

ALNYLAM PHARMACEUTICALS, INC.

Form S-3/A

December 16, 2005

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As filed with the Securities and Exchange Commission on December 16, 2005

Registration No. 333-129905

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

**AMENDMENT NO. 1
TO
FORM S-3
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933**

Alnylam Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in Its Charter)

**Delaware
(State or Other Jurisdiction of Incorporation or
Organization)**

**77-0602661
(I.R.S. Employer Identification Number)**

**300 Third Street
Cambridge, Massachusetts 02142
(617) 551-8200
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's
Principal Executive Offices)**

**John M. Maraganore, Ph.D.
President and Chief Executive Officer
Alnylam Pharmaceuticals, Inc.
300 Third Street
Cambridge, Massachusetts 02142
(617) 551-8200
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for
Service)**

***Copy to:*
Steven D. Singer, Esq.
Peter N. Handrinos, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
Telephone: (617) 526-6000
Telecopy: (617) 526-5000**

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. _____

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. _____

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, dated December 16, 2005

PRELIMINARY PROSPECTUS

\$75,000,000

ALNYLAM PHARMACEUTICALS, INC.

Common Stock

We may from time to time sell common stock in one or more offerings for an aggregate initial offering price of \$75,000,000. This prospectus describes the general manner in which our common stock may be offered using this prospectus. We will specify in the accompanying prospectus supplement the terms of the securities to be offered and sold. We may sell these securities to or through underwriters or dealers and also to other purchasers or through agents. We will set forth the names of any underwriters, dealers or agents in the accompanying prospectus supplement.

Our common stock is quoted on the Nasdaq National Market under the trading symbol **ALNY**. The reported last sale price of our common stock on the Nasdaq National Market on December 15, 2005 was \$12.90 per share.

Investing in our common stock involves risks. See Risk Factors on page 1 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

This prospectus may not be used to consummate sales of securities unless it is accompanied by a prospectus supplement.

Prospectus dated , 2005.

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You should rely only on the information contained in this prospectus and the documents incorporated by reference in this prospectus or to which we have referred you. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should not assume that the information contained in this prospectus or any document incorporated by reference is accurate as of any date other than the date on the front cover of the applicable document. Neither the delivery of this prospectus nor any distribution of securities pursuant to this prospectus shall, under any circumstances, create any implication that there has been no change in the information set forth or incorporated by reference into this prospectus or in our affairs since the date of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission using a shelf registration process. Under this shelf registration process, we may, from time to time, sell common stock in one or more offerings up to a total dollar amount of \$75,000,000. This prospectus describes the general manner in which our common stock may be offered by this prospectus. Each time we sell common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. If there is any inconsistency between the information in this prospectus and the accompanying prospectus supplement, you should rely on the information in the prospectus supplement. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. This prospectus, together with applicable prospectus supplements, includes all material information relating to this offering.

ALNYLAM PHARMACEUTICALS, INC.

Alnylam Pharmaceuticals, Inc. is 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. RNAi is a natural mechanism for selectively silencing genes. Genes provide cells with coded instructions for making proteins, and silencing a gene refers to stopping or reducing production of the protein specified, or encoded, by that gene. Using our intellectual property and the expertise we have built in RNAi, we are developing a set of biological and chemical methods and know-how that we expect to apply in a systematic way to develop RNAi therapeutics for a variety of diseases. We have initiated programs to develop RNAi therapeutics that will be administered directly to diseased parts of the body, which we refer to as Direct RNAi therapeutics. We currently have two development programs and a number of preclinical programs for Direct RNAi therapeutics. The development programs are focused on respiratory infections caused by human respiratory syncytial virus, or RSV, and influenza. In pre-clinical programs, we are also working on the inherited respiratory disease known as cystic fibrosis. We have additional pre-clinical programs in Direct RNAi focused on a central nervous system disorder known as Parkinson's disease and in spinal cord injury and neuropathic pain. We are also working to extend our capabilities to enable the development of RNAi therapeutics that travel through the bloodstream to reach diseased parts of the body, which we refer to as Systemic RNAi.

We were incorporated in Delaware in May 2003 as Alnylam Holding Co. In February 2004, we changed our name to Alnylam Pharmaceuticals, Inc. Alnylam Europe AG, which was incorporated in Germany in June 2000 under the name Ribopharma AG, and Alnylam U.S., Inc., which was incorporated in Delaware in June 2002, are wholly-owned subsidiaries of Alnylam Pharmaceuticals, Inc. We acquired Alnylam Europe AG in July 2003. Our principal executive offices are located at 300 Third Street, Cambridge, Massachusetts 02142 and our telephone number at that address is (617) 551-8200. Our website is www.alnylam.com. The information on our website is not incorporated by reference into this prospectus or any prospectus supplement and should not be considered to be a part of this prospectus or any prospectus supplement. We have included our website address as an inactive textual reference only.

Unless otherwise stated, all references to us, our, Alnylam, we, the Company and similar designations refer to Alnylam Pharmaceuticals, Inc. and our subsidiaries. Our logo, trademarks and service marks are the property of Alnylam. Other trademarks or service marks appearing in this prospectus, any prospectus supplement or any document incorporated by reference in this prospectus are the property of their respective holders.

RISK FACTORS

An investment in our common stock involves significant risks. You should carefully consider the risk factors contained in any prospectus supplement and in our filings with the Securities and Exchange Commission, as well as all of information contained in this prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus, before you decide to invest in our common stock. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, any prospectus supplement and the documents we incorporate by reference in this prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or

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the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. All statements, other than statements of historical facts, that we include in this prospectus, any prospectus supplement and in the documents we incorporate by reference in this prospectus, may be deemed forward-looking statements for purposes of the Securities Act and the Exchange Act. We use the words anticipate, believe, estimate, expect, intend, may, project, will, would and similar expressions to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and, accordingly, you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from the forward-looking statements that we make, including the factors included in the documents we incorporate by reference in this prospectus. You should read these factors and the other cautionary statements made in the documents we incorporate by reference as being applicable to all related forward-looking statements wherever they appear in this prospectus, any prospectus supplement and any document incorporated by reference. We caution you that we do not undertake any obligation to update forward-looking statements we make.

USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of our common stock under this prospectus for general corporate purposes, including research and development expenses, clinical trial costs, general and administrative expenses and potential acquisitions of companies, products and technologies that complement our business. We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of our common stock. Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

PLAN OF DISTRIBUTION

We may sell our common stock through underwriters or dealers, through agents, or directly to one or more purchasers. The accompanying prospectus supplement will describe the terms of the offering of our common stock, including:

the number of shares of common stock we are offering;

the name or names of any underwriters;

any securities exchange or market on which the common stock may be listed;

the purchase price of our common stock being offered and the proceeds we will receive from the sale;

any over-allotment options pursuant to which underwriters may purchase additional shares of common stock from us;

any underwriting discounts or agency fees and other items constituting underwriters or agents compensation; and

any discounts or concessions allowed or reallocated or paid to dealers.

If underwriters are used in the sale, they will acquire the common stock for their own account and may resell the common stock from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of the sale. The obligations of the underwriters to purchase the common stock will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the common stock to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the shares of common stock offered by the prospectus supplement. We may change from time to time the public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

We may sell our common stock directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of our common stock, and we will describe any commissions we will pay

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the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may provide underwriters and agents with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the underwriters or agents may make with respect to these liabilities. Underwriters and agents may engage in transactions with, or perform services for, us in the ordinary course of business. We will describe such relationships in the prospectus supplement naming the underwriter and the nature of any such relationship.

Rules of the Securities and Exchange Commission may limit the ability of any underwriters to bid for or purchase shares of common stock before the distribution of the shares of common stock is completed. However, underwriters may engage in the following activities in accordance with the rules:

Stabilizing transactions Underwriters may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

Over-allotments and syndicate covering transactions Underwriters may sell more shares of our common stock than the number of shares that they have committed to purchase in any underwritten offering. This over-allotment creates a short position for the underwriters. This short position may involve either covered short sales or naked short sales. Covered short sales are short sales made in an amount not greater than the underwriters over-allotment option to purchase additional shares in any underwritten offering. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing shares in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market, as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the shares that could adversely affect investors who purchase shares in the offering.

Penalty bids If underwriters purchase shares in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from other underwriters and selling group members who sold those shares as part of the offering.

Similar to other purchase transactions, an underwriter's purchases to cover the syndicate short sales or to stabilize the market price of our common stock may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our common stock. As a result, the price of the shares of our common stock may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of shares if it discourages resales of the shares.

If commenced, the underwriters may discontinue any of these activities at any time.

Our common stock is quoted on the Nasdaq National Market. One or more underwriters may make a market in our common stock, but the underwriters will not be obligated to do so and may discontinue market making at any time without notice. We cannot give any assurance as to liquidity of the trading market for our common stock.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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In compliance with guidelines of the National Association of Securities Dealers, or NASD, the maximum consideration or discount to be received by any NASD member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

The validity of the common stock offered will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2004 have been so incorporated in reliance on the reports of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other documents with the Securities and Exchange Commission. You may read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room.

The SEC also maintains an Internet site, the address of which is www.sec.gov. That site also contains our annual, quarterly and current reports, proxy statements, information statements and other information.

We have filed this prospectus with the SEC as part of a registration statement on Form S-3 under the Securities Act. This prospectus does not contain all of the information set forth in the registration statement because some parts of the registration statement are omitted in accordance with the rules and regulations of the SEC. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

We also maintain an Internet site at www.alnylam.com, through which you can access our SEC filings. The information set forth on our Internet site is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

We are incorporating by reference certain documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information in the documents incorporated by reference is considered to be part of this prospectus. Statements contained in documents that we file with the SEC and that are incorporated by reference in this prospectus will automatically update and supersede information contained in this prospectus, including information in previously filed documents or reports that have been incorporated by reference in this prospectus, to the extent the new information differs from or is inconsistent with the old information.

We have filed or may file the following documents with the SEC. These documents are incorporated herein by reference as of their respective dates of filing:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2004, as filed with the SEC on March 30, 2005;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2005, as filed with the SEC on May 16, 2005;

Our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2005, as filed with the SEC on August 11, 2005;

Our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2005, as filed with the SEC on November 14, 2005;

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Our Current Report on Form 8-K, as filed with the SEC on January 3, 2005;

Our Current Report on Form 8-K, as filed with the SEC on February 10, 2005;

Our Current Report on Form 8-K, as filed with the SEC on May 17, 2005;

Our Current Report on Form 8-K, as filed with the SEC on June 10, 2005;

Our Current Report on Form 8-K, as filed with the SEC on June 16, 2005;

Our Current Report on Form 8-K, as filed with the SEC on June 24, 2005;

Our Current Report on Form 8-K, as filed with the SEC on July 13, 2005;

Our Current Report on Form 8-K, as filed with the SEC on July 14, 2005;

Our Current Report on Form 8-K, as filed with the SEC on September 12, 2005;

Our Current Report on Form 8-K, as filed with the SEC on September 26, 2005;

Our Current Report on Form 8-K, as filed with the SEC on October 12, 2005;

Our Current Report on Form 8-K, as filed with the SEC on December 13, 2005;

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (1) after the date of the filing of this registration statement and prior to its effectiveness and (2) until all of the common stock to which this prospectus relates has been sold or the offering is otherwise terminated, except in each case for information contained in any such filing where we indicate that such information is being furnished and is not to be considered filed under the Exchange Act, will be deemed to be incorporated by reference in this prospectus and the accompanying prospectus supplement and to be a part hereof from the date of filing of such documents; and

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on May 5, 2004, as amended by Amendment No. 1 to Form 8-A on Form 8-A/A filed with the SEC on June 3, 2004 and Amendment No. 2 to Form 8-A on Form 8-A/A filed with the SEC on July 14, 2005.

You may request, orally or in writing, a copy of any of these documents, which will be provided to you at no cost, by contacting Cynthia Clayton, Director, Investor Relations and Corporate Communications, Alnylam Pharmaceuticals, Inc., 300 Third Street, Cambridge, MA 02142, telephone (617) 551-8200.

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PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following table sets forth the various expenses to be incurred in connection with the registration of the common stock being registered hereby, all of which will be borne by Alnylam. All amounts shown are estimates, except for the SEC registration fee.

	Amount
SEC registration fee	\$ 8,828
Printing and engraving expenses	2,000
Legal fees and expenses	30,000
Accounting fees and expenses	10,000
Transfer agent's fees and expenses	
Miscellaneous	4,172
Total expenses	\$ 55,000

Item 15. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law allows a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit.

Section 145 of the General Corporation Law of Delaware provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against amounts paid and expenses incurred in connection with an action or proceeding to which he is or is threatened to be made a party by reason of such position, if such person shall have acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal proceeding, if such person had no reasonable cause to believe his conduct was unlawful; provided that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that such indemnification is proper under the circumstances.

Our restated certificate of incorporation includes a provision that eliminates the personal liability of its directors for monetary damages for breach of fiduciary duty as a director, except for liability:

for any breach of the director's duty of loyalty to Alnylam or its stockholders;

for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

under section 174 of the Delaware General Corporation Law regarding unlawful dividends and stock purchases;
or

for any transaction from which the director derived an improper personal benefit.

Our restated certificate of incorporation also provides that:

we must indemnify our directors and officers to the fullest extent permitted by Delaware law;

we may indemnify our other employees and agents to the same extent that we indemnified our officers and directors, unless otherwise determined by our Board of Directors; and

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we must advance expenses, as incurred, to our directors and executive officers in connection with a legal proceeding to the fullest extent permitted by Delaware law.

The indemnification provisions contained in our restated certificate of incorporation are not exclusive of any other rights to which a person may be entitled by law, agreement, vote of stockholders or disinterested directors or otherwise.

In addition, we maintain insurance on behalf of our directors and executive officers insuring them against any liability asserted against them in their capacities as directors or officers or arising out of such status.

Item 16. Exhibits.

Exhibit Number	Description
1.1	Form of Underwriting Agreement (To be filed as an Exhibit to a Current Report on Form 8-K and incorporated herein by reference).
4.1	Restated Certificate of Incorporation of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Quarterly Report on Form 10-Q (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference).
4.2	Amended and Restated By-Laws of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-113162), and incorporated herein by reference).
4.3	Form of Common Stock Certificate (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-113162), and incorporated herein by reference).
4.4	Rights Agreement dated as of July 13, 2005 between the Registrant and EquiServe Trust Company, N.A., as Rights Agent, which includes as Exhibit A the Form of Certificate of Designations of Series A Junior Participating Preferred Stock, as Exhibit B the Form of Rights Certificate and as Exhibit C the Summary of Rights to Purchase Preferred Stock (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Current Report on Form 8-K filed on July 14, 2005 (File No. 000-50743) and incorporated herein by reference).
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel to the Registrant.
23.1	Consent of PricewaterhouseCoopers LLP.
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in the opinion filed as Exhibit 5.1).
24.1*	Powers of Attorney (included on signature pages).

* Previously filed

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental

change in the information set forth in the registration statement. Notwithstanding the foregoing, any

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increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; *provided, however*, that paragraphs (i), (ii) and (iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities:

The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the

Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Cambridge, Commonwealth of Massachusetts, as of December 16, 2005.

ALNYLAM PHARMACEUTICALS, INC.

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

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 1 to Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ John M. Maraganore John M. Maraganore, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	December 16, 2005
/s/ Barry E. Greene Barry E. Greene	Chief Operating Officer and Treasurer (Principal Financial and Accounting Officer)	December 16, 2005
*	Director	December 16, 2005
Peter Barrett, Ph.D.		
*	Director	December 16, 2005
John K. Clarke		

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Signature	Title	Date
Vicki L. Sato, Ph.D.	Director	
*	Director	December 16, 2005
Paul R. Schimmel, Ph.D.		
*	Director	December 16, 2005
Phillip A. Sharp, Ph.D.		
*	Director	December 16, 2005
Kevin P. Starr		
*	Director	December 16, 2005

James L. Vincent

* By: /s/ John M. Maraganore

Name: John M. Maraganore, Ph.D.

Title: Attorney-in-fact

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EXHIBIT INDEX

Exhibit Number	Description
1.1	Form of Underwriting Agreement (To be filed as an Exhibit to a Current Report on Form 8-K and incorporated herein by reference).
4.1	Restated Certificate of Incorporation of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Quarterly Report on Form 10-Q (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference).
4.2	Amended and Restated By-Laws of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-113162), and incorporated herein by reference).
4.3	Form of Common Stock Certificate (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-113162), and incorporated herein by reference).
4.4	Rights Agreement dated as of July 13, 2005 between the Registrant and EquiServe Trust Company, N.A., as Rights Agent, which includes as Exhibit A the Form of Certificate of Designations of Series A Junior Participating Preferred Stock, as Exhibit B the Form of Rights Certificate and as Exhibit C the Summary of Rights to Purchase Preferred Stock (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Current Report on Form 8-K filed on July 14, 2005 (File No. 000-50743) and incorporated herein by reference).
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel to the Registrant.
23.1	Consent of PricewaterhouseCoopers LLP.
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in the opinion filed as Exhibit 5.1).
24.1*	Powers of Attorney (included on signature pages).

* Previously filed