 ADDITIONAL DEVELOPMENT PROGRAMS. Within [**] after the Effective Date, the JSC will select [**] Additional Program Targets. Within [**] after the selection of each Additional Program Target, the JSC will agree upon a Program Workplan for a Program to research and develop one or more Ophthalmic Products directed to each such Additional Program Target (each such Program, an "Additional Program"). The focus of the Program Workplans for the Additional

Programs will be on generating, characterizing and optimizing Ophthalmic Products directed to the Additional Program Targets for further Development in the Field, including Clinical Studies, and as appropriate, the conduct of these studies. Each Party will contribute to each Additional Program any Ophthalmic Products directed to the applicable Additional Program Target that have been generated by such Party prior to the selection of the applicable Additional Program Target. The Program Workplan for each Additional Program will identify such Ophthalmic Products (if any) and Schedule 2.3 will be updated to include such Ophthalmic Products.

2.5 COLLABORATION ACTIVITIES. The Program Workplans shall allocate Development tasks between the Parties consistent with their respective capabilities and, to the extent possible and scientifically sound, in a manner to maximize the expeditious and cost-effective Development and Manufacture of Ophthalmic Products. With respect to each Ophthalmic Product and Program, ALNYLAM will be responsible for the following activities under the applicable Program Workplan: (a) [**] activities, and (b) [**] studies [**]. In addition, with respect to the VEGF Product that is at the most advanced stage of Development (the "Lead VEGF Product"), ALNYLAM will be primarily responsible for [**] activities and pursuant to Section 2.10.2 below, [**]. With respect to each Ophthalmic Product and Program, MERCK shall be responsible for the following activities under the applicable Program Workplan: (i) [**] Products [**], (ii) [**] activities [**] and (iii) [**] Products [**] (including, without limitation, [**] in accordance with the applicable Program Workplan).

2.6 THIRD PARTIES.

2.6.1 PERFORMANCE OF COLLABORATION ACTIVITIES. The Parties shall be entitled to utilize the services of Third Parties (including Third Party contract research organizations) to perform their respective Development and Manufacturing activities under the Program Workplans; provided that each Party shall remain at all times fully liable for its respective responsibilities under the Program Workplans. Neither Party shall use Third Party contract resources to conduct part or all of its obligations under the Ophthalmic Collaboration unless the non-contracting Party's rights under the agreement with the Third Party contract research organization guarantee the non-contracting Party the same rights under this Agreement as if the contracting Party had done the work itself, and any such Third Party agreement shall include confidentiality and non-use provisions which are no less stringent than those set forth in Article 9 of this Agreement.

2.6.2 COLLABORATIONS. In addition, the Parties agree that it may be necessary or useful to enter into Third Party collaborations which provide technology, information, data or know-how, patentable or otherwise, which is necessary or useful for MERCK and/or ALNYLAM to perform its obligations under the Ophthalmic Collaboration. Such Third

Party collaborations shall not conflict with the terms and conditions of this Agreement. In the event that any such Third Party collaborations are contemplated in connection with the Ophthalmic Collaboration, the JSC shall discuss, subject to Third Party confidentiality obligations, and agree upon entering into such Third Party collaborations, and the applicable Program Workplan shall be amended to include such Third Party collaborations. The Parties shall use good faith efforts to ensure that, to the extent possible, all such Third Party collaborations

shall provide that any and all data and results, discoveries and inventions, whether patentable or not, arising out of the Third Party collaboration may be used by bona fide collaborators of the Party entering into the Third Party collaboration agreement and shall include confidentiality and non-use provisions which are no less stringent than those set forth in Article 9 of this Agreement. In addition, the Party entering into such Third Party collaborations shall use reasonable efforts to obtain a right to sublicense to the other Party and its Related Parties any intellectual property arising out of the Third Party collaboration for use in connection with the Ophthalmic Collaboration.

2.7 DILIGENCE. Each Party shall use Commercially Reasonable Efforts to perform its respective Development and Manufacturing activities under the Program Workplans in accordance with this Agreement according to the priorities established by the Program Workplans and the JSC.

2.8 RECORDS. Each Party shall maintain scientific records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, which shall fully and properly reflect all work done and results achieved in the performance of the Ophthalmic Collaboration by such Party. Each Party shall have the right, during normal business hours and upon reasonable notice, to inspect and copy (or request the other Party to copy) all records of the other Party maintained in connection with the work done and results achieved in the performance of the Programs, but solely to the extent to which such records relate to a Profit-Sharing Product or to the extent access to such records is necessary for a Party to exercise its rights under this Agreement. All such records and the information disclosed therein shall be maintained in confidence by the recipient in accordance with Article 9.

2.9 AVAILABILITY OF EMPLOYEES. Each Party (the "Requested Party") shall make available its employees engaged in the Programs upon reasonable notice during normal business hours and at their respective places of employment to consult with the other Party on the progress of the Programs, as coordinated through the Requested Party's Collaboration Manager or such other individual as may be designated by the Requested Party.

2.10 REGULATORY MATTERS AND COMPLIANCE FOR PROFIT-SHARING PRODUCTS.

2.10.1 OWNERSHIP AND REFERENCE RIGHT. Subject to Section 2.10.2, [**] the Regulatory Approvals and related regulatory documents submitted to the applicable Regulatory Authorities for all Profit-Sharing Products. The Party owning any Regulatory Approval and related regulatory documents shall license, including for cross-reference purposes, transfer, provide a letter of reference with respect to, or take other action necessary to make available such Regulatory Approvals and related regulatory documents to the

other Party as may be reasonably necessary to enable such other Party to fulfill its obligations under the applicable Program Workplan and/or Commercialization Plan and exercise its rights under this Agreement with respect to the Development and Commercialization of such Profit-Sharing Products in the Field in the Territory.

2.10.2 VEGF PRODUCT IND. Notwithstanding the general provisions of Section 2.10.1, [**] filing the IND for the Lead VEGF Product. [**] preparing and promptly supplying the [**] information for such IND

and [**] preparing and promptly supplying [**], including without limitation, the [**]. Promptly after acceptance of such IND by the applicable Regulatory Authority, [**].

2.10.3 REGULATORY COORDINATION. Except as otherwise provided in Section 2.10.2, Section 2.10.4, Section 5.7 or the applicable Program Workplan, [**] (a) [**], (b) be responsible for [**], and (c) [**] under this Section 2.10, and to comply with its disclosure requirements under applicable securities laws. Except as otherwise provided in Section 2.10.2, Section 2.10.4 or Section 5.7, [**] shall have the right [**] with respect to Profit-Sharing Products.

2.10.4 MANUFACTURING REGULATORY COMMUNICATIONS. Notwithstanding any provisions of Section 2.10.3 to the contrary, with respect to all regulatory issues related to the Manufacture of Profit-Sharing Products, including all matters relating to cGMP compliance, (a) in the case of supply of a Profit-Sharing Product [**], and (b) in the case of supply of a Profit-Sharing Product for [**]:

(i) be primarily responsible for [**], each Regulatory Authority;

(ii) be primarily responsible for [**] each Regulatory Authority;

(iii) be responsible for [**];

(iv) notify [**] a Regulatory Authority [**]; and

(v) provide to the [**] Regulatory Authority [**].

2.10.5 REPORTING ADVERSE EXPERIENCES. The Parties will develop and agree upon safety data exchange procedures governing the coordination of collection, investigation, reporting, and exchange of information concerning any adverse experiences, and any product quality and product complaints involving adverse experiences, related to a Profit-Sharing Product, sufficient to permit each Party to comply with its legal obligations.

2.10.6 COMPLIANCE. Each Party shall conduct the Ophthalmic Collaboration and the Development, Manufacture and Commercialization of Profit-Sharing Products in accordance with all applicable laws, rules and regulations, including without limitation current governmental regulations concerning good laboratory practices, good clinical practices and good manufacturing practices.

2.11 FUNDING OF THE DEVELOPMENT COLLABORATION.

2.11.1 From the Effective Date, with respect to each Profit-Sharing Product, the Parties will each bear fifty percent (50%) of all Development Expenses incurred in the conduct of

the Program Workplan for such Profit-Sharing Product in order to generate data primarily to support Regulatory Approval of such Profit-Sharing Product in the United States ("U.S. Development Expenses"). For the avoidance of doubt, U.S. Development Expenses may include expenses related to Clinical Studies performed outside of the United States in support of Regulatory Approval in the United States. The applicable Program Workplan will identify each Clinical Study that is primarily in support of Regulatory Approval of a Profit-Sharing Product in the United States. Prior to the Initiation of the first Phase III Study with respect to each Profit-Sharing Product, each Party has a one-time option to reduce its percentage share of U.S. Development Expenses related to such

Profit-Sharing Product ("Expense Share Reduction Option"); provided, however, that in no event will such percentage share be less than [**] percent ([**]%). A Party may exercise such option by providing [**] prior written notice to the other Party of such exercise and the percentage share of U.S. Development Expenses to be borne by such Party. In the event that [**] exercises its Expense Share Reduction Option with respect to any Profit-Sharing Product, [**] over the Development, Manufacturing and Commercialization activities for such Profit-Sharing Product with respect to the United States and the appropriate changes will be made to the provisions of this Agreement to reflect [**], including without limitation, the reallocation of responsibility for [**] with respect to the United States.

2.11.2 From the Effective Date, with respect to each Profit-Sharing Product, MERCK will bear one hundred percent (100%) of the Development Expenses incurred in the conduct of the Program Workplan for such Profit-Sharing Product in order to generate data primarily to support Regulatory Approval of such Profit-Sharing Product in the Territory outside the United States.

2.11.3 Each Program Workplan under the Ophthalmic Collaboration shall be accompanied by a budget prepared by the Parties setting forth the projected Development Expenses for such Program relating to the United States. Such Program Workplan budgets shall be reviewed and approved at least annually by the JSC pursuant to Section 3.1.4. U.S. Development Expenses identified within the budget for the applicable Program Workplan approved by the JSC shall initially be borne by the Party incurring the cost or expense, subject to reimbursement as provided in Section 2.11.4. ALNYLAM and MERCK shall report quarterly to each other on their U.S. Development Expenses with respect to the immediately preceding Calendar Quarter, if any, with such reports to be submitted within thirty (30) days after the end of each Calendar Quarter. The Parties shall seek to resolve any questions related to such U.S. Development Expenses within fifteen (15) days following receipt.

2.11.4 The Party that incurs more than its share of the total actual U.S. Development Expenses for a Profit-Sharing Product shall be paid by the other Party an amount sufficient to reconcile to its agreed percentage of actual U.S. Development Expenses in each Calendar Quarter; provided that total actual U.S. Development Expenses for both Parties for the Calendar Year to date have not exceeded [**]% of budgeted U.S. Development Expenses for such Profit-Sharing Product for the Calendar Year to date. If total actual U.S. Development Expenses exceeded budgeted U.S. Development Expenses by more than [**]% for the Calendar Year to date, the reimbursing Party shall

first pay the other Party an amount sufficient to cause the reimbursing Party to have borne its stated percentage of [**]% of the budgeted U.S. Development Costs. Actual U.S. Development Expenses in excess of [**]% of budgeted U.S. Development Expenses shall also be reimbursed if (i) both Parties approve the additional U.S. Development Expenses in advance or (ii) such excess U.S. Development Expenses are the result of work carried out in response to a governmental requirement to do such work and the Party incurring such excess U.S. Development Expenses has notified the other Party prior to incurring such excess U.S. Development Expenses. Subject to the foregoing clause (ii), any proposal to increase U.S. Development Expense for any Calendar Year by more than [**]% of the U.S. Development Expenses budgeted for such

Calendar Year, if the Parties are unable to reach consensus on such issue, after referral to the executive officers of the Parties pursuant to Section 13.6.1, shall not be approved. Reconciling payments under this Section 2.11.4 shall be made within thirty (30) days of receipt of the other Party's quarterly report.

2.12 PRE-CLINICAL DEVELOPMENT COLLABORATION TERM.

2.12.1 TERM. Except as otherwise provided herein, the term of the Pre-Clinical Development Collaboration shall commence on the Effective Date and continue until the[**]anniversary of the Effective Date (the "Pre-Clinical Development Collaboration Term"); provided, however, that the Parties will cooperate in the orderly cessation of any Clinical Studies of the Ophthalmic Products that are ongoing at the end of the Pre-Clinical Development Collaboration Term and mutually agree on sharing any associated expenses. The Parties may extend the Pre-Clinical Development Collaboration Term by mutual written agreement of authorized representatives of the Parties.

2.12.2 EFFECT OF EXPIRATION. No later than [**] prior to expiration of the Pre-Clinical Development Collaboration Term, the Parties, through the JSC, shall discuss any Ophthalmic Products that are not Royalty-Bearing Products and have not yet advanced to the Pre-IND Filing Opt-Out Period and shall mutually agree which Party shall be the Continuing Party for such Ophthalmic Product. Following the expiration of the Pre-Clinical Development Collaboration Term, such Ophthalmic Product shall be deemed a Royalty-Bearing Product under this Agreement. The Continuing Party shall be free to Develop, Manufacture and Commercialize such Royalty-Bearing Product in the Territory, with or without a partner or collaborator and without any further obligation to the other Party with respect to such activities under this Agreement, except for (a) the continuing obligations of the Parties set forth in Article 6 and (b) the obligation of the Continuing Party to pay the other Party [**]percent ([**]%) of the royalties that would be payable by the Continuing Party to the other Party under Section 8.3.2 had such Continuing Party exercised its Product Opt-Out Right with respect to such Royalty-Bearing Product during the Pre-IND Filing Opt-Out Period; provided, however, that if MERCK is the Continuing Party, in no event shall the royalties payable by MERCK to ALNYLAM with respect to Net Sales in a country for any Calendar Quarter be less than the amount of any royalties and any portions of milestones or other payments under the Existing ALNYLAM In-Licenses that are reasonably allocable to the Commercialization or Manufacture of such Royalty-Bearing Product in or for such country in the Field.

2.13 EXCLUSIVITY. Except as provided in Section 2.6 of this Agreement and the Research Collaboration and License Agreement dated September 8, 2003 among MERCK, ALNYLAM (formerly Alnylam Holding Co.) and Alnylam U.S. Inc. (formerly Alnylam Pharmaceuticals, Inc.),

(a) During the Pre-Clinical Development Collaboration Term, neither Party nor any of its Affiliates shall, alone or with a Third Party, [**]in the Field in the Territory;

(b) Until the [**] anniversary of the date of First Commercial Sale of the first Ophthalmic Product directed to a Program Target, neither Party nor any of its Affiliates shall, alone or with a Third Party, [**] in the Field in the Territory, provided that this obligation shall terminate in the event that no Ophthalmic Product directed to such Program Target is being Developed or Commercialized;

(c) Following the exercise by a Party of its Target Opt-Out Right with respect to a Program Target, the rights of each Party to research, develop, manufacture or commercialize with Third Parties RNAi Products directed to the applicable Program Target shall be governed by Section 4.3(e).

2.14 RIGHT OF FIRST NEGOTIATION. During the Pre-Clinical Development Collaboration Term, [**] (a) commencing the research, development and/or commercialization of any RNAi Product (i) within the Field and directed to a target gene or gene product [**]; or [**] shall include material information relating to [**] shall have [**], then the Parties shall [**] in an effort to [**] within such [**] within such [**].

2.15 IN-LICENSES. With respect to each Profit-Sharing Product, if either Party identifies any Necessary Third Party IP that at the time of identification is not Controlled by a Party, such Party shall notify the JSC and include in such notification a summary of such Necessary Third Party IP, the anticipated commercial terms of the necessary license and any other relevant information. The JSC shall discuss whether a license to such Necessary Third Party IP should then be obtained by taking into consideration any commercial advantages associated with the timing of licensing such Necessary Third Party IP, the usefulness or necessity of such Necessary Third Party IP to the success of the Development, Manufacture or Commercialization of the applicable Profit-Sharing Product and any other factors the JSC deems relevant. If the JSC determines that a license to such Necessary Third Party IP should be obtained, the JSC shall determine which Party shall be responsible for negotiating and entering into such license and such license, if executed, shall be an "In-License" of that Party; provided, however, that ALNYLAM shall be responsible for negotiating and entering into any licenses of Broad RNAi Technology that constitute Necessary Third Party IP. Prior to execution of any such license, the negotiating party shall present the license in substantially final form to the JSC for review and approval. If the JSC does not approve such license, such license shall not constitute an "In-License" under this Agreement. Each Party shall comply with all applicable terms and conditions of the In-Licenses of the other Party and shall take such actions as may be required to allow such Party to comply with its obligations

thereunder, including obligations relating to patent matters, confidentiality, indemnification and diligence. The Parties agree that this Section 2.15 shall not apply to any In-Licenses entered into by either Party or its Affiliates prior to the Effective Date of this Agreement. [**].

2.16 TRANSFER OF KNOW-HOW.

2.17 GENERAL. Each Party shall provide to the other Party, at such other Party's request, any and all Know-How related to Program Targets and Profit-Sharing Products directed to such Program Targets that is Controlled by such Party, or in the absence of such request, such Know-How Controlled by such Party as the providing Party reasonably believes is necessary for the other Party to perform its obligations or exploit its rights under this Agreement, including without limitation in the Development, Manufacture and Commercialization of Profit-Sharing Products. In particular, but without limiting the generality of the foregoing, each Party shall provide to the other all Know-How Controlled by such Party that it reasonably believes will assist the Parties in evaluating and selecting the Additional Program Targets. Each Party shall use such

Know-How solely for the purposes of performing its obligations or exploiting its rights under this Agreement with respect to such Program Targets and Profit-Sharing Products.

2.17.1 DEVELOPMENT MATERIALS. With respect to Know-How that consists of Development Materials, each Party may provide to the other Party Development Materials Controlled by the supplying Party for use by the other Party in furtherance of the Programs. Except as otherwise provided under this Agreement or explicitly authorized in writing by the supplying Party, all such Development Materials delivered to the receiving Party shall remain the sole property of the supplying Party, shall be used only in furtherance of the applicable Program and solely under the control of the receiving Party and shall not be used or delivered to or for the benefit of any Third Party without the prior written consent of the supplying Party. The Development Materials supplied under this Section 2.16.2 must be used with prudence and appropriate caution in any experimental work, since not all their characteristics may be known; however, the supplying Party shall notify the receiving Party of any health hazards of which it is or becomes aware relating to the use or handling of the Development Materials. THE DEVELOPMENT MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF SATISFACTORY QUALITY, MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE, OR SAVE AS SPECIFICALLY PROVIDED IN THIS AGREEMENT, ANY WARRANTY THAT THE USE OF THE DEVELOPMENT MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

3. COLLABORATION MANAGEMENT

3.1 JOINT STEERING COMMITTEE. The Parties hereby establish a committee to facilitate the Ophthalmic Collaboration as follows:

3.1.1 COMPOSITION OF THE JOINT STEERING COMMITTEE. The Ophthalmic Collaboration shall be conducted under the direction of a joint steering committee (the "JSC") comprised of three (3) named representatives of MERCK and three (3) named representatives of ALNYLAM. Each Party shall appoint its respective representatives to the JSC from time to time, and may substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. Each Party shall have at least one JSC representative who is a senior employee (director level or above), and all JSC representatives shall have appropriate research, preclinical, manufacturing, clinical development or commercialization expertise and ongoing familiarity with the Ophthalmic Collaboration. Additional representatives or consultants may from time to time, by mutual consent of the Parties, be invited to attend JSC meetings, subject to such representatives' and consultants' written agreement to comply with the requirements of Section 9.1. Each Party shall bear its own expenses relating to attendance at such meetings by its representatives.

3.1.2 JSC CHAIRPERSON. The "JSC Chairperson" shall rotate every twelve (12) months between ALNYLAM and MERCK. The initial JSC Chairperson shall be a representative of ALNYLAM. The JSC Chairperson's responsibilities shall include (a) scheduling meetings at least once per Calendar Quarter, but more frequently if the JSC determines it necessary; (b) setting agenda for meetings with solicited input from other members; (c) confirming and delivering minutes to the JSC for review and final approval; and (d) conducting effective meetings, including ensuring that objectives for each meeting are set and achieved.

3.1.3 MEETINGS. The JSC shall meet in accordance with a schedule established by mutual written agreement of the Parties, but no less frequently than once per Calendar Quarter, with the location for such meetings alternating between ALNYLAM and MERCK facilities (or such other locations as are determined by the JSC). Alternatively, the JSC may meet by means of teleconference, videoconference or other similar communications equipment, but at least two meetings per year shall be conducted in person.

3.1.4 JSC RESPONSIBILITIES. The JSC shall have the following responsibilities with respect to the Ophthalmic Collaboration:

(a) determining the overall Development strategy for the Programs and the Ophthalmic Products in the Field in the Territory;

(b) evaluating and selecting [**] Additional Program Targets by no later than [**] following the Effective Date;

(c) reviewing for approval the Program Workplans for the Additional Programs (including without limitation, identifying each Clinical Study in such Program Workplans that is primarily in support of Regulatory Approval of a Profit-Sharing Product in the United States) within sixty (60) days after the selection of the Additional Program Targets by the JSC, and reviewing for approval the related Development Expense budgets described in Section 2.11.3 within ninety

(90) days after the selection of the Additional Program Targets by the JSC, in each case with appropriate input from ALNYLAM and MERCK senior management;

(d) reviewing for approval (i) an annual update to each Program Workplan and the related Development Expense budgets described in Section 2.11.3, no later than December 31 of each Calendar Year, and (ii) any modifications to such Program Workplans and Development Expense budgets within thirty (30) days of each submission to the JSC (including without limitation, identifying each Clinical Study in such updates and modifications to such Program Workplans that is primarily in support of Regulatory Approval of a Profit-Sharing Product in the United States);

(e) determining each Party's responsibilities under the Program Workplans consistent with Section 2.5;

(f) facilitating the transfer of Know-How and Information between the Parties for purposes of conducting the Program Workplans;

(g) regularly assessing the progress of the Parties in their conduct of the Program Workplans and against the timelines and budgets contained therein, reviewing relevant data, considering issues of priority, and determining which Profit-Sharing Products to advance into clinical development;

(h) reviewing for approval any Manufacturing plans for Profit-Sharing Products and overseeing activities conducted thereunder;

(i) reviewing for approval, within the Parties' regular business cycles, but no later than [**] days after a proposal is made to the JSC by either Party, the entry of any Profit-Sharing Product into IND-Enabling GLP Toxicology Studies;

(j) reviewing for approval, within the Parties' regular business cycles, but no later than [**] days after a proposal is made to the JSC by either Party, the submission of an IND with respect to any Profit-Sharing Product;

(k) reviewing for approval the terms of any In-License under Section 2.15;

(l) reviewing for approval proposed Third Party collaborations in accordance with Section 2.6; and

(m) performing such other activities as are contemplated under this Agreement or that the Parties agree shall be the responsibility of the JSC.

3.2 APPOINTMENT OF SUBCOMMITTEES, PROJECT TEAMS AND COLLABORATION MANAGERS. The JSC shall be empowered to create such subcommittees of itself and additional project teams as it may deem appropriate or necessary. Each such subcommittee and project team shall report to the JSC, which shall have authority to approve or reject recommendations or actions proposed thereby subject to the terms of this Agreement.

Each Party shall also designate a "Collaboration Manager." The Collaboration Managers will be responsible for the day-to-day worldwide coordination of the Ophthalmic Collaboration and will serve to facilitate communication between the Parties. Each Party may change its designated Collaboration Manager from time to time upon written notice to the other Party.

3.3 REPORTS AND MINUTES. Each Party will provide the members of the JSC with written copies of all materials they intend to present at the JSC meeting. The JSC may also request at any time specific data or information related to Development activities or that a written report be prepared in advance of any meeting summarizing certain material data and information arising out of the conduct of the Development activities and the Party or appropriate committee to whom such request is made shall promptly provide to the other Party or JSC such report, data or information. A secretary shall be appointed for each meeting and shall prepare minutes of the meeting, which shall provide a description in reasonable detail of the discussions held at the meeting and a list of any actions, decisions or determinations approved by the JSC.

3.4 DECISION MAKING.

3.4.1 FINAL DECISION-MAKING. The JSC shall operate by consensus; provided, however, that the JSC shall not have final decision-making authority regarding issues relating to the following matters for each Profit-Sharing Product:

(a) [**];

(b) [**]; and

(c) [**];

provided, however, that if [**] with respect to any Profit-Sharing Product[**] such Profit-Sharing Product [**].

3.4.2 BUDGETS. As set forth in Sections 3.1.4(c) and (d), for Profit-Sharing Products, the JSC shall have primary responsibility

to review and approve Development Expense budgets for Program Workplans, including budgets related to Development activities over which one Party has final decision-making authority pursuant to Section 3.4.1. In recognition of the importance of budgets, each Party shall have the full opportunity to review and comment on budgets before final approval. Any disputes related to budgets shall be resolved in accordance with Section 3.5.2.

3.4.3 VOTING. With respect to decisions of the JSC, the representatives of each Party shall have collectively one vote on behalf of such Party. For each meeting of the JSC, at least two (2) representatives of each Party shall constitute a quorum. Action on any matter may be taken at a meeting, by teleconference, videoconference or by written agreement.

3.5 DISPUTES. The JSC shall attempt to resolve any and all disputes relating to the Ophthalmic Collaboration by unanimous consensus. [**].

3.5.1 With respect to a dispute concerning a matter provided for in Section 3.4.1, [**]; provided, however, that the [**] by the JSC [**] the JSC shall provide the [**] decision.

3.5.2 With respect to a dispute concerning a matter provided for in Section 3.4.2, [**]; provided, however, that [**] consideration by the JSC, [**] the JSC shall provide the [**] decision.

3.5.3 With respect to all other matters except those relating to the Cost of Goods Sold of an Ophthalmic Product as described in Section 1.21, if the JSC is unable to resolve such dispute, and the dispute is material, then the dispute shall be submitted to escalating levels of MERCK and ALNYLAM senior management for review. If the dispute cannot be resolved despite escalation, then the dispute resolution provisions of Section 13.6 shall apply.

3.6 DISSOLUTION OF JSC. The JSC shall be dissolved at the end of the Ophthalmic Collaboration.

4. OPT-OUT RIGHTS.

4.1 JOINT DEVELOPMENT AND COMMERCIALIZATION. Each Ophthalmic Product being jointly Developed and Commercialized by the Parties under this Agreement shall be referred to as a "Profit-Sharing Product", unless and until a Party exercises its Opt-Out Rights with respect to such Profit-Sharing Product.

4.2 SOLE PARTY DEVELOPMENT AND COMMERCIALIZATION. If either Party (the "Opt-Out Party") exercises its Opt-Out Rights with respect to a Profit-Sharing Product or a Program Target, and the other Party elects, by notice to the Opt-Out Party within [**] after the Target Opt-Out Point or the Product Opt-Out Point, as the case may be (each, an "Opt-Out Point"), to continue the Development and Commercialization of such product (such other Party after such election, a "Continuing Party"), such Profit-Sharing Product will thereafter be referred to as a "Royalty-Bearing Product."

4.3 TARGET OPT-OUT RIGHTS. Each Party shall have the right to narrow the Parties' collaboration hereunder to exclude a Program Target and all Ophthalmic Products directed to such Program Target (a "Target Opt-Out Right"), subject to the following terms and conditions:

(i) a party may exercise its Target Opt-Out Right with respect to a Program by giving the other Party [**] prior written notice

of the Opt-Out Party's intent to exercise its Target Opt-Out Right; provided, however, that a Party may not exercise its Target Opt-Out Right with respect to a Program until after completion of the final IND-Enabling GLP Toxicology Study for the most advanced Ophthalmic Product in such Program, and such Target Opt-Out Right shall not apply to any Ophthalmic Product in such Program after the expiration of the End of Phase II Completion Opt-Out Period for such Product. On the effective date of the exercise of such Target Opt-Out Right (the "Target Opt-Out Point"):

(a) the definition of Program Targets shall thereafter be narrowed to exclude the applicable Program Target, the definition of Programs shall thereafter be narrowed to exclude the Program for such Program Target, and if the Party that is not the Opt-Out Party does not elect to become the Continuing Party for any Ophthalmic Products in the Program, the definition of Ophthalmic Product shall thereafter be narrowed to exclude any such Ophthalmic Products;

(b) if the Party that is not the Opt-Out Party elects to become the Continuing Party for one or more Ophthalmic Products in such Program, then such Ophthalmic Products will be deemed Royalty-Bearing Products and the provisions of Section 12.3 shall apply to each such Royalty-Bearing Product;

(c) if the Party that is not the Opt-Out Party does not elect to become the Continuing Party for any Ophthalmic Products in such Program, then except for the provisions of this Agreement that survive termination of this Agreement pursuant to Section 12.4 and this Section 4.3, the financial, license and other terms of this Agreement shall no longer apply to such Program Target or Program or the Development, Manufacture and Commercialization of Ophthalmic Products in such Program;

(d) the Continuing Party shall be free to Develop, Manufacture and Commercialize the Royalty-Bearing Products directed against such Program Target, in the Field in the Territory, with or without a partner or collaborator and without any further obligation to the Opt-Out Party with respect to such activities under this Agreement, subject to the continuing obligations of the Parties with respect to Royalty-Bearing Products set forth in Article 6 and Sections 8.1.3.2 and 8.3.2;

(e) provided that the Party that is not the Opt-Out Party elects to become the Continuing Party for one or more Ophthalmic Products in such Program, for a period of two (2) years after the Target Opt-Out Point neither the Opt-Out Party nor any of its Affiliates shall, alone or with a Third Party, research, develop, manufacture or commercialize RNAi Products directed to such Program Target in the Field in the Territory; and

(f) the licenses granted to the Opt-Out Party by the Continuing Party with respect to such Ophthalmic Product set forth in Article 7 shall terminate and the licenses granted to the Continuing Party by the Opt-Out Party with respect to such Ophthalmic Product set forth in Article 7 shall continue in full force and effect.

4.4 PRODUCT OPT-OUT RIGHTS. Each Party shall have the right to elect not to participate in the Development and Commercialization of any Ophthalmic Product (a "Product Opt-Out Right") subject to the

following terms and conditions:

4.4.1 A Party may exercise its Product Opt-Out Right with respect to a Profit-Sharing Product by giving the other Party [**] prior written notice of such exercise during any of the following periods:

(a) after [**] such Profit-Sharing Product, [**] for such Profit-Sharing Product [**] Opt-Out Period");

(b) within [**] such Profit-Sharing Product ("[**] Opt-Out Period"); or

(c) within [**] such Profit-Sharing Product ("[**] Opt-Out Period").

The [**] Opt-Out Period, [**] Opt-Out Period and [**] Opt-Out Period are each referred to as an "Opt-Out Period" and collectively as the "Opt-Out Periods."

4.4.2 Upon the exercise by a Party of its Product Opt-Out Rights with respect to a Profit-Sharing Product,

(a) the effective date of such exercise shall be deemed the "Product Opt-Out Point" for such Profit-Sharing Product;

(b) if the Party that is not the Opt-Out Party elects to become the Continuing Party for such Profit-Sharing Product, such Profit-Sharing Product will be deemed a Royalty-Bearing Product, the provisions of Section 12.3 shall apply to such Royalty-Bearing Product, and the Continuing Party shall be free to Develop, Manufacture and Commercialize such Royalty-Bearing Product in the Field in the Territory, with or without a partner or collaborator and without any further obligation to the Opt-Out Party with respect to such activities under this Agreement, subject to the continuing obligations of the Parties with respect to Royalty-Bearing Products set forth in Article 6 and Sections 8.1.3.2 and 8.3.2;

(c) if the Party that is not the Opt-Out Party does not elect to become the Continuing Party for such Profit-Sharing Product, the definition of Ophthalmic Product shall thereafter be narrowed to exclude such product and the financial, license and other terms of this Agreement shall no longer apply to such product or the Development, Manufacture and Commercialization of such product;

(d) the exclusivity provisions of Section 2.13 shall continue to apply to the applicable Program Target for such product (but not the product itself) until a Party has exercised its Target Opt-Out Right with respect to such Program Target, or the Parties have exercised their Product Opt-Out Rights with respect to each Ophthalmic Product in the Program for such Program Target; and

(e) the licenses granted to the Opt-Out Party by the Continuing Party with respect to such Ophthalmic Product set forth in Article 7 shall terminate and the licenses granted to the Continuing Party by the Opt-Out Party with respect to such Ophthalmic Product set forth in Article 7 shall continue in full force and effect.

5. COMMERCIALIZATION AND MANUFACTURE OF PROFIT-SHARING PRODUCTS

The rights and obligations set forth in this Article 5 shall apply to both Parties, as applicable, in respect of each Profit-Sharing Product.

5.1 JOINT COMMERCIALIZATION COMMITTEE. Within [**]following the earliest Co-Promotion Option Exercise Date, the Parties will establish a Joint Commercialization Committee ("JCC") to oversee Commercialization activities in the United States relating to Profit-Sharing Products. The JCC will be chaired by MERCK and shall be comprised of three (3) named representatives of MERCK and three (3) named representatives of ALNYLAM. Each Party shall appoint its respective representatives to the JCC from time to time, and may substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. All JCC representatives shall have appropriate marketing or commercialization expertise and ongoing familiarity with the Profit-Sharing Products. Each Party shall bear its own expenses relating to attendance at such meetings by its representatives. The responsibilities of the JCC shall include overseeing the Commercialization of the Profit-Sharing Product, reviewing the Commercialization Plan and related budget for each Profit-Sharing Product and facilitating implementation of such Commercialization Plans and other related activities; provided, however, that [**]; provided, further, that [**]. Any disputes related to Commercialization budgets shall be resolved as described in Section 3.5.2, but with the substitution of the JCC for the JSC. The meeting schedule and additional responsibilities of the JCC shall be determined upon establishment of the JCC.

5.2 DILIGENCE. MERCK agrees to use Commercially Reasonable Efforts to Commercialize each Profit-Sharing Product in the Territory. Upon exercise by ALNYLAM of its U.S. Co-Promotion Option with respect to a Profit-Sharing Product, (a) the Parties agree to diligently collaborate in the Commercialization of such Profit-Sharing Product in the Field in the United States and (b) ALNYLAM agrees to use Commercially Reasonable Efforts to Commercialize such Profit-Sharing Product in the United States. Except as otherwise set forth in this Article 5, all activities shall be undertaken by the Parties in accordance with the Commercialization Plan developed under Section 5.4 and all sales shall be made under Product Trademark(s) selected by MERCK and approved by the JSC, using only professional sales representatives who are employees of the Parties, in the United States, or outside the United States, using professional sales representatives who are employees or direct independent contractors of MERCK.

5.3 LEAD COMMERCIALIZATION PARTY; CERTAIN ALNYLAM RIGHTS. MERCK shall be responsible for developing a suitable global marketing strategy for each Profit-Sharing Product in the Territory and for sales activities, the development of marketing materials and the implementation of operational matters related to such activities including marketing, sales, supply and distribution of each Profit-Sharing Product in the Territory. MERCK shall be responsible for booking sales and shall warehouse and distribute the Profit-Sharing Product in the Territory. In the event that ALNYLAM exercises its U.S. Co-Promotion Option pursuant to Section 5.5, ALNYLAM shall have the right (but not the obligation) to field Health Science Associates in support of Profit-Sharing Products. The number and deployment of such Health Science Associates shall be detailed in the Commercialization Plan for each Profit-Sharing Product, and any Health Science Associates fielded by ALNYLAM shall be fully integrated into the efforts of MERCK's Health Science Associates. Regardless of whether ALNYLAM has exercised its U.S.

Co-Promotion Option, the Parties shall mutually agree (such agreement not to be

unreasonably withheld) upon the participation of key opinion leaders and/or investigators from time to time in meetings with investors sponsored by ALNYLAM.

5.4 COMMERCIALIZATION PLAN. Prior to [**] a Profit-Sharing Product, MERCK shall prepare a statement of interest with respect to such Profit-Sharing Product for submission to the JSC. The statement of interest shall provide general marketing guidance, and shall contain [**]in the therapeutic area targeted by such Profit-Sharing Product. After submission of the statement of interest, but prior to submission of the marketing needs report to the JSC as described below, routine documents prepared by MERCK's marketing group to support the Development of such Profit-Sharing Product shall be submitted to the JSC as they become available. [**] with respect to such Profit-Sharing Product, MERCK shall prepare a marketing needs report for submission to the JSC. The marketing needs report will highlight the [**] for such Profit-Sharing Product and outline [**]such Profit-Sharing Product. Thereafter on an annual basis (until such time as such responsibility shifts to the JCC pursuant to Section 5.1), MERCK shall prepare a rolling multiyear (not less than [**] year) plan (a "Commercialization Plan") for Commercializing such Profit-Sharing Product in the Field in the United States. The initial Commercialization Plan for such Profit-Sharing Product shall include [**] The subsequent Commercialization Plan will contain greater detail with respect to Commercialization activities in the United States with respect to such Profit-Sharing Product and shall contain increasing levels of detail regarding the foregoing matters in each yearly update. Such subsequent Commercialization Plan is expected to include, without limitation, [**] for the Profit-Sharing Product. The Commercialization Plan shall also include, as an appendix, a budget for [**] in and for the United States after the First Commercial Sale of the relevant Profit-Sharing Product in the United States.

5.5 U.S. CO-PROMOTION OPTION FOR PROFIT-SHARING PRODUCTS. Except in the event that ALNYLAM has exercised its Expense Share Reduction Option with respect to a Profit-Sharing Product, ALNYLAM shall have the option to Co-Promote such Profit-Sharing Product with MERCK in the United States (the "U.S. Co-Promotion Option"), which option shall be exercisable at any time (the "Co-Promotion Option Exercise Date"), but no later than [**] prior to the target launch date for such Profit-Sharing Product in the United States. If ALNYLAM exercises the U.S. Co-Promotion Option, the Parties' respective Co-Promotion responsibilities in the United States shall be [**] prior to the target launch date for such Profit-Sharing Product in the United States. Such [**] terms substantially similar to those set forth in Schedule 5.5.

5.6 MANUFACTURE. [**] shall be responsible for the Manufacture and supply of each Profit-Sharing Product for Commercialization purposes. [**] shall have the right to Manufacture the Profit-Sharing Product or have the Profit-Sharing Product Manufactured by an Affiliate or Third Party; provided that [**] shall remain at all times fully liable for the Manufacture of the Profit-Sharing Product. In the event that [**] uses a Third Party to fulfill its obligations hereunder, such Third Party shall be bound by confidentiality and non-use obligations which are no less stringent than those set forth in Article 9 of this Agreement.

5.7 MANUFACTURING REGULATORY COMMUNICATIONS RELATING TO SUPPLY OF PROFIT-SHARING PRODUCTS [**]. Notwithstanding any provisions of Section 2.10.3 to the contrary, with respect to all regulatory issues related to the Manufacture of Profit-Sharing Products [**], including all matters relating to cGMP compliance, [**] (i) oversee, monitor and coordinate all regulatory actions, communications and filings with, and submissions to, each Regulatory Authority, (ii) be responsible for interfacing, corresponding and meeting with each Regulatory Authority, (iii) be responsible for maintaining all regulatory filings, (iv) [**] as soon as possible, but in any event within [**] business days, of any action by a Regulatory Authority in Canada, the European Union, Japan or the United States that would prohibit the marketing or the continued marketing of such Profit-Sharing Product or that would result in any shortage or projected shortage of such Profit-Sharing Product and (v) [**] a written report once per Calendar Quarter of all material communications with any Regulatory Authority in Canada, the European Union, Japan and the United States.

5.8 REGULATORY COORDINATION; REPORTING ADVERSE EXPERIENCES; COMPLIANCE. The Commercialization and Manufacture of Profit-Sharing Products shall be subject to the provisions of Sections 2.10.5 and 2.10.6. In addition, except with respect to regulatory issues related to the Manufacture of Profit-Sharing Products for Phase III Study, Post-Approval Study or Commercialization purposes, which are the subject of Section 5.7, the Commercialization of Profit-Sharing Products shall be subject to the provisions of Section 2.10.3.

6. DEVELOPMENT, MANUFACTURE AND COMMERCIALIZATION OF ROYALTY-BEARING PRODUCTS.

The rights and obligations set forth in this Article 6 shall apply to the Continuing Party with respect to the Development, Manufacture and Commercialization of each Royalty-Bearing Product.

6.1 DEVELOPMENT AND COMMERCIALIZATION. Upon designation of a Royalty-Bearing Product pursuant to Section 4.2, the Continuing Party shall be solely responsible for all Development and Commercialization activities relating to such Royalty-Bearing Product and shall bear one hundred percent (100%) of all expenses for the Development, Manufacture and Commercialization of such Royalty-Bearing Product incurred after the Opt-Out Point and the JSC and JCC shall cease to have oversight or management responsibility with respect to such Royalty-Bearing Product.

6.2 DEVELOPMENT AND DILIGENCE BY THE CONTINUING PARTY. After the Opt-Out Point, the Continuing Party shall use Commercially Reasonable Efforts to Develop and Commercialize the Royalty-Bearing Product. All Development and Commercialization activities with respect to such Royalty-Bearing Product shall be conducted at the Continuing Party's sole cost and expense and in accordance with all applicable laws, rules and regulations, including without limitation current governmental regulations concerning good laboratory practices, good clinical practices and good manufacturing practices.

6.3 REPORTS FOR ROYALTY-BEARING PRODUCTS. After the Opt-Out Point, the Continuing Party shall prepare and deliver to the Opt-Out Party, by no later than each November 1, a written plan that describes the Development and Commercialization activities to be undertaken in the next Calendar Year and the dates by which such activities are

targeted to be accomplished. In addition, the Continuing Party shall prepare and deliver to the Opt-Out Party, by no later than each February 28 (for the period ending December 31 of the prior Calendar Year), written reports which shall update any prior report filed hereunder, including a summary of the Continuing Party's Development and Commercialization activities performed to date, as applicable. The Continuing Party shall provide the Opt-Out Party with written notice of (i) all filings and submissions for Regulatory Approval regarding Royalty-Bearing Products in a timely manner; and (ii) all Regulatory Approvals obtained or denied within [**] days of receipt of written notice of such obtaining or denial; provided, however, that for filings and submissions for Regulatory Approval, and Regulatory Approvals obtained or denied, in the United States, the European Union, Japan, and Canada, the Continuing Party will notify the Opt-Out Party as soon as reasonably possible, but in any event within [**] business days of the Continuing Party's receipt of notice of such filing or submission for Regulatory Approval, or of the obtaining or denial of such Regulatory Approval, as the case may be. At the Opt-Out Party's reasonable request from time to time and without unduly burdening the Continuing Party, the Continuing Party shall also provide such other information and shall agree to meet with the Opt-Out Party as needed (but not more than once each year) to keep the Opt-Out Party reasonably informed of the Continuing Party's Development and Commercialization activities.

6.4 CLINICAL AND COMMERCIAL SUPPLY. In the event that [**] with respect to a Royalty-Bearing Product [**] Manufacture and supply such Royalty-Bearing Product [**] after the applicable Opt-Out Point or such earlier time as may be agreed[**]. In the event that [**] with respect to a Royalty-Bearing Product [**] Manufacture and supply such Royalty-Bearing Product to [**] for [**] after such Opt-Out Point or such earlier time as may be agreed[**]; provided that [**] such Royalty-Bearing Product [**]The Continuing Party shall pay[**]the Opt-Out Party for any such Royalty-Bearing Product supplied pursuant to this Section 6.4 at the Cost of Goods Sold of such Royalty-Bearing Product.

6.5 REGULATORY APPROVALS. Notwithstanding anything to the contrary contained in Section 2.10, after the Opt-Out Point for a Royalty-Bearing Product, the Continuing Party shall be the holder of all Regulatory Approvals (including IND and NDA submissions) for such Royalty-Bearing Product. To the extent permitted by law, the Opt-Out Party will assign to the Continuing Party, as soon as practical after the Opt-Out Point, all regulatory filings related to such Royalty-Bearing Product to the extent requested by the Continuing Party, including any draft IND documents, and copies of all correspondence and notes of any oral communication with Regulatory Authorities regarding such Royalty-Bearing Product. The Opt-Out Party will execute such further instruments, documents or certificates, as may be required to more effectively assign the regulatory filings to the Continuing Party. To the extent the Opt-Out Party cannot transfer all such Regulatory Approvals, the Opt-Out Party shall permit the Continuing Party to use and cross-reference such regulatory filings.

6.6 MANUFACTURING REGULATORY COMMUNICATIONS RELATING TO ROYALTY-BEARING PRODUCTS. Notwithstanding any provisions of Section 2.10.3 or Section 2.10.4 to the contrary, with respect to all Manufacturing issues related to Royalty-Bearing Products, including all matters relating to cGMP compliance, the Continuing Party shall (i) oversee, monitor and coordinate all regulatory actions, communications and filings with, and submissions to, each Regulatory Authority, (ii) be responsible for interfacing,

corresponding and meeting with each Regulatory Authority and (iii) be responsible for maintaining all regulatory filings.

6.7 CONTINUATION OF LICENSES GRANTED UNDER IN-LICENSES. With respect to In-Licenses of the Opt-Out Party that Cover the applicable Royalty-Bearing Product, the Opt-Out Party will determine whether (i) such In-Licenses may be assigned to the Continuing Party subject to Third Party consent(s) and (ii) the Opt-Out Party's interest in retaining certain rights to exploit products other than such Royalty-Bearing Product. If the Opt-Out Party determines that such In-Licenses are assignable, the Opt-Out Party will assign such In-Licenses to the Continuing Party subject to any Third Party consents. With respect to such In-Licenses which are not assignable, the Opt-Out Party shall maintain these licenses for the duration of the sublicense granted by the Opt-Out Party to the Continuing Party under this Agreement. All amounts payable with respect to such non-assignable In-Licenses shall be shared by the Opt-Out Party and the Continuing Party in proportion to the rights being utilized by the Opt-Out Party and the Continuing Party under such In-Licenses; provided that all amounts allocable to the rights sublicensed to the Continuing Party shall be paid by the Opt-Out Party subject to reimbursement by the Continuing Party pursuant to Section 8.3.6. Such sublicense shall remain in full force and effect under the terms of this Agreement so long as the Continuing Party complies with all obligations relevant to such In-Licenses.

6.8 TECHNOLOGY TRANSFER. For a period of [**] the applicable Opt-Out Point, each Party shall provide to the other Party, at such other Party's request, any and all Know-How related to the Royalty-Bearing Products necessary for the other Party to perform its obligations or exploit its rights under this Agreement. Such technology transfer shall include, but not be limited to, technical assistance. The costs and expenses directly related to such provision of Know-How and technical assistance shall be calculated in accordance with the provisions related to Development Expenses and Commercialization Expenses, as applicable, and shall be borne equally by the Opt-Out Party and the Continuing Party. Each Party shall use such Know-How of the other Party solely for the purposes of performing its obligations or exploiting its rights under this Agreement with respect to the Royalty-Bearing Products.

7. LICENSES

7.1 LICENSE GRANTS.

7.1.1 PROFIT-SHARING PRODUCTS.

7.1.1.1 DEVELOPMENT LICENSES. Subject to the terms and conditions of this Agreement, solely for the purpose of conducting each Program, ALNYLAM hereby grants MERCK a co-

exclusive (with ALNYLAM), royalty-free license under ALNYLAM Technology to Develop Profit-Sharing Products in the Field in the Territory. Subject to the terms and conditions of this Agreement, solely for the purpose of conducting each Program, MERCK hereby grants ALNYLAM a co-exclusive (with MERCK), royalty-free license under MERCK Technology to Develop Profit-Sharing Products in the Field in the Territory. Such licenses shall include the right for both Parties to grant sublicenses and licenses as provided in Section 7.2 below.

7.1.1.2 COMMERCIALIZATION LICENSES. Subject to the terms and conditions of this Agreement, including without limitation ALNYLAM's U.S. Co-Promotion Option set forth in Section 5.5, ALNYLAM hereby grants MERCK a license under ALNYLAM Technology to Commercialize Profit-Sharing Products in the Field. Such license shall be exclusive in the United States with respect to each Profit-Sharing Product, unless ALNYLAM exercises its U.S. Co-Promotion Option, in which case such license shall be co-exclusive (with ALNYLAM). Such license shall be exclusive and royalty-bearing in the Territory outside the United States. Subject to the terms and conditions of this Agreement, upon ALNYLAM's exercise of its U.S. Co-Promotion Option, MERCK hereby grants ALNYLAM a co-exclusive (with MERCK) license under MERCK Technology to Commercialize Profit-Sharing Products in the Field in the United States. Such licenses shall include the right for both Parties to grant sublicenses and licenses as provided in Section 7.2 below.

7.1.1.3 MANUFACTURING LICENSES. Subject to the terms and conditions of this Agreement, only as permitted and solely for the purposes set forth in Sections [**] ALNYLAM hereby grants MERCK a non-exclusive license under ALNYLAM Technology to Manufacture Profit-Sharing Products in the Field for the Territory. Subject to the terms and conditions of this Agreement, only as permitted and solely for the purposes set forth in Sections [**] MERCK hereby grants ALNYLAM a non-exclusive license under MERCK Technology to Manufacture Profit-Sharing Products in the Field for the Territory. Such licenses shall include the right for both Parties to grant sublicenses and licenses as provided in Section 7.2 below.

7.1.1.4 PRODUCT TRADEMARK LICENSES. Subject to the terms and conditions of this Agreement, upon ALNYLAM's exercise of its U.S. Co-Promotion Option with respect to a Profit-Sharing Product, MERCK hereby grants ALNYLAM a co-exclusive license (with MERCK) to use the Product Trademark(s) selected by MERCK and approved by the JSC for such Profit-Sharing Product to Commercialize such Profit-Sharing Product in the Field in the United States. Furthermore, in the event that MERCK makes public use of Product Trademark(s) in the Development of a Profit-Sharing Product, MERCK shall grant ALNYLAM a co-exclusive license (with MERCK) to use such Product Trademark(s) to perform its Development obligations under this Agreement with respect to such Profit-Sharing Product. Such licenses shall include the right for both Parties to grant sublicenses and licenses as provided in Section 7.2 below.

7.1.2 ROYALTY-BEARING PRODUCTS. Subject to the terms and conditions of this Agreement, in relation to each Royalty-Bearing Product, the Opt-Out Party hereby grants the Continuing Party a license under ALNYLAM Technology or MERCK Technology, as

the case may be, to Develop, Manufacture and Commercialize such Royalty-Bearing Product in the Field in the Territory. Such license shall be exclusive and royalty-bearing for the royalty term of such Royalty-Bearing Product as set forth in Section 8.3.3 in each country in the Territory, and shall thereafter be a non-exclusive, royalty-free license to Develop, Manufacture and Commercialize such Royalty-Bearing Product in the Field in such country. Such licenses shall include the right to grant sublicenses and licenses as provided in Section 7.2 below.

7.1.3 BROAD RNAI TECHNOLOGY LICENSE. Subject to the rights granted each Party under this Agreement and the obligations set forth in Section 2.13, each Party (the "Granting Party") hereby grants the other Party a non-exclusive, royalty-free license, with the right to grant

sublicenses, under ALNYLAM Collaboration IP or MERCK Collaboration IP (collectively, "Collaboration IP") Controlled by the Granting Party comprising Broad RNAi Technology for the purpose of research, development, manufacture, use, import, or sale of RNAi Products; provided, that with respect to target validation and/or target identification research, neither Party shall have the right to provide any Third Party as part of a research collaboration with Collaboration IP Controlled by the other Party comprising Broad RNAi Technology, nor to use such Collaboration IP Controlled by the other Party comprising Broad RNAi Technology on behalf of any Third Party except in a collaboration whose primary purpose is the development of RNAi Products, and if Broad RNAi Technology is developed within such collaboration for use in target validation and/or target identification, then it may only be developed in the course of developing such RNAi Products.

7.2 SUBLICENSES AND LICENSES OF JOINT COLLABORATION IP.

7.2.1 AFFILIATES. Each Party shall be entitled to grant sublicenses of its rights under this Agreement (and licenses under any Joint Collaboration IP) to its Affiliates for so long as such entity remains an Affiliate.

7.2.2 PROFIT-SHARING PRODUCTS. With respect to Profit-Sharing Products, each Party shall be entitled to grant sublicenses of its rights under Section 7.1.1 (and licenses under any Joint Collaboration IP) in connection with its activities under a Program Workplan or Commercialization Plan to academic collaborators, and contract service organizations, that in each case are approved by the JSC in accordance with Section 2.6 to perform its obligations under such Program Workplan or Commercialization Plan.

7.2.3 ROYALTY-BEARING PRODUCTS. Subject to the terms of Section 7.2.5, the Continuing Party shall be entitled to grant sublicenses of its rights under this Agreement (and licenses under any Joint Collaboration IP) with respect to Royalty-Bearing Products to Third Parties to Develop and Commercialize such Royalty-Bearing Products. The Continuing Party shall notify the Opt-Out Party following the grant of any such sublicense or license, as the case may be.

7.2.4 MANUFACTURING SUBLICENSES. Subject to the terms of Section 7.2.5, each Party entitled to Manufacture Ophthalmic Products under the terms and conditions of this Agreement shall be entitled to grant sublicenses of its rights under this Agreement (and licenses

under any Joint Collaboration IP) to Third Parties to Manufacture such Ophthalmic Products; provided, that such Party shall remain primarily responsible with respect to such sublicense. Each such sublicense with respect to a Profit-Sharing Product shall require the approval of the JSC or JCC, as applicable. Each such sublicense with respect to a Royalty-Bearing Product shall be discussed between the Parties for a period of up to [**]; provided, however, that the Continuing Party may thereafter grant such sublicense in its sole discretion.

7.2.5 TERMS. Each sublicense granted by a Party pursuant to Section 7.2.3 or Section 7.2.4 shall be subject and subordinate to the terms and conditions of this Agreement and shall contain terms and conditions consistent with those in this Agreement. Agreements with any Commercializing Sublicensee shall contain the following provisions: (a) a requirement that such Sublicensee submit applicable sales or other reports consistent with those required hereunder; (b) an audit requirement similar to the requirement set forth in Section 8.4; and

(c) a requirement that such Sublicensee comply with the confidentiality and non-use provisions of Article 9 with respect to both Parties' Information.

7.2.6 LIABILITY. Each Party shall at all times be responsible for the performance of its Sublicensees under this Agreement.

7.3 JOINT COLLABORATION IP. Subject to the rights granted each Party under this Agreement and the obligations set forth in Section 2.13, each Party shall have the right to use, sell, keep, license or assign its interest in Joint Collaboration IP and otherwise undertake all activities a sole owner might undertake with respect to such Joint Collaboration IP without the consent of and without accounting to the other Party.

7.4 IN-LICENSES. All licenses and other rights granted MERCK under this Article 7 are subject to the rights granted ALNYLAM under the ALNYLAM In-Licenses. All licenses and other rights granted ALNYLAM under this Article 7 are subject to the rights granted MERCK under the MERCK In-Licenses.

7.5 CERTAIN PATENT RIGHTS. Notwithstanding anything to the contrary herein, the licenses[**]to ALNYLAM Patent Rights hereunder initially shall[**]provided that if any such Patent Rights in-licensed by[**]ALNYLAM[**], as the case may be, [**] shall be amended accordingly.

7.6 NO OTHER RIGHTS. Except as otherwise expressly provided in this Agreement, under no circumstances shall a Party hereto, as a result of this Agreement, obtain any ownership interest or other right in any Know-How or Patent Rights of the other Party, including items owned, controlled or developed by the other Party, or provided by the other Party to the receiving Party at any time pursuant to this Agreement.

8. PAYMENTS; ROYALTIES AND REPORTS

8.1 PAYMENTS.

8.1.1 INITIAL PAYMENT. Within fifteen (15) business days following the Effective Date, MERCK shall pay ALNYLAM a non-refundable, non-creditable initial payment of [**] Dollars ($[**]).

8.1.2 DEVELOPMENT EXPENSE REIMBURSEMENT. Within fifteen (15) business days following the Effective Date, MERCK shall pay ALNYLAM a non-refundable, non-creditable payment of [**] Dollars ($[**]) as reimbursement for development expenses incurred by ALNYLAM prior to the Effective Date with respect to the VEGF Program.

8.1.3 MILESTONE FEES.

8.1.3.1 PROFIT-SHARING PRODUCTS. MERCK shall make the non-refundable, non-creditable milestone payments to ALNYLAM set forth below no later than thirty (30) calendar days after the earliest date on which the corresponding milestone event has been achieved with respect to the first Profit-Sharing Product in each Program to achieve such milestone event.

<TABLE>
<CAPTION>

Milestone Event	Payment
<S>	<C>

Initiation of IND-Enabling GLP Toxicology Studies	$[**]
Submission of IND	$[**]

8.1.3.2 ROYALTY-BEARING PRODUCTS.

(a) If (i) MERCK has exercised its Product Opt-Out Right during the [**] Opt-Out Period with respect to an Ophthalmic Product [**] and ALNYLAM is the Continuing Party with respect to such Royalty-Bearing Product, or (ii) ALNYLAM has exercised its Product Opt-Out Right during the [**] Opt-Out Period with respect to an Ophthalmic Product [**] and MERCK is the Continuing Party with respect to such Royalty-Bearing Product, then the Continuing Party shall make a non-refundable, non-creditable milestone payment to the Opt-Out Party in the amount of $[**] no later than twenty (20) business days after the earliest date on which the first NDA Filing for such Royalty-Bearing Product has been achieved.

(b) If either Party has exercised its Product Opt-Out Right with respect to an Ophthalmic Product in any Program during the [**] Opt-Out Period and the other Party is the Continuing Party with respect to such Royalty-Bearing Product, then the Continuing Party shall make the non-refundable, non-creditable milestone payments to the Opt-Out Party set forth below no later than twenty (20) business days after the earliest date on which the corresponding milestone event has been achieved for the first time with respect to such Royalty-Bearing Product.

MILESTONE EVENT	PAYMENT
Initiation of Phase III Study	$[**]
First NDA Filing	$[**]

8.2 U.S. OPERATING PROFIT/LOSS FOR PROFIT-SHARING PRODUCTS. The Parties shall share equally the U.S. Operating Profit/Loss for all Profit-Sharing Products; provided, however, that if a Party exercises its Expense Share Reduction Option pursuant to Section 2.11.1 to reduce its percentage share of U.S. Development Expenses with respect to a Profit-Sharing Product, the Parties' percentage shares of the U.S. Operating Profit/Loss for such Profit-Sharing Product shall be the same as their respective percentage shares of U.S. Development Expenses as adjusted pursuant to the Expense Share Reduction Option.

"U.S. Operating Profit/Loss" shall be calculated for each Profit-Sharing Product by determining Net Sales of such Profit-Sharing Product in the relevant time period in the United States and by then subtracting the Commercialization Expenses accrued by either Party in respect of such Profit-Sharing Product in the relevant time period in the United States.

Within sixty (60) days after submission of the first Commercialization Plan for such Profit-Sharing Product to the JCC, the Parties will discuss and agree upon the procedures for reporting, reconciliation and payments with respect to U.S.

Operating Profit/Loss.

8.3 ROYALTIES.

8.3.1 ROYALTIES PAYABLE ON PROFIT-SHARING PRODUCTS. Subject to the terms and conditions of this Agreement, MERCK shall pay to ALNYLAM royalties on aggregate Net Sales in the Territory outside the United States of each Profit-Sharing Product by MERCK or its Related Parties as follows:

<TABLE>
<CAPTION>

CALENDAR YEAR NET SALES OF THE PROFIT-SHARING PRODUCT IN THE TERRITORY OUTSIDE THE UNITED STATES	ROYALTY (AS A PERCENTAGE OF NET SALES)
<S>	<C>
$0 - $[**]	[**]%
$[**] - $[**]	[**]%
$[**] - $[**]	[**]%
Greater than $[**]	[**]%

</TABLE>

Royalties on aggregate Net Sales of the Profit-Sharing Products in the Territory outside the United States in a Calendar Year shall be paid at the rate applicable to the portion of Net Sales within each of the Net Sales levels above during such Calendar Year.

8.3.2 ROYALTIES PAYABLE ON ROYALTY-BEARING PRODUCTS. Subject to the terms and conditions of this Agreement, the Royalty Payor shall pay to the Royalty Recipient royalties on a country-by-country basis for Worldwide Sales of each Royalty-Bearing Product, such royalties to be calculated as set forth in Section 8.3.2.1.

8.3.2.1 GENERAL PROCEDURE FOR CALCULATION OF ROYALTIES. For each scenario under which royalties are due from one Party to the other, Sections 8.3.2.2 and 8.3.2.3 set forth values for the following parameters: Sublicense Revenue Fraction (expressed as a percentage), Royalty Rate One, Royalty Rate Two, Royalty Rate Three and Royalty Rate Four. The values set forth for these parameters in Sections 8.3.2.2 and 8.3.2.3 shall be used to calculate the royalties due under each scenario in relation to each Royalty-Bearing Product, as follows:

(a) In the event that all of the Worldwide Sales for the Royalty-Bearing Product are made by the Royalty Payor or its Related Parties, the Royalty Payor shall pay the Royalty Recipient royalties on Worldwide Sales as follows:

<TABLE>
<CAPTION>

WORLDWIDE SALES	ROYALTY (AS A PERCENTAGE OF WORLDWIDE SALES)
<S>	<C>
$0 to $[**]	Royalty Rate One
$[**] to $[**]	Royalty Rate Two
$[**] to $[**]	Royalty Rate Three

Greater than $[**]	Royalty Rate Four

</TABLE>

Royalties on Worldwide Sales in a Calendar Year shall be paid at the rate applicable to the portion of Worldwide Sales within each of the Worldwide Sales levels above. For example, if, during a Calendar Year, Worldwide Sales were equal to $[**], the royalties payable by the Royalty Payor would be calculated by adding (i) the royalties with respect to the first $[**] at Royalty Rate One, (ii) the royalties with respect to the next $[**] at Royalty Rate Two, and (iii) the royalties with respect to the final $[**] at Royalty Rate Three.

(b) In the event that all of the Worldwide Sales for the Royalty-Bearing Product are made through one or more Sublicensees of the Royalty Payor, the Royalty Payor shall pay the Royalty Recipient the lesser of (i) an amount equal to the Sublicense Revenue Fraction multiplied by the revenues received by the Royalty Payor from its Sublicensees in relation to such Worldwide Sales, and (ii) the amounts that would be due pursuant to Section 8.3.2.1(a) if all Worldwide Sales had been made directly by the Royalty Payor or its Related Parties, without a Sublicensee.

(c) In the event that some of the Worldwide Sales for the Royalty-Bearing Product are made directly by the Royalty Payor or its Related Parties, and some of the Worldwide Sales for the Royalty-Bearing Product, in one or more countries, are made through one or more Sublicensee(s), the royalties to be paid by the Royalty Payor to the Royalty Recipient shall be calculated as follows:

(i) The fraction of Worldwide Sales that were made in each country shall be determined by dividing Country Sales in such country by Worldwide Sales (such fraction, the "Country Fraction" for such country).

(ii) For each country:

a. "Level One Limit" shall be calculated by multiplying the Country Fraction for such country by $[**];

b. "Level Two Threshold" shall be calculated by adding one dollar to "Level One Limit";

c. "Level Two Limit" shall be calculated by multiplying the Country Fraction for such country by $[**];

d. Level Three Threshold" shall be calculated by adding one dollar to "Level Two Limit"; and

e. "Level Three Limit" shall be calculated by multiplying the Country Fraction for such country by $[**].

(iii) For each country in the Territory in which Country Sales are made by the Royalty Payor or its Related Parties and not by a Sublicensee, the Royalty Payor shall pay the Royalty Recipient royalties as follows:

<TABLE>
<CAPTION>

COUNTRY SALES IN COUNTRY IN THE TERRITORY	ROYALTY (AS A PERCENTAGE OF COUNTRY SALES)
<S>	<C>
$0 to Level One Limit for such country	Royalty Rate One
Level Two Threshold to Level Two Limit for such country	Royalty Rate Two
Level Three Threshold to Level Three Limit for such country	Royalty Rate Three
Greater than Level Three Limit for such country	Royalty Rate Four

</TABLE>

Royalties on Country Sales of the Royalty-Bearing Products in each country in the Territory in a Calendar Year shall be paid at the rate applicable to the portion of Country Sales within each of the Country Sales levels above during such Calendar Year. For example, if, during a

Calendar Year, Country Sales of a Royalty-Bearing Product were equal to $[**], and the Level One Limit is $[**], the Level Two Limit is $[**], and the Level Three Limit is $[**], then the royalties payable by the Royalty Payor would be calculated by adding (i) the royalties with respect to the first $[**] at Royalty Rate One, (ii) the royalties with respect to the next $[**] at Royalty Rate Two, (iii) the royalties with respect to the next $[**] at Royalty Rate Three, and (iv) the royalties with respect to the final $[**] at Royalty Rate Four.

(iv) For each country in which Country Sales are made through one or more Sublicensees of the Royalty-Payor, the Royalty Payor shall pay the Royalty Recipient the lesser of (x) an amount equal to the Sublicense Revenue Fraction multiplied by the revenues received by the Royalty Payor from its Sublicensees in relation to such Country Sales, and (y) the amounts that would be due pursuant to Section 8.3.2.1(c)(iii) if such Country Sales had been made directly by the Royalty Payor or its Related Parties, without a Sublicensee.

8.3.2.2 ALNYLAM IS THE CONTINUING PARTY FOR [**]. If MERCK has exercised its Product Opt-Out Right with respect to [**] and ALNYLAM is the Continuing Party with respect to such Royalty-Bearing Product that is [**] then ALNYLAM shall be the Royalty Payor, MERCK shall be the Royalty Recipient, and

(a) If such exercise by MERCK of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**] percent ([**]%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

(b) If such exercise by MERCK of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**] percent ([**]%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

(c) If such exercise by MERCK of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**] percent ([**]%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

8.3.2.3 ALNYLAM IS THE CONTINUING PARTY FOR AN OPHTHALMIC PRODUCT [**] OR MERCK IS THE CONTINUING PARTY FOR AN OPHTHALMIC PRODUCT [**] If (x) MERCK has exercised its Product Opt-Out Right with respect to an Ophthalmic Product [**] and ALNYLAM is the Continuing Party with respect to such Royalty-Bearing Product, or (y) ALNYLAM has exercised its Product Opt-Out Right with respect to an Ophthalmic Product [**] and MERCK is the Continuing Party with respect to such Royalty-Bearing Product, then the Continuing Party shall be the Royalty Payor and the Opt-Out Party shall be the Royalty Recipient, and

(a) If such exercise by MERCK or ALNYLAM of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**] percent (40%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

(b) If such exercise by MERCK or ALNYLAM of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**] percent ([**]%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

(c) If such exercise by MERCK or ALNYLAM of its Product Opt-Out Right occurred during the [**] Opt-Out Period, then

(i) The Sublicense Revenue Fraction shall be [**]percent ([**]%);

(ii) Royalty Rate One shall be [**] percent ([**]%);

(iii) Royalty Rate Two shall be [**] percent ([**]%);

(iv) Royalty Rate Three shall be [**] percent ([**]%); and

(v) Royalty Rate Four shall be [**] percent ([**]%).

8.3.2.4 EITHER PARTY IS CONTINUING PARTY AFTER EXERCISE OF TARGET OPT-OUT RIGHTS. If either Party exercises its Target Opt-Out Right with respect to a Program Target, and the other Party elects to be the Continuing Party with respect to any Ophthalmic Product in the Program for such Program Target, then such Ophthalmic Product shall be deemed to be a Royalty-Bearing Product and (a) with respect to the Royalty-Bearing Product in such Program that is at the most advanced stage of Development (the "Lead Royalty-Bearing Product"), the Royalty Payor shall pay the Royalty Recipient royalties calculated as set forth in Section 8.3.2.3 for Product Opt-Out Rights exercised during the Opt-Out Period in which the Target Opt-Out Point occurred, or if the Target Opt-Out Point did not occur in an Opt-Out Period, then for the exercise of Product Opt-Out Rights during the Opt-Out Period most recently preceding the Target Opt-Out Point; and (b) with respect to all other Royalty-Bearing Products in such Program, the Royalty Payor shall pay the Royalty Recipient [**] percent ([**]%) of the amount of royalties calculated as set forth in Section 8.3.2.3 for the exercise of Product Opt-Out Rights during the [**]Opt-Out Period; provided, however, that if ALNYLAM is the Opt-Out Party, in no event shall the royalties payable to ALNYLAM with respect to Net Sales in a country for any Calendar Quarter be less than the amount of any royalties and any portions of milestones or other payments under the Existing ALNYLAM In-Licenses that are reasonably allocable to the Commercialization or Manufacture of the Profit-Sharing Product in or for such country in the Field.

8.3.3 ROYALTY TERM. Royalties on each Ophthalmic Product at the rates set forth in Section 8.3.1 and 8.3.2 shall be effective as of the date of First Commercial Sale of such Ophthalmic Product in a country and shall continue until the later of (a) the expiration of the last Valid Claim covering the Manufacture or Commercialization of the Ophthalmic Product in the country of sale, or (b) [**] anniversary of the First Commercial Sale in such country, subject to the following conditions:

(a) only one royalty shall be due with respect to the same unit of Ophthalmic Product;

(b) no royalties shall be due upon the sale or other transfer among a Party or its Related Parties, but in such cases the royalty shall be due and calculated upon the Party's or its Related Party's Net Sales to the first independent Third Party;

(c) no royalties shall accrue on the sale or other disposition of the Ophthalmic Product by the Parties or their Related Parties for use in a Clinical Trial; and

(d) no royalties shall accrue on the disposition of Ophthalmic Product in reasonable quantities by a Party or its Related Parties as samples (promotion or otherwise) or as donations (for example, to non-profit institutions or government agencies for a non-commercial purpose).

8.3.4 CHANGE IN SALES PRACTICES. The Parties acknowledge that during the Agreement Term, a Royalty Payor's sales practices for the marketing and distribution of an Ophthalmic Product may change to the extent to which the calculation of the payment for royalties on Net Sales may become impractical or even impossible. In such event the Parties agree to meet and discuss in good faith new ways of compensating the Royalty Recipient to the extent currently contemplated under this Section 8.3.

8.3.5 COMPULSORY LICENSES. If a compulsory license is granted to a Third Party with respect to an Ophthalmic Product in any country in the Territory with a royalty rate lower than the applicable royalty rate set forth in this Section 8.3, then the royalty rate to be paid by the Royalty Payor on Net Sales in that country under this Section 8.3 shall be reduced to the rate paid by the compulsory licensee.

8.3.6 NECESSARY THIRD PARTY IP.

8.3.6.1 PROFIT-SHARING PRODUCTS. If the Development, Manufacture or Commercialization of a Profit-Sharing Product by a Party in accordance with this Agreement infringes Necessary Third Party IP then:

(a) The amount of any portions of milestones or other payments paid by either Party under all In-Licenses of such Necessary Third Party IP that are reasonably allocable to the Development of the Profit-Sharing Product in the Field (i) in the United States, shall be included in the U.S. Development Expenses for such Profit-Sharing Product and shared by the Parties pursuant to Section 2.11, and (ii) in the Territory outside the United States, shall be borne by MERCK.

(b) The amount of any royalties and any portions of milestones or other payments paid by either Party under all In-Licenses of such Necessary Third Party IP that are reasonably allocable to the Commercialization or Manufacture of the Profit-Sharing Product in or for the United States in the Field, shall be Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss for such Profit-Sharing Product pursuant to Section 8.2.

(c) The applicable royalties in each country in the Territory outside the United States payable by MERCK to ALNYLAM

pursuant to Section 8.3.1 will be (i) reduced by [**] percent ([**]%) of the amount paid by MERCK and (ii) increased by [**] percent ([**]%) of the amount paid by ALNYLAM, in each case, of any royalties and any portions of milestones or other payments under all In-Licenses of such Necessary Third Party IP that are reasonably allocable to the Commercialization or Manufacture of the Profit-Sharing Product in or for such country in the Field; provided, however, that, on a country-by-country basis, in no event shall the royalties payable to ALNYLAM with respect to Net Sales in a

country for any Calendar Quarter be reduced below the greater of (x) [**]percent ([**]%) of the royalties otherwise payable by MERCK to ALNYLAM for such Calendar Quarter as calculated pursuant to Section 8.3.1 or (y) the amount of any royalties and any portions of milestones or other payments under the Existing ALNYLAM In-Licenses that are reasonably allocable to the Commercialization or Manufacture of the Profit-Sharing Product in or for such country in the Field.

8.3.6.2 ROYALTY-BEARING PRODUCTS. If the Development, Manufacture or Commercialization of a Royalty-Bearing Product by a Continuing Party in accordance with this Agreement infringes Necessary Third Party IP, the applicable royalties in each country in the Territory payable to the Opt-Out Party pursuant to Section 8.3.2.1 will be (a) reduced by [**] percent ([**]%) of the amount paid by the Continuing Party and (b) increased by [**] percent ([**]%) of the amount paid by the Opt-Out Party (and not already reimbursed by the Continuing Party pursuant to Section 6.7), in each case, of any royalties and any portions of milestones or other payments under all In-Licenses of such Necessary Third Party IP that are reasonably allocable to the Development, Manufacture and Commercialization of the Royalty-Bearing Product in or for such country in the Field; provided, however, that, on a country-by-country basis, in no event shall the royalties payable to the Opt-Out Party with respect to Net Sales in a country for any Calendar Quarter be reduced below the greater of (i) [**] percent ([**]%) of the royalties otherwise payable by the Continuing Party to the Opt-Out Party for such Calendar Quarter as calculated pursuant to Section 8.3.2 or (ii) if ALNYLAM is the Opt-Out Party, the amount of any royalties and any portions of milestones or other payments under the Existing ALNYLAM In-Licenses that are reasonably allocable to the Commercialization or Manufacture of the Profit-Sharing Product in or for such country in the Field.

8.3.7 BLENDED ROYALTY RATES. The Parties acknowledge and agree that the Patent Rights and Know-How licensed pursuant to this Agreement justify royalty rates of differing amounts with respect to the sales of Ophthalmic Products, which rates could be applied separately to Ophthalmic Products involving the exercise of such Patent Rights and/or the incorporation of such Know-How, and that, if such royalties were calculated separately, royalties relating to Patent Rights and royalties relating to Know-How would last for different terms. Notwithstanding the foregoing, the Parties have determined, for reasons of convenience, that blended royalty rates for the Patent Rights and the Know-How licensed hereunder, as set forth above, will apply during a single royalty term. The Parties acknowledge and agree that nothing in this Agreement (including without limitation any exhibits or attachments hereto) shall be construed as

representing an estimate or projection of either (a) the number of Ophthalmic Products that will or may be successfully Developed or Commercialized or (b) anticipated sales or the actual value of any Ophthalmic Product, and that the figures set forth in this Section 8.3 or elsewhere in this Agreement or that have otherwise been discussed by the Parties are merely intended to define the Parties' royalty payment obligations to each other in the event such sales performance is achieved.

8.3.8 REPORTS; PAYMENT OF ROYALTY. During the Agreement Term, commencing upon the First Commercial Sale of each Ophthalmic Product, the Royalty Payor shall furnish to the Royalty Recipient (a) a monthly written report showing the estimated quantity of each Ophthalmic Product sold in each country (as measured in grams of active pharmaceutical ingredient or saleable units of product, as the Parties may agree) and the Net Sales of such Ophthalmic Product in each country (and any other detail reasonably available through the Royalty Payor's internal sales reporting system) for the previous month, in each case on an unaudited basis; and (b) a quarterly written report showing the quantity of each Ophthalmic Product sold in each country (as measured in grams of active pharmaceutical ingredient or saleable units of product, as the Parties may agree), the gross sales of such Ophthalmic Product in each country, total deductions for such Ophthalmic Product for each country included in the calculation of Net Sales, the Net Sales in each country of such Ophthalmic Product subject to royalty payments sold by the Royalty Payor or its Related Parties during the reporting period and the royalties payable under this Agreement. Quarterly reports shall be due no later than [**] following the close of each Calendar Quarter. Royalties shown to have accrued by each royalty report shall be due and payable on the date such royalty report is due. Each Party shall keep complete and accurate records in sufficient detail to enable the royalties and other payments payable hereunder to be determined, including without limitation records of the items underlying U.S. Development Expenses and U.S. Operating Profit/Loss.

8.4 AUDITS.

8.4.1 Upon the written request of a Party and not more than once in each Calendar Year, the other Party and/or its Related Parties shall permit an independent certified public accounting firm of nationally-recognized standing selected by the requesting Party and reasonably acceptable to the other Party, at the requesting Party's expense except as set forth below, to have access during normal business hours to such of the records of the other Party as may be reasonably necessary to verify the accuracy of the royalty and other reports hereunder for any year ending not more than [**] months prior to the date of such request for the sole purpose of verifying the basis and accuracy of payments made under Sections 2.11 and 13.2 and this Article 8.

8.4.2 If such accounting firm identifies a discrepancy made during such period, the appropriate Party shall pay the other Party the amount of the discrepancy within twenty (20) business days of the date the requesting Party delivers to the other Party such accounting firm's written report so concluding, or as otherwise agreed by the Parties in writing. Such written report shall be binding upon the Parties. The fees charged by such accounting firm shall be paid by the requesting Party, unless such discrepancy represents an underpayment by the other Party of the lesser of [**] U.S. dollars ($[**]) or [**] percent ([**]%) of the total amounts due hereunder, in which case such fees shall be paid by the other Party.

8.4.3 The Royalty Payor shall include in each sublicense granted by it

pursuant to this Agreement a provision requiring the sublicensee to make reports to the Royalty Payor, to keep and maintain records of sales made pursuant to such sublicense and to grant

access to such records by the Royalty Recipient's independent accountant to the same extent required of the Royalty Payor under this Agreement.

8.4.4 Unless an audit for such year has been commenced upon the expiration of [**] months following the end of any year, the calculation of royalties and other payments payable with respect to such year shall be binding and conclusive upon both Parties, and the Royalty Payor and its Related Parties shall be released from any further liability or accountability with respect to royalties for such year.

8.4.5 Each Party shall treat all financial information subject to review under this Section 8.4 or under any sublicense agreement in accordance with the confidentiality and non-use provisions of this Agreement, and shall cause its accounting firm to enter into an acceptable confidentiality agreement with the other Party and/or its Related Parties obligating it to retain all such information in confidence pursuant to such confidentiality agreement.

8.5 PAYMENT EXCHANGE RATE. All payments to be made under this Agreement shall be made in United States dollars and shall be paid by bank wire transfer in immediately available funds to such bank account in the United States as may be designated in writing by the receiving Party from time to time. In the case of sales outside the United States by each Party and its Related Parties, the rate of exchange to be used in computing the amount of currency equivalent in United States dollars due shall be made at the rate of exchange utilized by such Party in its worldwide accounting system, prevailing on the third to the last business day of the month preceding the month in which such sales are recorded.

8.6 INCOME TAX WITHHOLDING. If laws, rules or regulations require withholding of income taxes or other taxes imposed upon payments set forth in this Article 8, the paying Party shall make such withholding payments as required and subtract such withholding payments from the payments set forth in this Article 8. The paying Party shall submit appropriate proof of payment of the withholding taxes to the receiving Party within a reasonable period of time. At the request of the receiving Party, the paying Party shall, at its cost, give the receiving Party such reasonable assistance, which shall include the provision of appropriate certificates of such deductions made together with other supporting documentation as may be required by the relevant tax authority, to enable the receiving Party to claim exemption from such withholding or other tax imposed or obtain a repayment thereof or reduction thereof and shall upon request provide such additional documentation from time to time as is reasonably required to confirm the payment of tax.

9. CONFIDENTIALITY AND PUBLICATION

9.1 NONDISCLOSURE OBLIGATION. All Information disclosed by one Party to the other Party hereunder shall be maintained in confidence by the receiving Party and shall not be disclosed to a non-Party or used for any purpose except as set forth herein without the prior written consent of the disclosing Party, except to the extent that such Information:

(a) is known by the receiving Party at the time of its receipt, and not through a prior disclosure by the disclosing Party, as documented by the receiving Party's business records;

(b) is in the public domain by use and/or publication before its receipt from the disclosing Party, or thereafter enters the public domain through no fault of the receiving Party;

(c) is subsequently disclosed to the receiving Party by a Third Party who may lawfully do so and is not under an obligation of confidentiality to the disclosing Party;

(d) is developed by the receiving Party independently of Information received from the disclosing Party, as documented by the receiving Party's business records;

(e) is deemed necessary by counsel to the receiving Party to be disclosed to such Party's attorneys or independent accountants for the sole purpose of enabling such attorneys or independent accountants to provide advice to the receiving Party, on the condition that such attorneys and independent accountants agree to be bound by confidentiality and non-use obligations substantially similar to those contained in this Agreement; provided, however, that the term of confidentiality for such attorneys and independent accountants shall be no less than [**]; or

(f) is deemed necessary by a Party to be disclosed to Related Parties, agents, consultants, and/or other Third Parties for the Development, Manufacturing or Commercialization of Ophthalmic Product (or for such entities to determine their interest in performing such activities) in accordance with this Agreement on the condition that such Third Parties agree to be bound by confidentiality and non-use obligations substantially similar to those contained in this Agreement provided, however, that the term of confidentiality for such Third Parties shall be no less than [**].

Any combination of features or disclosures shall not be deemed to fall within the foregoing exclusions merely because individual features are published or available to the general public or in the rightful possession of the receiving Party unless the combination itself and principle of operation are published or available to the general public or in the rightful possession of the receiving Party.

Notwithstanding the obligations of confidentiality and non-use set forth above, a receiving Party may provide Information disclosed to it to (i) governmental or other Regulatory Authorities in order to obtain patents or to gain or maintain approval to conduct Clinical Studies or to otherwise Develop, Manufacture or Commercialize Ophthalmic Products; provided, that such disclosure shall be subject to the prior written consent of the Party whose Information is intended to be disclosed (which consent shall not be unreasonably withheld), and such Information shall be disclosed only to the extent reasonably necessary to obtain patents or authorizations, (ii) the extent required

by applicable law, including without limitation by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or Nasdaq, (iii) any bona fide actual or prospective underwriters, investors, lenders or other financing sources who are obligated to keep such information

confidential, to the extent reasonably necessary to enable such actual or prospective underwriters, investors, lenders or other financing sources to determine their interest in underwriting or making an investment in, or otherwise providing financing to, the receiving Party; provided, however, that in the case of an investor that is a Significant Pharmaceutical Company, such disclosure shall be subject to the prior written consent of the Party whose Information is intended to be disclosed (which consent shall not be unreasonably withheld), and (iv) in the event that the Party seeking to provide Information of the other Party is the Continuing Party with respect to a Royalty-Bearing Product, any bona fide actual or prospective collaborators or strategic partners with respect to the Development or Commercialization of such Royalty-Bearing Product, who are obligated to keep such information confidential; provided, however, that the Party and/or its Affiliates shall only disclose to actual or prospective collaborators and strategic partners the general subject matter of this Agreement, the licenses granted hereunder, the provisions set forth in Section 2.13 and 13.2, the provisions of Articles 8, 9 and 11, and such Know-How and Patent Rights relating to such Royalty-Bearing Product as the receiving Party, in its reasonable judgment, considers necessary for such actual or prospective collaborators or strategic partners to evaluate their interest in such Royalty-Bearing Product.

If a Party is required by judicial or administrative process to disclose Information that is subject to the non-disclosure provisions of this Section 9.1 or Section 9.2, such Party shall promptly inform the other Party of the disclosure that is being sought in order to provide the other Party an opportunity to challenge or limit the disclosure obligations. Information that is disclosed by judicial or administrative process shall remain otherwise subject to the confidentiality and non-use provisions of this Section 9.1 and Section 9.2, and the Party disclosing Information pursuant to law or court order shall take all steps reasonably practical, including without limitation seeking an order of confidentiality, to ensure the continued confidential treatment of such Information. In addition to the foregoing restrictions on public disclosure, if either Party concludes that a copy of this Agreement must be filed with the Securities and Exchange Commission, such Party shall provide the other Party with a copy of this Agreement showing any sections as to which the Party proposes to request confidential treatment, will provide the other Party with an opportunity to comment on any such proposal and to suggest additional portions of the Agreement for confidential treatment, and will take such Party's reasonable comments into consideration before filing the Agreement.

9.2 PUBLICATION. MERCK and ALNYLAM each acknowledge the other Party's interest in publishing the results of the Development. Each Party also recognizes the mutual interest in obtaining valid patent protection and in protecting business interests and trade secret information. Consequently, except for disclosures permitted pursuant to Section 9.1, either Party, its Affiliates, or their respective employees or consultants wishing to make a publication or a disclosure to a Third Party relating to the Ophthalmic Collaboration or any Profit-Sharing Product shall deliver to the other Party a copy of the

proposed written publication or an outline of an oral disclosure at least thirty (30) days prior to submission for publication or presentation. The reviewing Party shall have the right (a) to propose modifications to the publication or presentation for patent reasons, trade secret reasons or business reasons, or (b) to request

a reasonable delay in publication or presentation in order to protect patentable information. If the reviewing Party requests a delay, the publishing Party shall delay submission or presentation for a period of sixty (60) days to enable patent applications protecting each Party's rights in such information to be filed in accordance with Article 11 below. Upon expiration of such sixty (60) days, the publishing Party shall be free to proceed with the publication or presentation. If the reviewing Party requests modifications to the publication or presentation, the publishing Party shall edit such publication to prevent disclosure of trade secret or proprietary business information prior to submission of the publication or presentation. With respect to any proposed publications or disclosures by investigators or academic or non-profit collaborators, such materials shall be subject to review under this Section 9.2 to the extent that MERCK or ALNYLAM, as the case may be, has the right and ability (after using reasonable efforts) to do so. For the avoidance of doubt, subject to its obligations under Section 9.1, the Continuing Party with respect to a Royalty-Bearing Product may make publications and disclosures to Third Parties relating to such Royalty-Bearing Product without any obligation to permit the Opt-Out Party to review or comment on such publication or disclosure. Furthermore, subject to its rights under Section 9.1, the Opt-Out Party with respect to a Royalty-Bearing Product shall have no right to make any publications and disclosures to Third Parties relating to such Royalty-Bearing Product.

9.3 PUBLICITY/USE OF NAMES. No disclosure of the existence of, or the terms of, this Agreement may be made by either Party, and no Party shall use the name, trademark, trade name or logo of the other Party or its employees in any publicity, news release or disclosure relating to this Agreement or its subject matter, without the prior express written permission of the other Party, except as may be required by law or expressly permitted by the terms hereof.

Notwithstanding the foregoing, prior to the execution of this Agreement by both Parties, the Parties shall agree in writing upon a press release to be issued jointly by the Parties publicizing the Ophthalmic Collaboration. After such initial press release, neither Party shall issue a press release or public announcement relating to the Ophthalmic Collaboration or this Agreement without the prior written approval of the other Party, which approval shall not be unreasonably withheld, except that a Party may (a) once a press release or other written statement is approved in writing by both Parties, make subsequent public disclosure of the information contained in such press release or other written statement without the further approval of the other Party, and (b) issue a press release or public announcement as required, in the reasonable judgment of such Party, by applicable law, including without limitation by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or Nasdaq, in each case after first notifying the other Party of such planned press release or public announcement at least seven (7) business days in advance of issuing such press release or making such public announcement (or, with respect to press releases and public announcements made

pursuant to the foregoing clause (b), with as much advance notice as possible under the circumstances if it is not possible to provide notice at least seven (7) business days in advance) for the sole purpose of allowing the other Party to review the proposed press release or public announcement for the inclusion of Confidential Information or the use of its name.

10. REPRESENTATIONS AND WARRANTIES; INDEMNIFICATION

10.1 MUTUAL REPRESENTATIONS AND WARRANTIES. Each Party represents and warrants to the other Party that as of the Effective Date of this Agreement:

10.1.1 It is duly-organized and validly existing under the laws of its jurisdiction of incorporation or formation, and has full corporate or other power and authority to enter into this Agreement and to carry out the provisions hereof.

10.1.2 It is duly-authorized to execute and deliver this Agreement and to perform its obligations hereunder, and the person or persons executing this Agreement on its behalf has been duly-authorized to do so by all requisite corporate action.

10.1.3 This Agreement is legally binding upon it and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by it does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party and by which it may be bound.

10.1.4 It has not, and will not during the Agreement Term, grant any right to any Third Party which would conflict with the rights granted to the other Party hereunder. It has (or will have at the time performance is due) maintained and will maintain and keep in full force and effect all agreements (including license agreements) and filings (including patent filings) necessary to perform its obligations hereunder.

10.1.5 If any human primary cell lines, human tissue, human clinical isolates or similar human-derived materials ("Human Materials") have been or are to be collected and/or used in the Ophthalmic Collaboration, each Party represents and warrants (i) that it has complied, or shall comply, with all applicable laws, guidelines and regulations relating to the collection and/or use of the Human Materials, and (ii) that it has obtained, or shall obtain, all necessary approvals and appropriate informed consents, in writing, for the collection and/or use of such Human Materials. Each Party shall provide documentation of such approvals and consents upon the other Party's request. Each Party further represents and warrants that such Human Materials may be used as contemplated in this Agreement without any obligation to the individuals or entities ("Providers") who contributed the Human Materials, including without limitation any obligation of compensation to such Providers or any other Third Party for the intellectual property associated with the Human Materials or commercial use thereof for any purposes.

10.1.6 Neither Party nor any of its Affiliates has been debarred or is subject to debarment and neither Party nor any of its Affiliates will use in any capacity, in connection with the Development, Manufacture or Commercialization of an Ophthalmic Product, any person

or entity that has been debarred pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act, or that is the subject of a conviction described in such section. Each Party agrees to inform the other Party in writing immediately if it or any person or entity that is performing activities under the Ophthalmic Collaboration is debarred or is the subject of a conviction described in Section 306, or if any action, suit,

claim, investigation or legal or administrative proceeding is pending or, to the best of such Party's knowledge, is threatened, relating to the debarment or conviction of such Party or any person or entity used in any capacity by such Party or any of its Affiliates in connection with the Development, Manufacture or Commercialization of an Ophthalmic Product.

10.2 ALNYLAM REPRESENTATIONS AND WARRANTIES. ALNYLAM represents and warrants to MERCK that as of the Effective Date of this Agreement:

10.2.1 To the best of ALNYLAM's knowledge, the ALNYLAM Patent Rights exist and are not invalid or unenforceable, in whole or in part;

10.2.2 It has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in the ALNYLAM Technology in a manner that conflicts with any rights granted to MERCK hereunder; and

10.2.3 Except as set forth in Section 10.2.3 of Schedule 10 to this Agreement, there are no claims, judgments or settlements against or owed by ALNYLAM or its Affiliates or pending or threatened claims or litigation relating to the ALNYLAM Technology.

10.3 MERCK REPRESENTATIONS AND WARRANTIES. MERCK represents and warrants to ALNYLAM that as of the Effective Date of this Agreement:

10.3.1 To the best of MERCK's knowledge, the MERCK Patent Rights exist and are not invalid or unenforceable, in whole or in part;

10.3.2 It has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in the MERCK Technology in a manner that conflicts with the rights granted to ALNYLAM hereunder; and

10.3.3 There are no claims, judgments or settlements against or owed by MERCK or its Affiliates or pending or threatened claims or litigation relating to the MERCK Technology that are expected to impact the Ophthalmic Collaboration or any Ophthalmic Product.

10.4 WARRANTY DISCLAIMER. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY WITH RESPECT TO ANY TECHNOLOGY, OPHTHALMIC PRODUCTS, GOODS, SERVICES, RIGHTS OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND HEREBY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT WITH RESPECT TO ANY AND ALL OF

THE FOREGOING. EACH PARTY HEREBY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE DEVELOPMENT, MANUFACTURE OR COMMERCIALIZATION OF ANY OPHTHALMIC PRODUCT PURSUANT TO THIS AGREEMENT WILL BE SUCCESSFUL OR THAT ANY PARTICULAR SALES LEVEL WITH RESPECT TO THE OPHTHALMIC PRODUCTS WILL BE ACHIEVED.

10.5 INDEMNIFICATION.

10.5.1 GENERAL INDEMNIFICATION BY MERCK. MERCK shall indemnify, hold harmless, and defend ALNYLAM, its Affiliates, and their respective directors, officers, employees and agents ("ALNYLAM Indemnitees") from and against any and all Third Party claims, suits, losses, liabilities, damages, costs, fees and expenses (including reasonable attorneys' fees) (collectively, "Losses") arising out

of or resulting from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by MERCK in this Agreement, or any breach or violation of any covenant or agreement of MERCK in or pursuant to this Agreement, or (b) the negligence or willful misconduct by or of MERCK, its Affiliates and their respective Sublicensees, and their respective directors, officers, employees and agents. This indemnification excludes Losses arising out of Third Party Infringement Claims resulting from MERCK's exercise in accordance with the terms of this Agreement of any intellectual property rights granted by ALNYLAM hereunder. Furthermore, MERCK shall have no obligation to indemnify the ALNYLAM Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by ALNYLAM in this Agreement, or any breach or violation of any covenant or agreement of ALNYLAM in or pursuant to this Agreement, or the negligence or willful misconduct by or of any of the ALNYLAM Indemnitees.

10.5.2 GENERAL INDEMNIFICATION BY ALNYLAM. ALNYLAM shall indemnify, hold harmless, and defend MERCK, its Affiliates and their respective directors, officers, employees and agents ("MERCK Indemnitees") from and against any and all Losses arising out of or resulting from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by ALNYLAM in this Agreement, or any breach or violation of any covenant or agreement of ALNYLAM in or pursuant to this Agreement, or (b) the negligence or willful misconduct by or of ALNYLAM, its Affiliates and their respective Sublicensees, and their respective directors, officers, employees and agents. This indemnification excludes Losses arising out of Third Party Infringement Claims resulting from ALNYLAM's exercise in accordance with the terms of this Agreement of any intellectual property rights granted by MERCK hereunder. Furthermore, ALNYLAM shall have no obligation to indemnify the MERCK Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by MERCK in this Agreement, or any breach or violation of any covenant or agreement of MERCK in or pursuant to this Agreement, or the negligence or willful misconduct by or of any of the MERCK Indemnitees.

10.5.3 PRODUCT LIABILITY.

(a) MERCK shall indemnify and hold harmless the ALNYLAM Indemnitees from, against and in respect of any and all Losses arising out of Third Party product liability claims incurred or suffered by the ALNYLAM Indemnitees, or any of them, directly or indirectly relating to an Ophthalmic Product and resulting from or arising out of the negligence, willful misconduct, or breach of this Agreement of or by MERCK or any of the other MERCK Indemnitees, except to the extent caused by the negligence, willful misconduct or breach of this Agreement of or by ALNYLAM or any of the other ALNYLAM Indemnitees.

(b) ALNYLAM shall indemnify and hold harmless the MERCK Indemnitees from, against and in respect of any and all Losses arising out of Third Party product liability claims incurred or suffered by the MERCK Indemnitees, or any of them, directly or indirectly relating to an Ophthalmic Product and resulting from or arising out of the negligence, willful misconduct, or breach of this Agreement of or by ALNYLAM or any of the other ALNYLAM Indemnitees, except to the extent caused by the negligence, willful misconduct or

breach of this Agreement of or by MERCK or any of the other MERCK Indemnitees.

(c) Any Losses arising out of Third Party product liability claims (other than such claims entitled to indemnification under Sections 10.5.3(a) or (b)) shall (i) be borne by the Continuing Party, to the extent such Losses were incurred with respect to the Development, Manufacture or Commercialization of a Royalty-Bearing Product, (ii) be included in U.S. Development Expenses and shared by the Parties pursuant to Section 2.11, to the extent such Losses were incurred with respect to the Development (and/or related Manufacture) of a Profit-Sharing Product in the United States, (iii) be included in Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss pursuant to Section 8.2, to the extent such Losses were incurred with respect to the Commercialization (and/or related Manufacture) of a Profit-Sharing Product in the United States, or (iv) be borne by MERCK, to the extent such Losses were incurred with respect to Development, Manufacture or Commercialization of a Profit-Sharing Product in the Territory outside the United States.

10.5.4 INDEMNIFICATION PROCEDURE. In the event of any such claim against any MERCK Indemnitee or ALNYLAM Indemnitee (individually, an "Indemnitee"), the indemnified Party shall promptly notify the other Party in writing of the claim and the indemnifying Party shall manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnitee shall cooperate with the indemnifying Party and may, at its option and expense, be represented in any such action or proceeding. The indemnifying Party shall not be liable for any settlements, litigation costs or expenses incurred by any Indemnitee without the indemnifying Party's written authorization. Notwithstanding the foregoing, if the indemnifying Party believes that any of the exceptions to its obligation of indemnification of the Indemnitees set forth in Sections 10.5.1, 10.5.2 or 10.5.3 may apply, the indemnifying Party shall promptly notify the Indemnitees, which shall then have the right to be represented in any such action or proceeding by separate counsel at their expense; provided, that the indemnifying Party shall be responsible for

payment of such expenses if the Indemnitees are ultimately determined to be entitled to indemnification from the indemnifying Party.

11. INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION AND RELATED MATTERS

11.1 INVENTORSHIP. Inventorship for patentable inventions conceived or reduced to practice during the course of the performance of activities pursuant to this Agreement shall be determined in accordance with United States patent laws for determining inventorship.

11.2 OWNERSHIP. ALNYLAM shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered solely by employees or consultants of ALNYLAM or acquired solely by ALNYLAM in the course of conducting the Ophthalmic Collaboration. MERCK shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered solely by employees or consultants of MERCK or acquired

solely by MERCK in the course of conducting the Ophthalmic Collaboration. The Parties shall jointly own any inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered jointly in the course of conducting the Ophthalmic Collaboration.

11.3 PROSECUTION AND MAINTENANCE OF PATENT RIGHTS.

11.3.1 MERCK TECHNOLOGY. MERCK has the sole responsibility to, at MERCK's discretion, file, conduct ex parte and inter partes prosecution, and maintain (including the defense of any interference or opposition proceedings) in the Territory, all Patent Rights comprising MERCK Technology (other than Joint Collaboration IP), in MERCK's name.

11.3.2 ALNYLAM TECHNOLOGY. ALNYLAM has the sole responsibility to, at ALNYLAM's discretion, file, conduct ex parte and inter partes prosecution, and maintain (including the defense of any interference or opposition proceedings) in the Territory, all Patent Rights comprising ALNYLAM Technology (other than Joint Collaboration IP), in ALNYLAM's name.

11.3.3 JOINT COLLABORATION IP. Subject to ALNYLAM's continuing right to the prior review of, comment on, revision to and approval of material documents, which shall not be unreasonably delayed or withheld, MERCK has the sole responsibility to, at MERCK's discretion, file, conduct ex parte and inter partes prosecution, and maintain (including the defense of any interference or opposition proceedings) in the Territory, all Patent Rights comprising Joint Collaboration IP (other than Broad RNAi Technology Collaboration IP), in the names of both ALNYLAM and MERCK. Notwithstanding the foregoing, if ALNYLAM is the Continuing Party with respect to a Royalty-Bearing Product, then ALNYLAM shall have the sole responsibility to, at ALNYLAM's discretion, file, conduct ex parte and inter partes prosecution, and maintain (including the defense of any interference or opposition proceedings) in the Territory, all Patent

Rights comprising Joint Collaboration IP Covering, claiming or relating to such Royalty-Bearing Product, in the names of both ALNYLAM and MERCK. Each Party shall use Commercially Reasonable Efforts to make available to the Prosecuting Party or its authorized attorneys, agents or representatives, such of its employees as the Prosecuting Party in its reasonable judgment deems necessary in order to assist it in obtaining patent protection for such Joint Collaboration IP. Each Party shall sign, or use Commercially Reasonable Efforts to have signed, all legal documents necessary to file and prosecute patent applications or to obtain or maintain patents in respect of such Joint Collaboration IP, at no cost to the Prosecuting Party.

11.3.4 BROAD RNAI TECHNOLOGY COLLABORATION IP. Notwithstanding Section 11.3.3, subject to MERCK's continuing right to the prior review of, comment on, revision to and approval of material documents relating to Joint Collaboration IP, which shall not be unreasonably delayed or withheld, ALNYLAM has the sole responsibility to, at ALNYLAM's discretion, file, conduct ex parte and inter partes prosecution, and maintain, including the defense of any interference or opposition proceedings, in the Territory, all Patent Rights comprising Broad RNAi Technology Collaboration IP in the names of both ALNYLAM and MERCK. MERCK shall use Commercially Reasonable Efforts to make available to ALNYLAM or its authorized attorneys, agents or representatives, such of its

employees as ALNYLAM in its reasonable judgment deems necessary in order to assist it in obtaining patent protection for such Broad RNAi Technology Collaboration IP. MERCK shall sign or use Commercially Reasonable Efforts to have signed all legal documents necessary to file and prosecute patent applications or to obtain or maintain patents in respect of such Broad RNAi Technology Collaboration IP, at no cost to ALNYLAM.

11.3.5 CONTINGENT RIGHTS. The Party having the right to prosecute and maintain patents under Sections 11.3.1, 11.3.2, 11.3.3 and 11.3.4 shall be referred to as the "Prosecuting Party". In the event the Prosecuting Party elects not to seek or continue to seek or maintain patent protection on any ALNYLAM Collaboration IP, MERCK Collaboration IP or Joint Collaboration IP which are subject to the other Party's licensed rights under Section 7 in the Territory, the other Party shall have the right (but not the obligation), at its expense, to prosecute and maintain in any country within the Territory patent protection on such ALNYLAM Collaboration IP, MERCK Collaboration IP or Joint Collaboration IP in the name of ALNYLAM, MERCK or both Parties as set forth in Sections 11.3.1, 11.3.2, 11.3.3 and 11.3.4. The previously Prosecuting Party shall use Commercially Reasonable Efforts to make available to the other Party or its authorized attorneys, agents or representatives, such of its employees as are reasonably necessary to assist the other Party in obtaining and maintaining the patent protection described under this Section 11.3.5. The previously Prosecuting Party shall sign or use Commercially Reasonable Efforts to have signed all legal documents necessary to file and prosecute such patent applications or to obtain or maintain such patents.

11.3.6 COOPERATION. Each Party hereby agrees: (a) to make its employees, agents and consultants reasonably available to the other Party (or to the other Party's authorized attorneys, agents or representatives), to the extent reasonably necessary to enable such Party to undertake patent prosecution; (b) to provide the other Party with copies of all

material correspondence pertaining to prosecution with the patent offices; (c) to cooperate, if necessary and appropriate, with the other Party in gaining patent term extensions wherever applicable to Patent Rights; and (d) to endeavor in good faith to coordinate its efforts with the other Party to minimize or avoid interference with the prosecution and maintenance of the other Party's patent applications.

11.3.7 PATENT EXPENSES. The patent filing, prosecution and maintenance expenses incurred after the Effective Date with respect to Patent Rights comprised of ALNYLAM Technology and MERCK Technology ("Patent Expenses") shall be borne by each Party having the right to file, prosecute and maintain such Patent Rights under this Section 11.3, except that Patent Expenses incurred (a) by the Opt-Out Party with respect to a Royalty-Bearing Product shall be reimbursed in full by the Continuing Party, (b) by a Party with respect to a Profit-Sharing Product in the United States prior to the First Commercial Sale of such product in the United States shall be included in U.S. Development Expenses for such product and shared by the Parties pursuant to Section 2.11, (c) by a Party with respect to a Profit-Sharing Product in the United States after the First Commercial Sale of such product in the United States shall be included in Commercialization Expenses for such product for purposes of calculating U.S. Operating Profit/Loss pursuant to Section 8.2, and (d) by ALNYLAM with

respect to a Profit-Sharing Product in the Territory outside the United States shall be reimbursed in full by MERCK.

11.4 THIRD PARTY INFRINGEMENT.

11.4.1 NOTICES. Each Party shall promptly report in writing to the other Party during the Agreement Term any (a) known or suspected infringement of any ALNYLAM Technology or MERCK Technology being used in the Ophthalmic Collaboration, including without limitation any Joint Collaboration IP or (b) unauthorized use or misappropriation of any Information by a Third Party of which it becomes aware, and shall provide the other Party with all available evidence supporting such infringement, or unauthorized use or misappropriation

11.4.2 RIGHTS TO ENFORCE.

11.4.2.1 MERCK'S FIRST RIGHT. Subject to the provisions of Section 11.4.2.2(b) and the provisions of any Third Party agreement under which MERCK's rights in MERCK Technology are granted or ALNYLAM's rights in ALNYLAM Technology are granted and of any In-License, in respect of each (a) Profit-Sharing Product in the Field in the Territory and (b) Royalty-Bearing Product in the Field in the Territory for which MERCK is the Continuing Party, MERCK shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-How, comprising (i) MERCK Technology or ALNYLAM Technology that is licensed to MERCK under Section 7.1 with respect to such Profit-Sharing Product or Royalty-Bearing Product, as the case may be or (ii) Joint Collaboration IP Covering, claiming or relating to such Profit-Sharing Product or Royalty-Bearing Product, as the case may be.

11.4.2.2 ALNYLAM'S FIRST RIGHT.

(a) Subject to the provisions of any Third Party agreement under which ALNYLAM's rights in ALNYLAM Technology or MERCK's rights in MERCK Technology are granted and of any In-License, in respect of each Royalty-Bearing Product in the Field in the Territory for which ALNYLAM is the Continuing Party, ALNYLAM shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-How, comprising ALNYLAM Technology or MERCK Technology that is licensed to ALNYLAM under Section 7.1 with respect to such Royalty-Bearing Product or Joint Collaboration IP Covering, claiming or relating to such Royalty-Bearing Product.

(b) ALNYLAM shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-How, comprising Broad RNAi Technology Collaboration IP.

11.4.3 STEP-IN RIGHTS. Subject to the provisions of any Third Party license agreement under which ALNYLAM's rights in ALNYLAM

Technology are granted or MERCK's rights in MERCK Technology are granted, and of any In-Licenses, if the Party with the first right to enforce (the "Initial Enforcement Rights Party") ALNYLAM Technology, MERCK Technology, Joint Collaboration IP or Broad RNAi Technology Collaboration IP under Section 11.4.2 fails to initiate a suit or take other appropriate action that it has the initial right to initiate or take pursuant thereto within ninety (90) days after becoming aware of the basis for such suit or action, then the other Party (the "Secondary Enforcement Rights Party") may, in its discretion, provide the Initial Enforcement Rights Party with written notice of such Secondary Enforcement Rights Party's intent to initiate a suit or take other appropriate action. If the Secondary Enforcement Rights Party provides such notice and the Initial Enforcement Rights Party fails to initiate a suit or take such other appropriate action within thirty (30) days after receipt of such notice from the Secondary Enforcement Rights Party, then the Secondary Enforcement Rights Party shall have the right to initiate a suit or take other appropriate action that it believes is reasonably required to protect its ownership interest in and to, or licensed interest under, as applicable, ALNYLAM Technology and MERCK Technology, including without limitation, Joint Collaboration IP and Broad RNAi Technology Collaboration IP.

11.4.4 PROCEDURES; EXPENSES AND RECOVERIES. The Party having the right to initiate any infringement suit under Section 11.4.2 above shall have the sole and exclusive right to select counsel for any such suit and shall pay all expenses of the suit, including attorneys' fees and court costs and reimbursement of the other Party's reasonable out-of-pocket expense in rendering assistance requested by the initiating Party, except that such expenses in respect of any Profit-Sharing Product in the United States (i) prior to

the First Commercial Sale of such Profit-Sharing Product in the United States shall be included in U.S. Development Expenses for such product and shared by the Parties pursuant to Section 2.11, and (ii) after the First Commercial Sale of such Profit Sharing Product in the United States shall be Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss pursuant to Section 8.2. If required under applicable law in order for the initiating Party to initiate and/or maintain such suit, or if either Party is unable to initiate or prosecute such suit solely in its own name or it is otherwise advisable to obtain an effective legal remedy, in each case, the other Party shall join as a party to the suit and will execute and cause its Affiliates to execute all documents necessary for the initiating Party to initiate litigation to prosecute and maintain such action. In addition, at the initiating Party's request, the other Party shall provide reasonable assistance to the initiating Party in connection with an infringement suit at no charge to the initiating Party except for reimbursement by the initiating Party of reasonable out-of-pocket expenses incurred in rendering such assistance. The non-initiating Party shall have the right to participate and be represented in any such suit by its own counsel at its own expense. If the Parties obtain from a Third Party, in connection with such suit, any damages, license fees, royalties or other compensation (including any amount received in settlement of such litigation), such amounts shall be allocated as follows:

(a) In all cases, to reimburse each Party for all expenses of the suit, including attorneys' fees and disbursements,

court costs and other litigation expenses; and

(b) If the infringement by the Third Party is related to a Profit-Sharing Product in the United States (i) prior to the First Commercial Sale of the Profit-Sharing Product in the United States, the balance shall be applied to reimburse the Parties for U.S. Development Expenses in accordance with their share of such expenses as set forth in Section 2.11 and (ii) after the First Commercial Sale of the Profit-Sharing Product in the United States, the balance shall be deemed Net Sales for the purpose of calculating U.S. Operating Profit/Loss for such Profit-Sharing Product pursuant to Section 8.2; or

(c) If the infringement by the Third Party is related to a Profit-Sharing Product in the Territory outside the United States, the remaining amount shall be treated as if it were Net Sales of MERCK, with ALNYLAM receiving a royalty on such remaining amount pursuant to the terms of Section 8.3.1, and the balance being retained by MERCK; or

(d) If the infringement by the Third Party is related to a Royalty-Bearing Product, the remaining amount shall be treated as if it were Net Sales of the Continuing Party, with the other Party receiving a royalty on such remaining amount pursuant to the terms of Section 8.3.2, and the balance being retained by the Continuing Party.

11.5 CLAIMED INFRINGEMENT.

11.5.1 NOTICE. In the event that a Third Party at any time provides written notice of a claim to, or brings an action, suit or proceeding against, any Party, or any of their respective Affiliates or Sublicensees, claiming infringement of its patent rights or unauthorized use or misappropriation of its know-how, based upon an assertion or claim arising out of the Development, Manufacture or Commercialization of Ophthalmic Products in the Field in the Territory ("Infringement Claim"), such Party shall promptly notify the other Party of the claim or the commencement of such action, suit or proceeding, enclosing a copy of the claim and all papers served. Each Party agrees to make available to the other Party its advice and counsel regarding the technical merits of any such claim at no cost to the other Party and to offer reasonable assistance to the other Party at no cost to the other Party.

11.5.2 PROFIT-SHARING PRODUCTS. Any Infringement Claim brought against either Party or its Affiliates or Sublicensees arising out of the Development, Manufacture or Commercialization of any Profit-Sharing Product in the Field in the Territory, shall be defended by MERCK if it so desires; provided, however, that ALNYLAM shall defend any such Infringement Claim relating to Broad RNAi Technology, if it so desires. All litigation costs and expenses incurred by the Defending Party (defined below) in connection with such Infringement Claim, and all damages, payments and other amounts awarded against, or payable by, either Party under any settlement with such Third Party (a) with respect to the United States (i) prior to the First Commercial Sale of the Profit-Sharing Product in the United States, shall be U.S. Development Expenses for such Profit-Sharing Product as set forth in Section 2.11 and (ii) after the First Commercial Sale of the Profit-Sharing Product in the United States, shall be Commercialization Expenses for purposes of calculating U.S.

Operating Profit/Loss in respect of such Profit-Sharing Product pursuant to Section 8.2, and (b) with respect to the Territory outside the United States, shall be borne by MERCK.

11.5.3 ROYALTY-BEARING PRODUCTS. In respect of any Royalty-Bearing Product, the applicable Continuing Party shall assume full responsibility for any Infringement Claims brought against either Party or its Affiliates or Sublicensees arising out of the Development, Manufacture or Commercialization of such Royalty-Bearing Product. All liabilities, damages, costs and expenses arising out of such Third Party Infringement Claims shall be borne by the Continuing Party.

11.5.4 PROCEDURE. The Party having the initial right to defend an Infringement Claim shall be referred to as the "Defending Party." The Defending Party shall have the sole and exclusive right to select counsel for any Infringement Claim; provided, that it shall consult with the other Party with respect to selection of counsel for such defense. The Defending Party shall keep the other Party informed, and shall from time to time consult with the other Party regarding the status of any such claims and shall provide the other Party with copies of all documents filed in, and all written communications relating to, any suit brought in connection with such claims. The other Party shall also have the right to participate and be represented in any such claim or related suit, at its own expense. The other Party shall have the sole and exclusive right to control the defense of an Infringement Claim in the event the Defending Party fails to exercise its right to assume such defense within thirty (30) days following written notice from the other

Party of such Infringement Claim. No Party shall settle any claims or suits involving rights of another Party without obtaining the prior written consent of such other Party, which consent shall not be unreasonably withheld.

11.5.5 LIMITATIONS. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN ARTICLE 10, THE FOREGOING STATES THE ENTIRE RESPONSIBILITY OF ALNYLAM AND MERCK, AND THE SOLE AND EXCLUSIVE REMEDY OF ALNYLAM OR MERCK, AS THE CASE MAY BE, IN THE CASE OF ANY CLAIMED INFRINGEMENT OF ANY THIRD PARTY PATENT RIGHTS OR UNAUTHORIZED USE OR MISAPPROPRIATION OF ANY THIRD PARTY'S KNOW-HOW.

11.6 OTHER INFRINGEMENT RESOLUTIONS. In the event of a dispute or potential dispute that has not ripened into a demand, claim or suit of the types described in Sections 11.4 and 11.5 of this Agreement (e.g., actions seeking declaratory judgments and revocation proceedings), the same principles governing control of the resolution of the dispute, consent to settlements of the dispute, and implementation of the settlement of the dispute (including the sharing in and allocating the payment or receipt of damages, license fees, royalties and other compensation) shall apply.

11.7 PRODUCT TRADEMARKS.

11.7.1 OWNERSHIP OF PRODUCT TRADEMARKS. MERCK shall own the Product Trademarks for Profit-Sharing Products in the Territory and shall be responsible for filing and maintaining the Product Trademarks in the Territory (including payment of costs associated therewith), subject to reimbursement of such costs in the United States as Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss for such Profit-Sharing Product

pursuant to Section 8.2. Each Party shall have the right to monitor the quality of such products in accordance with reasonable procedures to be agreed upon by the Parties. The Continuing Party shall own the Product Trademarks for Royalty-Bearing Products and shall be solely responsible for filing and maintaining the Product Trademarks in the Territory (including payment of costs associated therewith). Promptly after exercising its Opt-Out Right with respect to such Royalty-Bearing Product, MERCK shall assign to ALNYLAM all Product Trademarks for such Royalty-Bearing Product Controlled by MERCK in accordance with terms and conditions to be negotiated by the Parties in good faith.

11.7.2 THIRD PARTY INFRINGEMENT.

(a) PROFIT-SHARING PRODUCTS. In the event that either Party becomes aware of any infringement of a Product Trademark for a Profit-Sharing Product by a Third Party, it shall promptly notify the other and the Parties shall consult with each other and jointly determine the best way to prevent such infringement, including without limitation by the institution of legal proceedings against such Third Party. All out-of-pocket costs, including attorneys' fees, relating to such legal proceedings incurred (a) with respect to the United States (i) prior to the First Commercial Sale of the Profit-Sharing Product in the United States shall be

included in U.S. Development Expenses for such Profit-Sharing Product and shared by the Parties pursuant to Section 2.11 and (ii) after the First Commercial Sale of the Profit-Sharing Product in the United States shall be included in Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss for such Profit-Sharing Product pursuant to Section 8.2 and (b) in the Territory outside the United States shall be borne solely by MERCK.

(b) ROYALTY-BEARING PRODUCTS. The applicable Continuing Party shall assume full responsibility, at its sole cost and expense, for any infringement of a Product Trademark for a Royalty-Bearing Product by a Third Party.

11.7.3 CLAIMED INFRINGEMENT. If a Third Party challenges the Parties' right to commercialize a Profit-Sharing Product under the selected Product Trademark, the JSC shall consider the grounds for such challenge and recommend to MERCK a course of action in the affected market based on an assessment of the legal merits of such Third Party claim. The foregoing procedure shall also be followed in the event of an objection to the selected Product Trademark raised by a Regulatory Authority. In the case of a Royalty-Bearing Product, the Continuing Party will defend and indemnify the Opt-Out Party for and against any claims of infringement of the rights of a Third Party by the use of a Product Trademark in connection with such Royalty-Bearing Product.

11.8 PATENT TERM EXTENSIONS. The Parties shall use reasonable efforts to obtain all available supplementary protection certificates ("SPC") and other extensions of Patent Rights (including those available under the Hatch-Waxman Act). Each Party shall execute such authorizations and other documents and take such other actions as may be reasonably requested by the other Party to obtain such extensions. The Parties shall cooperate with each other in gaining patent term restorations, extensions and/or SPCs wherever applicable to Patent Rights. The Party first eligible to

seek patent term restoration or extension of any such Patent Rights or any SPC related thereto shall have the right to do so; provided, that if in any country the first Party has an option to extend the patent term for only one of several patents, the first Party shall consult with the other Party before making the election. If more than one patent is eligible for extension or patent term restoration, the JSC shall agree upon a strategy that shall maximize patent protection and commercial value for Ophthalmic Products. All filings for such extensions and certificates shall be made by the Party to whom responsibility for prosecution and maintenance of the Patent Rights are assigned, provided, that in the event that the Party to whom such responsibility is assigned elects not to file for an extension or SPC, such Party shall (i) inform the other Party of its intention not to file and (ii) grant the other Party the right to file for such extension or SPC in the patentee's name and such Party shall provide all necessary assistance in connection therewith.

11.9 PATENT CERTIFICATION. To the extent required by law or permitted by law, the Parties shall use Commercially Reasonable Efforts to maintain with the applicable Regulatory Authorities during the Agreement Term correct and complete listings of applicable Patent Rights for Ophthalmic Products being commercialized, including all so called "Orange Book" listings required under the Hatch-Waxman Act.

12. TERM AND TERMINATION

12.1 TERM AND EXPIRATION.

12.1.1 EXPIRATION OF OPHTHALMIC COLLABORATION. The Ophthalmic Collaboration shall commence on the Effective Date and expire on the date on which no Profit-Sharing Products are being Developed or Commercialized by the Parties. Expiration of the Ophthalmic Collaboration shall only affect the terms, responsibilities and activities undertaken in accordance with the Ophthalmic Collaboration and shall not affect the other terms of this Agreement.

12.1.2 TERMINATION OF AGREEMENT. This Agreement shall be effective as of the Effective Date and, unless terminated earlier pursuant to Section 12.2 below, this Agreement shall continue in effect until expiration of all royalty obligations hereunder ("Agreement Term"). Upon expiration of the Agreement Term, all licenses of the Parties under Article 7 then in effect shall become fully paid-up, perpetual, non-exclusive licenses.

12.2 TERMINATION FOR CAUSE.

12.2.1 CAUSE FOR TERMINATION. This Agreement may be terminated at any time during the Agreement Term:

(a) upon written notice by either Party (the "Non-Breaching Party") if the other Party (the "Breaching Party") is in breach of its material obligations hereunder by causes and reasons within its control and has not cured such breach within ninety (90) days after notice requesting cure of the breach; provided, however, in the event of a good faith dispute with respect to the existence of a material breach, the ninety (90) day cure period shall be tolled until such time as the Dispute is resolved pursuant to Section 13.6 hereof; or

(b) by either Party upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party; provided, however, that in the event of any involuntary bankruptcy or receivership proceeding such right to terminate shall only become effective if the Party consents to the involuntary bankruptcy or receivership or such proceeding is not dismissed within ninety (90) days after the filing thereof.

12.2.2 EFFECT OF TERMINATION FOR CAUSE.

(a) MATERIAL BREACH RELATING TO THE DEVELOPMENT OR COMMERCIALIZATION OF A ROYALTY-BEARING PRODUCT. If the material breach has, or is reasonably likely to have, a material adverse effect on the Development, Manufacture or Commercialization of a Royalty-Bearing Product in a Region or Regions, then this Agreement shall not terminate in its entirety, nor with respect to such Royalty-Bearing Product in the Territory outside of such Region(s), provided that with respect to such Region(s):

(i) except to the extent such licenses are necessary for the Breaching Party to perform its obligations under clause (iii) below, the licenses granted to the Breaching Party under this Agreement with respect to the Development, Manufacture and Commercialization of such Royalty-Bearing Product in such Region(s) shall terminate;

(ii) the Breaching Party hereby grants to the Non-Breaching Party an exclusive (even as to the Breaching Party), non-royalty-bearing perpetual license under ALNYLAM Technology if the Breaching Party is ALNYLAM, or under MERCK Technology, if the Breaching Party is MERCK, to Develop, Manufacture and Commercialize such Royalty-Bearing Product in the Field in such Region(s); provided, however, that to the extent such license to a Party's Technology includes a sublicense under Necessary Third Party IP, including without limitation the Existing ALNYLAM In-Licenses, the non-Breaching Party shall be fully responsible for all royalties, milestones or other payments under such In-Licenses reasonably allocable to such Royalty-Bearing Product in such Region(s);

(iii) in the event that the Breaching Party is Manufacturing and supplying the Royalty-Bearing Product pursuant to Section 6.4, the Breaching Party shall have the obligation, if requested by the Non-Breaching Party, to continue to Manufacture and supply the Royalty-Bearing Product for such Region(s) in accordance with, and for the time period described in, Section 6.4; and

(iv) in the event that the Non-Breaching Party is Manufacturing and supplying the Royalty-Bearing Product pursuant to Section 6.4, the Breaching Party shall have the obligation to reimburse the Non-Breaching Party for any committed and non-refundable or non-creditable costs or expenses incurred by the Non-Breaching Party, as of the date of

notice of termination, with respect to the supply of such Royalty-Bearing Product for the Breaching Party for such Region(s), and shall purchase, at the Cost of Goods Sold, any Royalty-Bearing Product Manufactured and supplied by the Non-Breaching Party for such Region(s), as well as any work in progress, raw materials, intermediates or components relating to the Royalty-Bearing Product, in each case in accordance with, and for the time period described in Section 6.4.

(b) MATERIAL BREACH RELATING TO THE DEVELOPMENT OR COMMERCIALIZATION OF A PROFIT-SHARING PRODUCT. If the material breach has, or is reasonably likely to have, a material adverse effect on the Development, Manufacture or Commercialization of a Profit-Sharing Product in a Region or Regions, then this Agreement shall not terminate in its entirety, nor with respect to such Profit-Sharing Product in the Territory outside of such Region(s), provided that with respect to such Region(s):

(i) the licenses granted to the Breaching Party under this Agreement with respect to the Development, Manufacture and Commercialization of such Profit-Sharing Product in such Region(s) shall terminate;

(ii) the licenses granted to the Non-Breaching Party by the Breaching Party with respect to such Profit-Sharing Product in such Region(s) pursuant to Article 7 shall continue in full force and effect;

(iii) the Non-Breaching Party shall have the right to Develop, Manufacture and Commercialize such Profit-Sharing Product in the Field in such Region(s), either alone or in collaboration with Third Parties, without any financial obligation to the Breaching Party; provided, however, that to the extent the licenses in Section 12.2.2(b)(ii) include a sublicense under Necessary Third Party IP, including without limitation the Existing ALNYLAM In-Licenses, the non-Breaching Party shall be fully responsible for all royalties, milestones or other payments under such In-Licenses reasonably allocable to such Profit-Sharing Product in such Region(s); and

(iv) the exclusivity covenant in Section 2.13 shall not apply to the Non-Breaching Party with respect to the applicable Program in such Region(s).

(c) TERMINATION UPON BANKRUPTCY OF A PARTY. If this Agreement is terminated by either Party (the "Non-Bankrupt Party") pursuant to Section 12.2.1(b) due to the rejection of this Agreement by or on behalf of the other Party (the "Bankrupt Party") under Section 365 of the United States Bankruptcy Code (the "Code"), all licenses and rights to licenses granted under or pursuant to this Agreement by the Bankrupt Party to the Non-Bankrupt Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Code, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Code. The Parties agree that the Non-Bankrupt Party, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Code, and that upon

commencement of a bankruptcy proceeding by or against the Bankrupt Party under the Code, the Non-Bankrupt Party shall be entitled to a complete duplicate of, or complete access to (as the Non-Bankrupt Party deems appropriate), any such intellectual property and all embodiments of such intellectual property. Such intellectual property and all embodiments thereof shall be promptly delivered to the Non-Bankrupt Party (i) upon any such commencement of a bankruptcy proceeding upon written request therefor by the Non-Bankrupt Party, unless the Bankrupt Party elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under (i) above, upon the rejection of this Agreement by or on behalf of the Bankrupt Party upon written request therefor by the Non-Bankrupt Party. The foregoing provisions are without prejudice to any rights the Non-Bankrupt Party may have arising under the Code or other applicable law.

(d) For purposes of this Article 12, "Region" shall mean any of the following regions in the Territory: (i) the United States; (ii) the European Union, (iii) the

region comprised of the following countries: Australia, Bangladesh, Bhutan, Brunei, Darussalam, Burma, Cambodia, China (including Hong Kong), India, Indonesia, Japan, Laos, Macao, Malaysia, Mongolia, Nepal, New Zealand, Papua New Guinea, Pakistan, Philippines, Republic of Korea, Singapore, Sri Lanka, Taiwan, Thailand and Vietnam; and (iv) the region comprised of the countries of the world not included in clauses (i), (ii) or (iii) above.

12.3 OTHER CONSEQUENCES OF TERMINATION OR THE EXERCISE OF OPT-OUT RIGHTS.

12.3.1 OTHER CONSEQUENCES OF TERMINATION. For purposes of this Section 12.3.1, "Transferring Party" shall mean the Breaching Party or the Opt-Out Party, as the case may be, and "Receiving Party" shall mean the Non-Breaching Party or the Continuing Party, as the case may be. In addition to the consequences set forth in Sections 4.3, 4.4 and 12.2 and without limiting any other legal or equitable remedies that a Party may have, in the event of a termination pursuant to Section 12.2 with respect to the Region(s) to which such termination applies, or upon the exercise by a Party of its Opt-Out Rights pursuant to Sections 4.3 or 4.4:

(a) with respect to each Ophthalmic Product that is the subject of the material breach or the exercise of an Opt-Out Right, the Transferring Party shall:

(i) promptly provide, or cause to be provided, to the Receiving Party all Know-How it Controls that pertains to the applicable Ophthalmic Product not previously provided by it to the Receiving Party reasonably necessary for the practice of the license rights granted to such other Party under this Agreement;

(ii) promptly transfer, or cause to be transferred, to the Receiving Party, subject to the completion of the on-going Clinical Studies under subsection (c) below, as applicable, all [**];

(iii) promptly transfer, or cause to be transferred, to the Receiving Party any and all tangible manifestations

and embodiments of the other Party's Know-How and other materials provided by it pursuant to this Agreement in respect of such Ophthalmic Product (provided that in the event of termination pursuant to Section 12.2, such transfer shall only be to the extent necessary to enable the Receiving Party to exercise its rights with respect to the terminated Region(s));

(iv) promptly assign, or cause to be assigned, to the Receiving Party upon the Receiving Party's request, any Third Party agreements to which the Transferring Party is a party, to the extent such agreements relate to the Development, Manufacture or Commercialization of the applicable Ophthalmic Product (in the terminated Region(s), in the event of termination pursuant to Section 12.2);

(b) The Breaching Party will allow the Non-Breaching Party, [**] (with respect to the terminated Region(s), in the event of termination pursuant to Section 12.2), or if this is not reasonably practicable, the Breaching Party will [**]. At the option of the Non-Breaching Party, the Breaching Party will assign to the Non-

Breaching Party, [**] (with respect to the terminated Region(s), in the event of termination pursuant to Section 12.2), to the extent legally permissible; and

(c) The Transferring Party will cooperate in any reasonable manner requested by the Receiving Party to achieve a smooth transition of the development, manufacturing, marketing and sales of the Ophthalmic Product to it or its licensees as contemplated by Section 4.3, 4.4 or 12.2, as applicable, such as transfer of its Know-How relating to Manufacturing and assistance in connection with regulatory matters relating to the transfer of the Ophthalmic Product.

12.4 EFFECT OF EXPIRATION OR TERMINATION; SURVIVAL. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including without limitation the obligation to pay royalties for Ophthalmic Products sold prior to such expiration or termination. The provisions of Articles 9, 11, 13 and Sections 2.12.1 (as it relates to the orderly cessation of Development activities), 10.5, 12.2.2, 12.3.1 and 12.4 shall survive any expiration or termination of this Agreement. Except as set forth in this Article 12, upon termination or expiration of this Agreement all other rights and obligations cease.

13. MISCELLANEOUS

13.1 FORCE MAJEURE. Neither Party shall be held liable to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in performing any obligation under this Agreement to the extent that such failure or delay is caused by or results from causes beyond the reasonable control of the affected Party, potentially including without limitation embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other

labor disturbances, fire, floods, or other acts of God, or acts, omissions or delays in acting by any governmental authority or the other Party. The affected Party shall notify the other Party of such force majeure circumstances as soon as reasonably practical, and shall promptly undertake all reasonable efforts necessary to cure such force majeure circumstances.

13.2 ASSIGNMENT/CHANGE OF CONTROL.

13.2.1 ASSIGNMENT. Except as provided in this Section 13.2, this Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the consent of the other Party. Either Party may, without the other Party's consent, assign this Agreement and its rights and obligations hereunder in whole or in part to an Affiliate. In any event, the assigning Party shall remain responsible for the performance by its Affiliate of this Agreement or any obligations hereunder so assigned to such Affiliate, and such assignment shall terminate, and all rights so assigned shall revert to the assigning Party, if and when such

Affiliate ceases to be an Affiliate of the assigning Party. Furthermore, in connection with a Change of Control (as defined below) of a Party, such Party may assign this Agreement and its rights and obligations hereunder in whole to the surviving entity or acquiror upon ninety (90) days' prior written notification to the other Party. Any attempted assignment not in accordance with this Section 13.2.1 shall be void.

13.2.2 CHANGE OF CONTROL. In the event of a Change of Control of a Party, such Party (the "Acquired Party") shall provide prompt written notice to the other Party (the "Non-Acquired Party") of the effective date of such Change of Control ("Change of Control Notice").

13.2.2.1 For each Profit-Sharing Product [**], the Non-Acquired Party may elect, by written notice to the Acquired Party within [**] after receipt of the Change of Control Notice, [**], such Profit-Sharing Product shall be deemed [**] [**] with respect to such Royalty-Bearing Product; provided, however, that (a) [**]such Royalty-Bearing Product shall be [**], (b) [**], calculated as set forth in Sections 8.1.3.2 and 8.3.2.3, respectively, in each case [**], then for the [**].

13.2.2.2 For each Profit-Sharing Product [**] as of the effective date of the Change of Control:

(a) In the Territory outside of the United States, MERCK shall retain the right to Develop, Manufacture and Commercialize such Profit-Sharing Product and the obligation to pay royalties with respect thereto to ALNYLAM pursuant to Section 8.3.1.

(b) In the United States, the Non-Acquired Party may [**] after receipt of the Change of Control Notice, [**]. If the Non-Acquired Party [**], the provisions of Section 4.4.2 will apply to such Royalty-Bearing Product and [**] with respect to such Royalty-Bearing Product; provided, however, that (a) [**] such Royalty-Bearing Product shall be [**], and (b) the Acquired Party shall [**]; (ii) [**] with respect to such Royalty-Bearing Product; and (iii) royalties on Net Sales of such Royalty-Bearing Product calculated as

set forth in Section 8.3.2.1, with the following values:

(A) The Sublicense Revenue Fraction shall be [**] percent ([**]%);

(B) Royalty Rate One shall be [**] percent ([**]%);

(C) Royalty Rate Two shall be [**] percent ([**]%);

(D) Royalty Rate Three shall be [**] percent ([**]%); and

(E) Royalty Rate Four shall be [**] percent ([**]%).

13.2.2.3 For each Profit-Sharing Product with respect to which an NDA has been filed:

(a) In the Territory outside of the United States, MERCK shall retain the right to Develop, Manufacture and Commercialize such Profit-Sharing Product and the obligation to pay royalties with respect thereto to ALNYLAM pursuant to Section 8.3.1.

(b) In the United States, the Non-Acquired Party may elect, by written notice to the Acquired Party within thirty (30) days after receipt of the Change of Control Notice, to change the Commercialization arrangements for such Profit-Sharing Product such that [**]. If the Non-Acquired Party does not so elect within such period, the Commercialization arrangements between the Parties in existence in the United States for such Profit-Sharing Product on the effective date of the Change of Control shall continue.

(c) If the Non-Acquired Party elects to change the Commercialization arrangements between the Parties within the United States for such Profit-Sharing Product as set forth in clause (b) above, such change will be implemented during a transition period not to exceed [**] after the date of such election and the Parties will cooperate to ensure the orderly implementation of such transition. Furthermore, the Party receiving sole Commercialization rights (the "Sole Commercialization Party") shall pay to the other Party (the "Divesting Party") in respect of such Profit-Sharing Product, [**] shall be reported and paid on a quarterly basis. Each quarterly report of [**] provided to the Divesting Party shall include information about Net Sales of the Profit-Sharing Product comparable to the information specified for royalty reports in Section 8.3.8, and shall also include information in summary form concerning the Commercialization Expenses deducted from Net Sales of such Profit-Sharing Product to calculate [**] during the applicable Calendar Quarter. Quarterly reports shall be due no later than the twenty-fifth (25th) day following the close of each Calendar Quarter. If the Divesting Party believes in good faith that [**] the Parties shall discuss the Divesting Party's concerns and the Sole Commercialization Party shall consider the Divesting Party's concerns in good faith.

13.2.2.4 For purposes of this Section 13.2.2, a "CHANGE OF CONTROL" of a Party shall be deemed to occur if such Party is involved in a merger, reorganization or consolidation in which its shareholders immediately prior to such transaction would hold fifty percent (50%) or less of the securities or other ownership

or voting interests representing the equity of the surviving entity immediately after such merger, reorganization or consolidation, or if there is a sale of all or substantially all of such Party's assets or business relating to this Agreement, or if a "Significant Pharmaceutical Company" (as defined below) effectively acquires control of the management and policies of such Party. A "Significant Pharmaceutical Company" is a pharmaceutical company, biotechnology company, or group of such companies acting in concert, with annual sales of human pharmaceutical products greater than [**] U.S. dollars ($[**]).

13.3 SEVERABILITY. If any one or more of the provisions contained in this Agreement is held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein shall not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affects the substantive rights of the Parties. The Parties shall in such an instance use their best efforts to replace the invalid, illegal or unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practical, implement the purposes of this Agreement.

13.4 NOTICES. All notices which are required or permitted hereunder shall be in writing and sufficient if delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by nationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to ALNYLAM, to:
ALNYLAM PHARMACEUTICALS, INC.
300 Third Street
Cambridge, MA 02142
Attention: Chief Executive Officer
Facsimile No.: (617) 551-8101

and:
FABER DAEUFER & ROSENBERG, P.C.
One Broadway, 14th Floor
Cambridge, MA 02142
Attention: Sumy Daeufer
Facsimile No.: (617) 507-5858

If to MERCK, to:
MERCK & CO., INC.
One Merck Drive
P.O. Box 100, WS3A-65
Whitehouse Station, NJ 08889-0100
Attention: Office of Secretary
Facsimile No.: (908) 735-1246

and:
MERCK & CO., INC.
One Merck Drive
P.O. Box 100, WS2A-30
Whitehouse Station, NJ 08889-0100
Attention: Chief Licensing Officer
Facsimile: (908) 735-1214

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such notice shall be deemed to have been given: (a) when delivered if personally delivered or sent by facsimile on a business day (or if delivered or sent on a non-business day, then on the next business day); (b) on receipt if sent by nationally-recognized overnight courier; and/or (c) on receipt if

sent by mail.

13.5 APPLICABLE LAW. The Agreement shall be governed by and construed in accordance with the laws of the State of New York and the patent laws of the United States without reference to any rules of conflict of laws or renvoi.

13.6 DISPUTE RESOLUTION.

13.6.1 DISPUTES. The Parties shall negotiate in good faith and use reasonable efforts to settle any dispute, controversy or claim arising from, or related to, this Agreement or to the breach hereof (collectively, "Dispute"). In particular, the CEO of ALNYLAM and the Executive Vice President of Worldwide Basic Research for MERCK shall attempt to resolve all Disputes. In the event that the CEO and the Executive Vice President cannot reach an agreement regarding a Dispute, and a Party wishes to pursue the matter, each such Dispute that is not an "Excluded Claim" shall be finally resolved by binding arbitration in accordance with the Commercial Arbitration Rules and Supplementary Procedures for Large Complex Disputes of the American Arbitration Association ("AAA") and Section 13.6.2 below, and judgment on the arbitration award may be entered in any court having jurisdiction thereof. As used in this Section 13.6, the term "Excluded Claim" shall mean a dispute that concerns (a) the validity or infringement of a patent, trademark or copyright, or (b) any antitrust, anti-monopoly or competition law or regulation, whether or not statutory.

13.6.2 ARBITRATION. The arbitration shall be conducted by a panel of three (3) persons experienced in the pharmaceutical business who are independent of both Parties and neutral with respect to the Dispute presented for arbitration. Within thirty (30) days after initiation of arbitration, each Party shall select one person to act as arbitrator and the two Party-selected arbitrators shall select a third arbitrator within thirty (30) days of their appointment. If the arbitrators selected by the Parties are unable or fail to agree upon the third arbitrator, the third arbitrator shall be appointed by the AAA. The place of arbitration shall be New York, New York, and all proceedings and communications shall be in English.

Either Party may apply to the arbitrators for interim injunctive relief until the arbitration award is rendered or the controversy is otherwise resolved. Either Party also may, without waiving any remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending the arbitration award. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages. Each Party shall bear its own costs and expenses and attorneys' fees, and the Party that does not prevail in the arbitration proceeding shall pay the arbitrators' and any administrative fees of arbitration. Except to the extent necessary to confirm an award or as may be required by law, neither a Party nor an arbitrator may disclose the existence, content, or results of an arbitration without the prior written consent of both Parties. In no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the dispute, controversy or claim would be barred by the applicable New York statute of limitations.

(a) The Parties agree that, in the event of a Dispute over the nature or quality of performance under this Agreement, neither Party may terminate this Agreement until final resolution of the Dispute through arbitration or other judicial determination. The Parties further agree that any payments made pursuant to this Agreement pending resolution of the Dispute shall be refunded promptly if an arbitrator or court determines that such payments are not due.

(b) The Parties hereby agree that any disputed performance or suspended performances pending the resolution of the arbitration that the arbitrator determines to be required to be performed by a Party must be completed within a reasonable time period following the final decision of the arbitrator.

(c) The Parties hereby agree that any monetary payment to be made by a Party pursuant to a decision of the arbitrator shall be made in United States dollars, free of any tax or other deduction. The Parties further agree that the decision of the arbitrator shall be the sole, exclusive and binding remedy between them regarding determination of the matters presented to the arbitrator.

13.7 ENTIRE AGREEMENT; AMENDMENTS. The Agreement contains the entire understanding of the Parties with respect to the Ophthalmic Collaboration and licenses granted hereunder. All express or implied agreements and understandings, either oral or written, with regard to the Ophthalmic Collaboration and the licenses granted hereunder are superseded by the terms of this Agreement. This Agreement (including the Schedules hereto) may be amended, or any term hereof modified, only by a written instrument duly-executed by authorized representatives of both Parties hereto.

13.8 HEADINGS. The captions to the Articles and Sections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Articles and Sections hereof.

13.9 INDEPENDENT CONTRACTORS. It is expressly agreed that ALNYLAM and MERCK shall be independent contractors and that the relationship between ALNYLAM and MERCK shall not constitute a partnership, joint venture or agency. ALNYLAM shall not have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on MERCK, without the prior written consent of MERCK, and MERCK shall not have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on ALNYLAM without the prior written consent of ALNYLAM.

13.10 WAIVER. The waiver by either Party hereto of any right hereunder, or of the failure of the other Party to perform, or of a breach by the other Party, shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party, whether of a similar nature or otherwise.

13.11 CUMULATIVE REMEDIES. No remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

13.12 WAIVER OF RULE OF CONSTRUCTION. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement shall be construed against the

drafting Party shall not apply.

13.13 COUNTERPARTS. The Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

13.14 LIMITATION OF LIABILITY. NEITHER PARTY HERETO WILL BE LIABLE FOR SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT AS A RESULT OF A PARTY'S WILLFUL MISCONDUCT OR A MATERIAL BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN ARTICLE 9. NOTHING IN THIS SECTION 13.14 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY.

13.15 BINDING EFFECT. As of the Effective Date, this Agreement shall be binding upon and inure to the benefit of the Parties and their respective permitted successors and permitted assigns.

13.16 NO THIRD PARTY BENEFICIARIES. Except as expressly contemplated herein, no Third Party, including any employee of any Party to this Agreement, shall have or acquire any rights by reason of this Agreement.

[THE REMAINDER OF THIS PAGE HAS BEEN LEFT INTENTIONALLY BLANK]

IN WITNESS WHEREOF, the Parties have executed this Agreement as of the date first set forth above.

MERCK & CO., INC.	ALNYLAM PHARMACEUTICALS, INC.
BY: /s/Raymond V. Gilmartin	BY: /s/ John Maraganore
NAME: Raymond V. Gilmartin	NAME: John Maraganore
TITLE: Chairman, President and CEO	TITLE: President & CEO
DATE: 6/27/04	DATE: 6/29/04

SCHEDULE 1.6
ALNYLAM PATENT RIGHTS

1.6.1 [**]
[**]
1.6.2 [**]
[**]

TABLE 1.6.1

PATENTS AND PATENT APPLICATIONS OWNED BY ALNYLAM

OR LICENSED BY ALNYLAM FROM THIRD PARTIES OTHER THAN ISIS PHARMACEUTICALS, INC.

<TABLE>
<CAPTION>

Case No.	Filing Date	Country	Serial No.	Status	Title
<S>	<C>	<C>	<C>	<C>	<C>
[**]	[**]	[**]	[**]	[**]	[**]

</TABLE>

SCHEDULE 1.30

EXISTING ALNYLAM IN-LICENSES

Existing ALNYLAM In-Licenses shall include the following Third Party agreements:

1. [**].

2. [**].

SCHEDULE 2.2

VEGF PROGRAM WORKPLAN

The work plan for the VEGF program [**]

[**]

[**]

[**]

[**]

[**]

[**]

VEGF Program Budget Overview (TO END of [**])

<TABLE>

<S>	<C>
Full-time Merck Employees:	[**] FTE
Full-Time Alnylam Employees:	[**] FTE
TOTAL VEGF Program FTE:	[**] FTE
Biology (Merck)	[**] FTE
[**]	
[**]	
Biology (Alnylam)	[**] FTE
[**]	
[**]	
[**]	
Chemistry (Alnylam)	[**] FTE

[**]
[**]
[**]
[**]

Program Management (Alnylam) [**] FTE
Program Management (Merck) [**] FTE
</TABLE>

<TABLE>
<S> <C>
External costs: $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]

Consultants
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**]
[**] $[**] [Terms to be driven by workplan]
[**] $[**]
</TABLE>

These figures are current estimates of costs through calendar year [**] based on a preliminary work plan. FTE may be added at a later date as needed [**]. Separate budget proposals will cover [**].

Other Ocular Programs

[**]
[**]

VEGF Research Timeline

[Graphic showing research timeline.]

SCHEDULE 2.3

OPHTHALMIC PRODUCTS

ALNYLAM: The ALNYLAM duplexes numbered [**], inclusive.

MERCK: None.

SCHEDULE 5.5

U.S. CO-PROMOTION
AGREEMENT TERMS

Commercialization:

- ALNYLAM shall co-promote the Profit-Sharing Product in the United States by [**]. The costs of ALNYLAM's co-promotion efforts (consistent with the Commercialization Plan) shall be included in Commercialization Expenses for purposes of calculating U.S. Operating Profit/Loss.

- ALNYLAM shall [**] to support such Profit-Sharing Product in the United States as set forth in the definitive Co-Promotion Agreement relating to such Profit-Sharing Product that is executed by the Parties pursuant to Section 5.5 of this Agreement. In the event that [**] at the time of launch of such Profit-Sharing Product in the United States, the Parties[**] following the launch of such Profit-Sharing Product in the United States. MERCK will [**], ALNYLAM shall [**].

- ALNYLAM's U.S. Co-Promotion activity shall be fully integrated into MERCK's U.S. promotion effort for such Profit-Sharing Product.

- The Co-Promotion Agreement will also contain, without limitation, provisions with respect to the following matters: [**].

SCHEDULE 10

EXCEPTIONS TO REPRESENTATIONS AND WARRANTIES

Section 10.2.3:

[**]
[**]

Exhibit 31.1

CERTIFICATIONS

I, John M. Maraganore, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Alnylam Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly 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 quarterly report;

3. Based on my knowledge, the financial statements, and other financial information included in this quarterly 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 quarterly 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)) for the registrant and we 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 quarterly report is being prepared;

b. [Paragraph omitted in accordance with SEC transition instructions contained in SEC Release 34-47986].

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

d. Disclosed in this quarterly report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter 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 registrant's board of directors (or persons performing the equivalent functions):

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

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

Date: August 12, 2004

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

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

Exhibit 31.2

CERTIFICATIONS

I, Barry E. Greene, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Alnylam Pharmaceuticals, Inc.;

2. Based on my knowledge, this quarterly 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 quarterly report;

3. Based on my knowledge, the financial statements, and other financial information included in this quarterly 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 quarterly 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)) for the registrant and we 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 quarterly report is being prepared;

b. [Paragraph omitted in accordance with SEC transition instructions contained in SEC Release 34-47986].

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

d. Disclosed in this quarterly report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter 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 registrant's board of directors (or persons performing the equivalent functions):

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

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

Date: August 12, 2004

/s/ Barry E. Greene

Barry E. Greene
Chief Operating Officer and Treasurer

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 of Alnylam Pharmaceuticals, Inc. (the "Company") on Form 10-Q for the period ending June 30, 2004 as filed with the Securities and Exchange Commission (the "Report"), I, John M. Maraganore, President and Chief Executive Officer of the Company, certify, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that:

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 result of operations of the Company.

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

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

August 12, 2004

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 of Alnylam Pharmaceuticals, Inc. (the "Company") on Form 10-Q for the period ending June 30, 2004 as filed with the Securities and Exchange Commission (the "Report"), I, Barry E. Greene, Chief Operating Officer and Treasurer of the Company, certify, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that:

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 result of operations of the Company.

/s/ Barry E. Greene

Barry E. Greene
Chief Operating Officer and Treasurer

August 12, 2004