ALNYLAM PHARMACEUTICALS, INC.
Form S-3ASR
January 18, 2007

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**As filed with the Securities and Exchange Commission on January 18, 2007**
**Registration No. 333-_____**

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

# FORM S-3
# REGISTRATION STATEMENT
***UNDER THE SECURITIES ACT OF 1933***

**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 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:***
**Peter N. Handrinos, Esq.**
**Lia Der Marderosian, Esq.**
**WilmerHale**
**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. o

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. þ

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. o _____

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. o _____

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. þ

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. o

**CALCULATION OF REGISTRATION FEE**

| Title of Each Class of Securities to be Registered | Amounts to be Registered | Proposed Maximum Aggregate Offering Price Per Share (1) | Proposed Maximum Aggregate Offering Price (1) | Amount of Registration Fee (1) |
|---|---|---|---|---|
| Common Stock, par value $0.01 per share (including the associated preferred stock purchase rights) | 361,990 | $21.81 | $7,895,002 | $845 |

(1) Estimated solely for purposes of determining the registration fee pursuant to Rule 457(c) under the Securities Act based on the average of the high and low sales price for the Common Stock on January 16, 2007.

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PROSPECTUS

**ALNYLAM PHARMACEUTICALS, INC.**

361,990 Shares of Common Stock

This prospectus relates to the resale of shares of common stock previously issued by Alnylam Pharmaceuticals, Inc. to Inex Pharmaceuticals Corporation in connection with a license and collaboration agreement entered in by the parties on January 8, 2007.

We will not receive any proceeds from the sale of the shares.

The selling stockholder identified in this prospectus, or its pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or privately negotiated prices.

Our common stock is listed on the NASDAQ Global Market under the trading symbol ALNY. The reported last sale price of our common stock on the NASDAQ Global Market on January 17, 2007 was $22.04 per share. You are urged to obtain current market quotations for the common stock.

**Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 3 of this prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

**The date of this prospectus is January 18, 2007**

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In this prospectus, unless otherwise stated or required by the context, all references to Alnylam, we, us, and ou 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 or any document incorporated by reference in this prospectus are the property of their respective owners.

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholder is offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

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## PROSPECTUS SUMMARY

*This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors, before making an investment decision.*

### ALNYLAM PHARMACEUTICALS, INC.

Alnylam Pharmaceuticals, Inc. is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. RNAi is a naturally occurring mechanism within cells for selectively silencing and regulating specific genes. Since many diseases are caused by the inappropriate activity of specific genes, the ability to silence genes selectively through RNAi could provide a new way to treat a wide range of human diseases. We believe that drugs that work through RNAi have the potential to become a new major class of drugs, like small molecule, protein and antibody drugs. 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 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.

**Recent Developments**

On November 27, 2006, we announced that the United States Patent and Trademark Office had issued a patent covering certain chemical modifications of oligonucleotides used to introduce drug-like properties in antisense oligonucleotides, including small interfering RNAs, or siRNAs, the molecules that mediate RNAi. Isis Pharmaceuticals owns this patent and has exclusively licensed it to us for double-stranded RNAi therapeutic applications.

On November 28, 2006, we announced that we had initiated a human experimental infection study with a respiratory syncytial virus, or RSV, designed to establish a safe and reliable RSV infection of the upper respiratory tract in adult volunteers. We expect to begin the treatment phase of this study in the first half of 2007 and to present data from this study in the second half of 2007. Following determination of the optimal level of RSV inoculum, we plan to initiate a subsequent clinical protocol in the second half of 2007 to evaluate the anti-viral activity of ALN-RSV01, an RNAi therapeutic we are developing for the treatment of RSV infection.

On December 5, 2006, we announced that we plan to advance a systemically-delivered RNAi therapeutic for the treatment of hypercholesterolemia as our second clinical development program. This program is focused on evaluating new approaches for reducing LDL cholesterol levels using RNAi therapeutics directed to the disease target called proprotein convertase subtilisn/kexin type 9, or PCSK9. We expect to submit an investigational new drug, or IND, application for this program in 2007.

On January 8, 2007, we announced that we expect to publish or present human proof-of-concept data for an RNAi therapeutic within the next 12 to 18 months.

On January 9, 2007, we announced that Inex Pharmaceuticals Corporation, or Inex, had granted us an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics and that we granted Inex an option for three InterfeRx licenses, subject to our review and third-party obligations, to develop its own RNAi therapeutic products and exclusive access to our intellectual property to develop oligonucleotide drugs that do not function through an RNAi mechanism.

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Under the terms of the agreement Inex, we issued Inex 361,990 shares of our common stock in a private placement on January 16, 2007. In addition, on or about February 23, 2007, we will be required to make an additional cash payment to Inex equal to the amount by which the sum of the value of the shares held by Inex on or about February 16, 2007, plus the net proceeds to Inex from the sale of shares prior to such date, is less than $8,000,000. Under the agreement, we will make available to Inex a $5,000,000 loan for capital equipment expenditures related to manufacturing services performed by Inex for us and Inex will be eligible to receive $13,000,000 in potential milestone payments for each product developed by us utilizing technology licensed to us by Inex.

Pursuant to the terms of our investor rights agreement with Novartis, in connection with the sale of shares to Inex on January 16, 2007, Novartis has the right to purchase up to 70,431 shares of our common stock at a purchase price of $21.88 per share, which we refer to as the first market price, if Novartis exercises this purchase right within the 30-day period after January 12, 2007. If Novartis exercises its purchase right after this 30-day period, it may purchase the shares at a purchase price that is a 10% premium to the first market price or is a 10% premium to the market price at the time it purchases the shares, whichever is greater. We cannot provide any assurance as to the exact number of shares of our common stock that Novartis will purchase, if any, in connection with the private placement to Inex.

**THE OFFERING**

| | |
|---|---|
| Common Stock offered by selling stockholder ..... | 361,990 shares |
| Use of proceeds ..... | Alnylam will not receive any proceeds from the sale of shares in this offering. |
| NASDAQ Global Market symbol ..... | ALNY |

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## RISK FACTORS

*An investment in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below before purchasing our common stock. The risks and uncertainties described below are not the only ones facing the company. Additional risks and uncertainties may also impair our business operations. If any of the following risks actually occur, our business, financial condition, results of operations and prospects would likely suffer. In that case, the trading price of our common stock could fall, and you may lose all or part of your investment.*

### 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 small interfering RNAs, or siRNAs, the class of molecule we are trying to develop into drugs. The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Skepticism as to the feasibility of developing RNAi therapeutics has been expressed in scientific literature. For example, there are potential challenges to achieving safe RNAi therapeutics based on the so-called off-target effects and activation of the interferon response. There are also potential challenges to achieving effective RNAi therapeutics based on the need to achieve efficient delivery into cells and tissues in a clinically relevant manner and at doses that are cost-effective.

Very few drug candidates based on these discoveries have ever been tested in animals or humans. siRNAs may 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 may 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

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developing a marketable product. If we do not successfully develop and commercialize drugs based upon our technological approach, we may not become profitable and the value of our common stock will decline.

Further, our focus solely on RNAi technology for developing drugs as opposed to multiple, more proven technologies for drug development, increases the risks associated with the ownership of our common stock. If we are not successful in developing 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 September 30, 2006, we had an accumulated deficit of $132.1 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 to continue to incur annual net operating losses 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 or funding from contracts with the government, but cannot be certain that we will be able to secure or maintain these collaborations or contracts or to meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments. 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, including pre-clinical 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 pre-clinical 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 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;
- the timing, receipt and amount of funding under current and future government contracts, if any;
- our ability to establish and maintain additional collaborative arrangements;

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the resources, time and costs required to initiate and complete our pre-clinical 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 either collaborative arrangements, public or private equity offerings or debt financings, or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. In 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 stockholders will result. In addition, our investor rights agreement with Novartis provides Novartis with the right generally to maintain its ownership percentage in Alnylam. While the exercise of this right may provide us with additional funding under some circumstances, Novartis exercise of this right will also cause further dilution to our stockholders. 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.

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

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

**Risks Related to Our Dependence on Third Parties**

***Our collaboration with Novartis is important to our business. If this collaboration is unsuccessful, Novartis terminates this collaboration or this collaboration results in competition between us and Novartis for the development of drugs targeting the same diseases, our business could be adversely affected.***

In October 2005, we entered into a collaboration agreement with Novartis. Under this agreement, Novartis will select disease targets towards which the parties will collaborate to develop drug candidates. Novartis will pay a portion of the costs to develop these drug candidates and will commercialize and market any products derived from this collaboration. In addition, Novartis will pay us certain pre-determined amounts based on the achievement of pre-clinical and clinical milestones as well as royalties on the annual net sales of any products derived from this collaboration. This collaboration has an initial term of three years that may be extended by Novartis for two additional one-year terms. Novartis may elect to terminate this collaboration after two years under some circumstances or in the event of a material uncured breach by us. We expect that a substantial amount of the funding for our operations will come from this collaboration. If this collaboration is unsuccessful, or if it is terminated, our business could be adversely affected.

This agreement also provides Novartis with a non-exclusive option to integrate our intellectual property into Novartis operations and develop products without our involvement for a pre-determined fee. If Novartis elects to exercise this option, Novartis could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases. Novartis has significantly greater financial resources than we do and has far more experience in developing and marketing drugs, which could put us at a competitive disadvantage if we were to compete with Novartis in the development of RNAi-based drugs targeting the same disease. The exercise by Novartis of this option could adversely affect our business.

Our agreement with Novartis allows us to continue to develop products on our own with respect to targets not selected by Novartis for inclusion in the collaboration. We may need to form additional alliances to develop

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products. However, our agreement with Novartis provides Novartis with a right of first offer in the event that we propose to enter into an agreement with a third party with respect to such targets. This right of first offer may make it difficult for us to form future alliances with other parties, which could impair development of our own products. If we are unable to develop products independent of Novartis, our business could be adversely affected.

***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 have entered into alliances with other companies that can provide such capabilities and may need to enter into additional alliances in the future. 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 due to various factors including Novartis right of first offer. 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.

For certain drug candidates that we may develop, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaborations with Novartis, as well as collaborations with Merck, Medtronic, Biogen Idec, the National Institute of Allergy and Infectious Diseases, or the NIAID, a component of the National Institutes of Health, or NIH and Cystic Fibrosis Foundation Therapeutics, Inc. We may not, however, be able to enter into additional 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 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 its development programs, which could affect the collaborator s commitment to us; or

if it has marketing rights, choose to devote fewer resources to the marketing of our product candidates, if any are approved for marketing, than it does for product candidates of its own development.

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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.

***We depend on a government contract to partially fund our research and development efforts and may enter into additional government contracts in the future. If current or future government funding, if any, is reduced or delayed, our drug development efforts may be negatively affected.***

In September 2006, the NIAID, a component of the NIH, awarded us a contract for up to $23 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus. Of the $23 million, the government has committed to pay us $14.2 million over the first two years of the contract and, subject to budgetary considerations in future years, the remaining $8.8 million over the last two years of the contract. We cannot be certain that the government will appropriate the funds necessary for this contract in future budgets. In addition, the government can terminate the agreement in specified circumstances. If we do not receive the $23 million we expect to receive under this contract, we may not be able to develop therapeutics to treat Ebola.

***We have very limited 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 very limited manufacturing experience. Our internal manufacturing capabilities are limited to small-scale production of non-good manufacturing practice material for use in *in vitro* and *in vivo* experiments. Our products may also depend upon the use of specialized formulations, such as liposomes, whose scale-up and manufacturing could also be very difficult. We also have very limited experience of such scale-up and manufacturing, requiring us to depend on third parties, who might not be able to deliver at all or in a timely manner. 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 may manufacture clinical trial materials ourselves or we may rely on others to manufacture the materials we will require for any clinical trials that we initiate. Only a limited number of manufacturers supply synthetic RNAi. We currently rely on several contract manufacturers, including Dowpharma[sm] contract manufacturing services, a business unit of The Dow Chemical Company, for our supply of synthetic RNAi. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our contract manufacturers to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are synthesis and/or purification failures and contamination during the manufacturing process, both of which could result in unusable product and cause delays in our development process. In addition, to fulfill our RNAi requirements we may need to secure alternative suppliers of synthetic RNAi. The manufacturing process for any products that we may develop is an element of the U.S. Food and Drug Administration, or 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 commercial 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.

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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 with 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 pre-clinical testing into one that develops and commercializes drugs.***

Since we commenced operations in 2002, we have grown to over 110 full time equivalent 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

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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 to a point where they do not become commercially viable.***

Pre-clinical testing and clinical trials of new drug candidates are lengthy and expensive and the historical failure rate for drug candidates is high. We have one product candidate, ALN-RSV01, being developed for the treatment of respiratory syncytial virus, or RSV, infection for which we recently completed two Phase I clinical trials and for which another Phase I clinical trial began during October 2006. In addition, in November 2006, we announced we had initiated a human experimental infection study with RSV. We may not be able to further advance this or any other product candidates through clinical trials. If we successfully enter into clinical studies, the results from pre-clinical 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 age and condition of the patients, 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.

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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:

- delays in filing initial drug applications;
- 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 from our clinical trials or the clinical trials of others for drug candidates similar to ours;
- 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 by individuals using drugs similar to our product candidate; or
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or pre-clinical 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 that deliver RNAi therapeutics directly to diseased parts of the body. We believe that any product candidate we develop for Parkinson s disease, or PD, Huntington s disease or other central nervous system diseases may need to be administered using such a device. For neurodegenerative diseases, we have entered into a collaboration agreement with Medtronic to pursue potential development of drug-device combinations incorporating RNAi therapeutics. We may not achieve successful development results under this collaboration and may need to seek other collaboration partners to develop alternative drug delivery systems, or utilize existing drug delivery systems, for the direct delivery of RNAi therapeutics for these diseases. 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, or our collaborator, 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. In cases where we do not have an ongoing collaboration with the company that makes the device, obtaining such additional approvals or clearances and the cooperation of such other company could significantly delay and increase the cost of obtaining marketing approval, which could reduce the commercial viability of our drug candidate. In summary, we may be unable to find, or experience delays in finding, suitable drug delivery systems to administer RNAi therapeutics directly to diseased parts of the body, which could negatively affect our ability to successfully commercialize these RNAi therapeutics.

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***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 pre-clinical 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 very little 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 pre-clinical 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 product candidates that 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 policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we 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.

***If our pre-clinical testing does not produce successful results or our clinical trials do not demonstrate safety and efficacy in humans, we will not be able to commercialize our drug candidates.***

Before obtaining regulatory approval for the sale of our drug candidates, we must conduct, at our own expense, extensive pre-clinical tests and clinical trials to demonstrate the safety and efficacy in humans of our drug candidates. Pre-clinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and interim results of a clinical trial do not necessarily predict final results.

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

- regulators or IRBs may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;

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our pre-clinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional pre-clinical testing or clinical trials or we may abandon projects that we expect to be promising;

enrollment in our clinical trials may be slower than we currently anticipate or participants may drop out of our clinical trials at a higher rate than we currently anticipate, resulting in significant delays;

our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner;

we might have to suspend or terminate our clinical trials if the participants are being exposed to unacceptable health risks;

regulators or IRBs may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;

the cost of our clinical trials may be greater than we anticipate;

the supply or quality of our drug candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate; and

the effects of our drug candidates may not be the desired effects or may include undesirable side effects or the drug candidates may have other unexpected characteristics.

***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. We may manufacture clinical trial materials or we may contract a third party to manufacture these materials for us. 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 regulatory 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;

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the willingness of patients to accept relatively new routes 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 and the relative risks and/or benefits of the treatments.

***Even if we develop RNAi therapeutic products for the prevention or treatment of infection by pandemic flu virus and/or Ebola, governments may not elect to purchase such products, which could adversely affect our business.***

We expect that governments will be the only purchasers of any products we may develop for the prevention or treatment of pandemic flu virus or Ebola. In the future, we may also initiate additional programs for the development of product candidates for which governments may be the only or primary purchasers. However, governments will not be required to purchase any such products from us and may elect not to do so, which could adversely affect our business. For example, although the focus of our flu program is to develop RNAi therapeutic targeting gene sequences that are highly conserved across known flu viruses, if the sequence of any flu virus that emerges is not sufficiently similar to those we are targeting, any product candidate that we develop may not be effective against that virus. Accordingly, while we expect that any RNAi therapeutic we develop for the treatment of pandemic flu virus could be stockpiled by governments as part of their preparations for a flu pandemic, they may not elect to purchase such product.

***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 been approved by the FDA.

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 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

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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.

Some states and localities have established drug importation programs for their citizens. So far, these programs have not led to a large proportion of prescription orders to be placed for foreign purchase. The FDA has warned that importing drugs is illegal and in December 2004 began to take action to halt the use of these programs by filing a civil complaint against an importer of foreign prescription drugs. If such programs were to become more substantial and were not to be encumbered by the federal government, they could also 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 have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our drug candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business.

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

Our research 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:

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much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;

more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing 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 for RSV, flu, Ebola, PD, hypercholesterolemia, neuropathic pain, PML and CF. Virazole is currently marketed for the treatment of certain RSV patients, Tamiflu® and Relenza® are marketed for the treatment of flu patients, numerous drugs are currently marketed for the treatment of hypercholesterolemia, PD and neuropathic pain and two drugs, TOBI® and Pulmozyme®, are currently marketed for the treatment of CF. These drugs, or other of 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 ease with which our products can be administered and the extent to which patients accept relatively new routes of administration;

the timing and scope of regulatory approvals for these products;

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

price;

reimbursement coverage; and

patent position.

Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above or on other factors. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our 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 Merck, Nastech Pharmaceutical Company Inc., or Nastech, Acuity Pharmaceuticals, Inc., Nucleonics, Inc., SR Pharma Plc. and CytRx Corporation. In addition, we

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granted licenses to Isis Pharmaceuticals, Inc., or Isis, GeneCare Research Institute, Benitec, Nastech, Calando Pharmaceuticals, Inc., Quark Biotech, Inc. as well as others under which these companies may independently 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. Merck is currently one of our collaborators and a licensee under our intellectual property for specified disease targets. However, with its recent acquisition of Sirna Therapeutics, Inc., Merck, which has substantially more resources than we do, could become a direct competitor.

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 multiple antisense drug candidates in late-stage clinical trials. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for drugs that target mRNAs to silence specific genes.

**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 issuance of a patent does not guarantee that it is valid or enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, unenforceable or circumvented. Moreover, the United States Patent and Trademark Office, or USPTO, may commence interference proceedings involving our patents or patent applications. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications would be costly, would require significant time and attention of our management and could have a material adverse effect on our business.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. 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.

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***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, Inex Pharmaceuticals Corporation, Idera Pharmaceuticals, Inc., Carnegie Institution of Washington, Cancer Research Technology Limited, the Massachusetts Institute of Technology, the Whitehead Institute for Biomedical Research, Garching Innovation GmbH, representing the Max Planck Gesellschaft zur Förderung der Wissenschaften e.V., referred to as the Max Planck organization, Stanford University, Cold Spring Harbor Laboratory and the University of South Alabama. 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.

***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 and opposition 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. Any attempt to circumvent or invalidate our intellectual property rights would be costly, would require significant time and attention of our management and could have a material adverse effect on our business.

After the grant by the European Patent Office, or EPO, of the Kreutzer-Limmer patent, 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, or EPC. In oral proceedings in June 2006, the EPO opposition division in charge of the opposition proceedings upheld the patent with amended claims. This decision has been appealed by two opposers, including Sirna, which was recently acquired by Merck. If appealed, the Boards of Appeal of the EPO may choose to uphold, further amend or revoke the patent it in its entirety. However, because a European Patent represents a bundle of national patents for each of the designated member states and must be enforced on a country-by country-basis, even if upheld, a National Court in one or more of the EPC member states could subsequently rule the patent invalid or unenforceable. In addition, National Courts in different countries could come to differing conclusions in interpreting the scope of the upheld claims.

In addition, four parties have filed Notices of Opposition in the EPO against the Kreutzer-Limmer patent, published under the publication number EP 1214945, and one party has given notice to the Australian Patent Office, IP Australia, that it opposes the grant of our patent AU 778474, which derives from the same parent international patent application that gave rise to EP 1144623 and EP 1214945. The proceedings in the EPO and Australian Patent Office may take several years before an outcome becomes final.

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.

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

Third parties may sue us for infringing their patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others. 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 patents, owned in part or solely by the Max Planck organization of Germany, our amended licenses with Garching Innovation GmbH, a related entity to the Max Planck organization, require us to maintain a minimum level of employees in Germany. If we fail to comply with this condition, the owners of the patents that are the subject of these licenses may have the right to grant a similar license to one other company. We regard these patents 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.

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***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.

***Novartis ownership of our common stock could delay or prevent a change in corporate control***

Novartis held approximately 14% of our outstanding common stock as of December 31, 2006. 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 and our stockholder rights plan could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

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

- a classified board of directors;
- a prohibition on actions by our stockholders by written consent;
- limitations on the removal of directors; and

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advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings.

In addition our board of directors has adopted a stockholder rights plan, the provisions of which could make it difficult for a potential acquirer of Alnylam to consummate an acquisition transaction.

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.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus includes and incorporates forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). All statements, other than statements of historical facts, included or incorporated in this prospectus regarding our strategy, future operations, financial position, future revenues, projected costs, prospects, plans and objectives of management are forward-looking statements. The words anticipates, believes, estimates, expects, intends, may, plans, goals, projects, will, would and similar expressions are intended to identif 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 you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included or incorporated in this prospectus, particularly under the heading Risk Factors , that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. Any such forward-looking statements represent management s views as of the date of the document in which such forward-looking statement is contained. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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## USE OF PROCEEDS

We are filing the registration statement of which this prospectus is a part to permit a holder of the shares of our common stock described in the section entitled Selling Stockholder to resell such shares. We will not receive any proceeds from the resale of the shares by the selling stockholder. The selling stockholder will pay any underwriting discounts and commissions and expenses incurred by the selling stockholder for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholder in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, NASDAQ listing fees and fees and expenses of our counsel and auditors.

## SELLING STOCKHOLDER

We issued the shares of our common stock covered by this prospectus in a private placement on January 16, 2007 in connection with our license and collaboration agreement with Inex. The following table sets forth, to our knowledge, certain information about the selling stockholder as of January 17, 2007.

We do not know when or in what amounts the selling stockholder may offer shares for sale. The selling stockholder might not sell any or all of the shares offered by this prospectus. Because the selling stockholder may offer all or some of the shares pursuant to this offering and because, other than the agreement between us and Inex that it will not, without our consent, sell more than 40,000 shares covered by this prospectus in any one day, there are currently no agreements or understandings with respect to the sale of any shares, we cannot estimate the number of shares that will be held by the selling stockholder after completion of the offering. However, for purposes of this table, we have assumed that, after completion of this offering, none of the shares covered by this prospectus will be held by the selling stockholder.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission, or SEC, and includes voting or investment power with respect to shares. To our knowledge, the entity named in the table has sole voting and investment power with respect to its shares of common stock.

| Name of Selling Stockholder | Shares of Common Stock Beneficially Owned Prior to Offering | | Number of Shares of Common Stock Being Offered | Shares of Common Stock to be Beneficially Owned After Offering | |
|---|---|---|---|---|---|
| | Number | Percentage | | Number | Percentage |
| Inex Pharmaceuticals Corporation | 361,990 | * | 361,990 | | |

* Less than one percent.

(1) Ian Mortimer and Tim Ruane are the natural persons who exercise voting and/or investment control over the shares of our common stock held by Inex. The reference to these natural

persons herein does not constitute an admission of beneficial ownership of any shares of our common stock.

The selling stockholder has not, and none of its affiliates, officers, directors or holders of 5% or more of its common stock has held any position or office, or had any other material relationship, with us or any of our subsidiaries within the past three years. As described elsewhere in this prospectus, on January 8, 2007, we entered into a license and collaboration agreement with Inex.

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## PLAN OF DISTRIBUTION

The shares covered by this prospectus may be offered and sold from time to time by the selling stockholder. The term selling stockholder includes donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from the selling stockholder as a gift, pledge, distribution or other non-sale related transfer. The selling stockholder will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions. The selling stockholder may sell its shares by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of The Nasdaq Stock Market;
- in privately negotiated transactions;
- in options transactions; and
- by any other legally available means.

In addition, any shares that qualify for sale pursuant to Rule 144 may be sold under Rule 144 rather than pursuant to this prospectus.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with distributions of the shares or otherwise, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with the selling stockholder. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling stockholder may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged shares pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by the selling stockholder may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholder in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus, the selling stockholder and any broker-dealers who execute sales for the selling stockholder may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. Any profits realized by the selling stockholder and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions. Some of the underwriters or deemed underwriters or agents and their associates may be customers of, engage in transactions with, and perform services for us in the ordinary course of business.

In order to comply with the securities laws of certain states, if applicable, the shares must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration

or qualification requirement is available and is complied with.

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We have advised the selling stockholder that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholder and their affiliates. In addition, we will make copies of this prospectus available to the selling stockholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholder may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

At the time a particular offer of shares is made, if required, a prospectus supplement will be distributed that will set forth the number of shares being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

Pursuant to the terms of the license and collaboration agreement between us and Inex, Inex may not (1) without our consent, sell, transfer or otherwise dispose of more than 40,000 shares of our common stock, subject to adjustment in the event of a stock split, stock dividend or similar recapitalization of our common stock, in any one day or (2) directly or indirectly, sell, transfer or otherwise dispose of any shares of our common stock during the two trading days prior to the date on which we calculate the additional cash payment, if any, that we may be required to make to Inex.

We have agreed to indemnify the selling stockholder against certain liabilities, including certain liabilities under the Securities Act.

We have agreed with the selling stockholder to keep the registration statement of which this prospectus constitutes a part effective until the earliest of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement, (2) a date on which we are required to determine whether we continue to be a well-known seasoned issuer, as such term is defined in the Securities Act, and we determine we are not, and (3) January 18, 2008. Notwithstanding the foregoing obligations, we may, under specified circumstances, suspend the use of the registration statement, or any amendment or supplement thereto.

## LEGAL MATTERS

The validity of the shares offered by this prospectus has been passed upon by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

## EXPERTS

The financial statements and management s assessment of the effectiveness of internal control over financial reporting (which is included in Management s Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2005 have been so incorporated in reliance on the report 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 SEC. 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. You should call the SEC at 1-800-SEC-0330 for further information on the public reference room. Our SEC filings are also available to you on the SEC s Internet site at www.sec.gov.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. 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 CERTAIN DOCUMENTS BY REFERENCE

The SEC requires us to incorporate into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus.

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Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of this offering, 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.

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2005, as filed with the SEC on March 16, 2006;

Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2006, as filed with the SEC on May 9, 2006;

Our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2006, as filed with the SEC on August 4, 2006;

Our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2006, as filed with the SEC on November 8, 2006;

Our Current Report on Form 8-K, as filed with the SEC on January 25, 2006;

Our Current Report on Form 8-K, as filed with the SEC on February 1, 2006;

Our Current Report on Form 8-K, as filed with the SEC on February 24, 2006;

Our Current Report on Form 8-K, as filed with the SEC on March 17, 2006;

Our Current Report on Form 8-K, as filed with the SEC on April 6, 2006;

Our Current Report on Form 8-K, as filed with the SEC on June 23, 2006;

Our Current Report on Form 8-K, as filed with the SEC on July 10, 2006;

Our Current Report on Form 8-K, as filed with the SEC on September 18, 2006;

Our Current Report on Form 8-K, as filed with the SEC on September 26, 2006;

Our Current Report on Form 8-K, as filed with the SEC on October 27, 2006;

Our Current Report on Form 8-K, as filed with the SEC on December 13, 2006;

Item 3.02 of our Current Report on Form 8-K, as filed with the SEC on January 12, 2007; 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.

The SEC file number for each of the documents listed above is 000-50743.

A statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superceded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or in any other subsequently filed document which is also incorporated in this prospectus

modifies or replaces such statement. Any statements so modified or superceded shall not be deemed, except as so modified or superceded, to constitute a part of this prospectus.

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 (except any underwriting discounts and commissions and expenses incurred by the selling stockholder for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholder in disposing of the shares). All amounts shown are estimates, except for the SEC registration fee.

| | Amount |
|---|---|
| SEC registration fee | $ 845 |
| Legal fees and expenses | 10,000 |
| Accounting fees and expenses | 5,000 |
| Miscellaneous expenses | 2,155 |
| Total expenses | $ 18,000 |

**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. Alnylam has included such a provision in its restated certificate of incorporation.

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.

Alnylam s restated certificate of incorporation provides that:

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

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

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

The indemnification provisions contained in Alnylam s 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, Alnylam maintains insurance on behalf of its 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.

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**Item 16. Exhibits.**

| Exhibit Number | Description |
|---|---|
| 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 page). |

**Item 17. Undertakings.**

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 increase or decrease in the 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;

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*provided, however*, that paragraphs (1)(i), (1)(ii) and (1)(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 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.

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

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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.

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 registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on January 17, 2007.

ALNYLAM PHARMACEUTICALS, INC.

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

**SIGNATURES AND POWER OF ATTORNEY**

We, the undersigned officers and directors of Alnylam Pharmaceuticals, Inc., hereby severally constitute and appoint John M. Maraganore, Barry E. Greene and Patricia L. Allen, and each of them singly, our true and lawful attorneys-in-fact and agents, with full power to any of them, to sign for us and in our names in the capacities indicated below, any and all post-effective amendments to the registration statement on Form S-3 filed herewith, and generally to do all such things in our names and on our behalf in our capacities as officers and directors to enable Alnylam Pharmaceuticals, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys-in-fact and agents, or any of them, to said registration statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons as indicated below:

| Signature | Title | Date |
|---|---|---|
| /s/ John M. Maraganore<br>John M. Maraganore, Ph.D. | President, Chief Executive Officer and Director (Principal Executive Officer) | January 17, 2007 |
| /s/ Patricia L. Allen<br>Patricia L. Allen | Vice President, Finance and Treasurer (Principal Financial and Accounting Officer) | January 16, 2007 |
| /s/ Peter Barrett<br>Peter Barrett, Ph.D. | Director | January 17, 2007 |
| /s/ John K. Clarke<br>John K. Clarke | Director | January 16, 2007 |
| /s/ Vicki L. Sato<br>Vicki L. Sato, Ph.D. | Director | January 17, 2007 |

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| Signature | Title | Date |
|---|---|---|
| /s/ Paul R. Schimmel | Director | January 17, 2007 |
| Paul R. Schimmel, Ph.D. | | |
| /s/ Phillip A. Sharp | Director | January 16, 2007 |
| Phillip A. Sharp, Ph.D. | | |
| /s/ Kevin P. Starr | Director | January 16, 2007 |
| Kevin P. Starr | | |
| /s/ James L. Vincent | Director | January 16, 2007 |
| James L. Vincent | | |

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## EXHIBIT INDEX

| Exhibit Number | Description |
|---|---|
| 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 page). |