ALNYLAM PHARMACEUTICALS, INC.
Form 10-K
March 12, 2007

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)**
OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2006

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d)**
OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission File Number 000-50743

ALNYLAM PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**77-0602661**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

300 Third Street, Cambridge, MA 02142
(Address of principal executive offices) (Zip Code)

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

Securities registered pursuant to Section 12(b) of the Act:
Common Stock, $0.01 par value per share

Securities registered pursuant to Section 12(g) of the Act: None
(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No þ

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act (Check one):

Large accelerated filer o Accelerated filer þ Non-accelerated filer o

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

The aggregate market value of the voting Common Stock held by non-affiliates of the registrant, based on the last sale price of the registrant s Common Stock at the close of business on June 30, 2006, was $466,921,226.

As of February 28, 2007, the registrant had 37,470,628 shares of Common Stock, $0.01 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III (except for information required with respect to our executive officers, which is set forth under Part I, Item 1 Business Executive Officers of the Registrant) and the information required by Item 5 relating to our equity compensation plans have been omitted from this report, as we expect to file with the Securities and Exchange Commission, not later than 120 days after the close of our fiscal year ended December 31, 2006, a definitive proxy statement for our annual meeting of stockholders. The information required by Items 10, 11, 12, 13 and 14 of Part III and the information required by Item 5 relating to our equity compensation plans, which will appear in our definitive proxy statement, is incorporated by reference into this report.

ALNYLAM PHARMACEUTICALS, INC.
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This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, that involve risks and uncertainties. All statements other than statements relating to historical matters should be considered forward-looking statements. When used in this report the words believe, expect, anticipate, will, plan, target, goal and similar expressions are intended to identi forward-looking statements, although not all forward-looking statements contain these words. Our actual results could differ materially from those discussed in the forward-looking statements as a result of a number of important factors, including the factors discussed in this section and elsewhere in this Annual Report on Form 10-K, including those discussed in Item 1A of this report under the heading Risk Factors, and the risks discussed in our other filings with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements, which reflect management s analysis, judgment, belief or expectation only as of the date hereof. We assume no obligation to update these forward-looking statements to reflect events or circumstances that arise after the date hereof.

PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. RNAi is a naturally occurring biological pathway 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 are building a pipeline of RNAi therapeutics. Our lead program is in Phase I clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which we believe is the leading cause of hospitalization in infants in the United States and occurs in the elderly and in immune compromised adults.

In pre-clinical development programs, we are working on an RNAi therapeutic for the treatment of another respiratory infection, influenza, with Novartis Pharma AG, or Novartis. Independently, we are also developing an RNAi therapeutic for the treatment of hypercholesterolemia. We have additional pre-clinical discovery programs for RNAi therapeutics for the treatment of a broad range of diseases, including Parkinson s disease, Huntington s disease, neuropathic pain, progressive multifocal leukoencephalopathy, or PML, Ebola virus infection and cystic fibrosis, or CF. We are also working to extend our delivery capabilities to enable the broad development of RNAi therapeutics for the treatment of other diseases, including cancer.

In addition, we have formed alliances with leading companies, including Merck & Co., Inc., or Merck, Medtronic, Inc., or Medtronic, Novartis and Biogen Idec, Inc., or Biogen Idec. We have also entered into contracts with government agencies, including the National Institute of Allergy and Infectious Diseases, or NIAID, a component of the National Institute of Health, or NIH. Finally, we have also entered into over 20 license agreements with other biotechnology companies interested in developing RNAi therapeutic products and research companies that commercialize RNAi reagents or services.

RNA Interference

RNAi is a recently discovered biological pathway that occurs naturally within cells and can be harnessed to selectively silence the activity of specific genes. The discovery of RNAi first occurred in plants and worms, and two of the scientists who made this discovery, Dr. Andrew Fire and Dr. Craig Mello, received the 2006 Nobel Prize for Medicine or Physiology.

Genes provide cells with instructions for producing proteins. Proteins perform many of the vital functions of the cell and of the human body. Although the roles they play are generally beneficial, in certain circumstances,

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proteins can be harmful. Many human diseases are caused by the inappropriate behavior of proteins. A particular protein may, for example, be present in too great a quantity, be too active or appear in the wrong place or at the wrong time. In these circumstances, the ability to stop or reduce production of the protein by selectively silencing the gene that directs its synthesis could be very beneficial for the treatment of the disease.

Beginning in 1999, our scientific founders described and provided evidence that the RNAi mechanism occurs in mammalian cells and that its immediate trigger is a type of molecule known as small interfering RNA, or siRNA. They showed that laboratory-synthesized siRNAs could be introduced into the cell and suppress production of specific target proteins. Because it is possible, in theory, to design and synthesize siRNAs specific to any gene of interest, we believe that RNAi therapeutics have the potential to become a broad new class of drugs.

How RNA Interference Works

RNA is a crucial intermediary in the process by which the cell uses inherited genetic information. This information is passed from one generation to the next in the form of genes, which are made of a substance known as deoxyribonucleic acid, or DNA. Generally, each gene contains the instructions that tell the cell how to make one specific protein. These instructions are in a coded form. The code is based on the four different chemical building blocks from which DNA is made, usually designated by the first letters of their chemical names, A, C, G and T. It is the sequence in which these building blocks, or bases, occur in a gene that tells the cell what protein to make. Most gene sequences are thousands of bases long, and the variety possible in such long sequences allows the cell to produce a large number of different proteins.

One very important property of DNA is that it is double-stranded, consisting of two separate strands intertwined around each other in a double helix. The two strands are held together by base pairs that form between bases on the opposite strands. Strict rules govern the formation of these base pairs: an A on one strand can pair with a T on the other, and a G can pair with a C, but no other pairings are allowed. The double-stranded nature of DNA and the strict rules governing base-pairing are fundamental to ensuring that genetic information is copied accurately when it is handed down from one generation to the next.

Base-pairing rules are also fundamental to the process by which the cell uses, or expresses, genetic information to make a protein. To initiate this process, the cell makes a working copy of the gene that encodes the protein. This working copy is made not of DNA but of a closely related substance called ribonucleic acid, or RNA. The working copy is known as messenger RNA, or mRNA. Unlike DNA, mRNA has only one strand. However, the application of base-pairing rules during synthesis of this strand ensures that the sequence of bases in mRNA accurately reflects the base sequence, and thus the genetic information, in the gene being copied. This mRNA then associates with the cell s protein synthesis machinery, where it directs synthesis of a protein in such a way that the structure of the protein is directly determined by the sequence of bases in the mRNA, and thus in the gene. The protein specified by a particular gene or mRNA is said to be encoded by that gene or mRNA. When this protein is made, the gene is said to be active or expressed.

Although many RNA molecules, like mRNA, are single-stranded, RNA is capable of forming double-stranded molecules analogous to those formed by DNA. When it does so, base-pairing rules apply. As a result, only RNA molecules with complementary sequences can form double-stranded structures. Generally, every base on one strand has to line up with its permitted base-pair partner on the other strand, otherwise the double-stranded structure will be unstable.

Double-stranded RNA, or dsRNA, is crucial to the phenomenon of RNAi. A particular type of dsRNA interferes with the activity of specific genes by triggering the breakdown of mRNAs copied from these genes, preventing production of the proteins they encode. Selection of mRNAs for breakdown is driven by base-pairing between the target mRNAs

and the separated strands of the dsRNA. Thus, the mRNAs selected for breakdown are those which contain base sequences identical to base sequences in one strand of the dsRNA. As a result, RNAi leads to selective silencing of specific genes with relatively little impact on other genes whose mRNAs do not share base sequences with the dsRNA.

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In nature, the cell initiates RNAi by cutting longer dsRNAs into smaller dsRNA pieces that have 25 or fewer base pairs. These shorter dsRNAs are known as small interfering RNAs, or siRNAs. siRNAs are double-stranded along most of their length but have unpaired bases, or overhangs, at each end, which are important for their activity. siRNAs are the molecules that actually trigger RNA interference. They do so by a process that has three main steps as shown in the figure below.

Step 1. siRNAs associate with several proteins to form an assembly known as the RNA-induced silencing complex, or RISC. The two strands of the siRNA become separated as the RISC is formed, so that RISC contains an unpaired single-stranded RNA.

Step 2. The RISC then looks for mRNA molecules that contain base sequences complementary to the single-stranded RNA it contains that is, sequences within the mRNA whose bases can pair up exactly, using base-pairing rules, with the bases in the single-stranded RNA.

Step 3. Once this pairing occurs, the RISC complex cuts the mRNA into two separate pieces at the base-paired region, destroying its ability to direct protein synthesis. The RISC complex is then available to cut additional mRNA molecules that contain the appropriate base sequence.

Repetitive cycles through steps two and three lead to catalytic degradation of mRNAs that contain a sequence complementary to the siRNA strand in the RISC. The ability of each RISC complex to cut multiple mRNA molecules consecutively in a catalytic manner is one of the reasons why we believe RNAi will be effective at silencing gene activity.

Opportunity for Therapeutics Based on RNAi

In May 2001, one of our scientific founders, Dr. Thomas Tuschl, published the first scientific paper demonstrating that the siRNAs required to trigger RNA interference need not be generated inside the cell. Instead, siRNAs can be synthesized in the laboratory using chemical or biochemical methods and introduced into cells to silence the activity of a specific gene. As a result of the human genome project, complete base sequences are available for most human genes. With the sophisticated bioinformatics tools that were developed in conjunction with the genome project, it is possible to scan through the gene that encodes a particular protein and select base sequences that are of the appropriate length for siRNAs and unique to that gene. Several siRNAs targeted to the gene of interest can then be synthesized. Each synthesized siRNA will contain a sequence capable of base-pairing exactly with a short stretch of the sequence of the mRNA copied from the target gene. The synthetic siRNAs can then be tested to determine whether they silence the activity of this gene and suppress the synthesis of the protein it encodes.

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The use of siRNAs has been broadly adopted by academic and industrial researchers for the fundamental study of the function of genes. Important information about the function of a gene can often be deduced by suppressing, or knocking-down, its activity and examining the effect this has on the behavior of a cell or animal. There are now many examples in which such suppression of gene activity has been achieved, in whole or in part, using synthetic siRNAs. In just a few years after siRNAs were discovered, they have become the tools of choice for the selective knock-down of gene function by research scientists, and have largely displaced other methods previously used for this purpose. Reflecting this, siRNAs are a growing portion of the market for research reagents and related products and services.

One important application of such knock-down studies is to confirm the role of a particular gene or protein in a disease, a process often referred to as target identification or target validation. If silencing a gene with an siRNA leads to improvements in disease symptoms in an experimental disease model, this implies that the target gene or protein plays an important role in the disease.

It also implies that the siRNA that suppresses the gene in the model system may be a useful starting point for the development of a drug. We believe that it will be possible to develop these siRNAs into potent and specific drugs.

Broad Potential of siRNAs as Therapeutics

The success of siRNAs in silencing gene activity in experimental systems suggests that siRNAs could potentially be developed into a broad new class of human therapeutics. We believe this new class of drugs has the potential to become a major class of drugs because RNAi therapeutics could offer the following benefits:

Ability to treat a broad range of diseases. Given the availability of the base sequence of the entire human genome, it could be possible, in theory, to design siRNAs to suppress the production of virtually any human protein whose presence or activity causes disease. This suggests that RNAi therapeutics could potentially be used to treat a broad range of diseases.

Ability to target proteins that cannot be targeted effectively by existing drug classes. Many proteins that play important roles in disease cannot be targeted effectively with small molecules or with therapeutic proteins such as monoclonal antibodies. These proteins are commonly referred to as non-druggable targets. In the case of small molecule drugs, many proteins are non-druggable because it has proved difficult to synthesize drug candidates with appropriate specificity, potency and safety. In the case of protein drugs, the range of available targets is limited to targets on the surface of or outside the cell. These limitations on small molecule and protein drugs should not apply to siRNAs, which, in theory, can be synthesized to target any gene in the genome. Therefore, we believe RNAi therapeutics will be able to target proteins that small molecule and protein drugs cannot currently target effectively.

Inherently potent mechanism of action. One molecule of siRNA could potentially do the work of thousands of molecules of conventional drugs. With conventional drugs, one drug molecule is typically required for every protein molecule whose activity needs to be blocked. Accordingly, to block several thousand protein molecules, several thousand drug molecules are required. In contrast, a single siRNA molecule can potentially block the synthesis of many protein molecules. This is because each siRNA within a RISC complex can trigger destruction of multiple mRNA molecules, each of which could otherwise direct the synthesis of many protein molecules. This inherent potency of the RNAi mechanism suggests a potentially high degree of potency for RNAi therapeutics.

Simplified discovery of drug candidates. Identification of small molecule and protein drug candidates typically requires screening of a large number of potential candidates to find prospective leads. These leads

must then undergo significant optimization in order to become drug candidates. Particularly in the case of small molecule drug candidates, the optimization procedure can be very challenging, and has to be almost entirely repeated for each candidate. Identification of siRNA drug candidates has the potential to be much simpler and take considerably less time because, in theory, it will involve relatively standard processes that can be applied in a similar fashion to many successive product candidates.

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For these potential benefits of siRNA drugs to be realized, it will be necessary to create chemically synthesized siRNAs that are potent, specific, stable and safe and also capable of reaching, or achieving delivery into, the appropriate tissues and cells. The incorporation of such properties into siRNAs is the focus of our product platform. We have reported on our advances in developing siRNAs as potential drugs in a number of peer-reviewed publications and meetings, including publications by Alnylam scientists in the journals *Nature*, *Nature Medicine* and *Nature Chemical Biology.*

Our Business Strategy

Our business strategy is to develop and commercialize a pipeline of *proprietary* RNAi therapeutic products and, in parallel, to form alliances with pharmaceutical companies to develop and commercialize a pipeline of *partnered* RNAi therapeutic products. For our proprietary RNAi therapeutic products, our aim is to develop these products to later stages of clinical development and to commercialize them on our own or through alliances formed at these later stages. For our partnered RNAi therapeutic products, we have five discovery and development alliances with four separate companies: Novartis, Merck, Medtronic and Biogen Idec. Two of these alliances are with Novartis. The first of our Novartis alliances, formed in September 2005, is for the discovery, development and commercialization of RNAi therapeutics for a significant but defined number of targets in the Novartis research portfolio. In this alliance, we are eligible to receive substantial early funding in addition to future milestone and royalty payments. We are also eligible to receive additional payments if Novartis exercises a non-exclusive option to integrate our RNAi therapeutics platform into its internal efforts, in which case we would be eligible to receive future milestones and royalties on products resulting from those efforts. Our second alliance with Novartis, formed in February 2006, is for the discovery and development of RNAi therapeutics for pandemic flu. In this alliance, we and Novartis will jointly develop RNAi therapeutics for pandemic flu in the United States, with Novartis leading development outside the United States. Novartis will also lead commercialization efforts worldwide, with Alnylam actively involved, and in certain situations taking the lead, in commercialization within the United States. Our alliance with Merck was initiated in September 2003 and amended in July 2006, and is focused on RNAi therapeutics directed toward ten Merck proprietary targets. Our collaboration with Medtronic, formed in February 2005, is focused on the development of novel drug-device products incorporating RNAi therapeutics to treat diseases caused by degeneration of the nervous system. Our collaboration with Biogen Idec, formed in September 2006, is focused on research on the potential use of RNAi technology to discover and develop therapeutics to treat PML.

One of the key factors in our ability to form significant alliances with pharmaceutical companies is the strength of our intellectual property position relating to the development and commercialization of siRNAs as therapeutics. This includes ownership of, or exclusive rights to, issued patents and pending patent applications claiming fundamental features of siRNAs and RNAi therapeutics. The United States Patent and Trademark Office, or USPTO, has issued two patents in the Tuschl II patent series (U.S. Patent Nos. 7,056,704 and 7,078,196) that broadly cover methods of making siRNAs that have certain features that we believe are needed for their use as therapeutics, which we refer to as fundamental features. These issued Tuschl II patents are exclusively licensed to Alnylam on a worldwide basis for therapeutic applications. The European Patent Office, or EPO, has granted two patents from the Kreutzer-Limmer I patent series (EP 1144623 and EP 1214945) that broadly cover siRNA compositions, methods and uses. We own these granted Kreutzer-Limmer I patents, which stem from our July 2003 acquisition of Ribopharma AG. Additional patents and patent applications that relate to fundamental features of siRNAs and RNAi therapeutics and for which we have entered into licensing agreements include those called Crooke, Glover, Tuschl I and Hannon. Our patent estate also includes a broad portfolio of intellectual property relating to chemical modifications of siRNAs licensed from Isis Pharmaceuticals, Inc., or Isis, and a number of issued patents related to the formulation and delivery of siRNAs licensed from Inex Pharmaceuticals Corporation, or Inex. Finally, our patent estate also includes patents and pending patent applications claiming siRNAs directed to specific targets as treatments for particular diseases.

To realize additional value from our intellectual property, we also grant licenses to biotechnology companies with our InterfeRx[tm] program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. InterfeRx licensees include GeneCare Research Institute Co., Ltd., or GeneCare, Quark Biotech, Inc., or Quark, Calando Pharmaceuticals, Inc., or Calando, and Nastech

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Pharmaceutical Company Inc., or Nastech. Inex and Benitec Ltd., or Benitec, have options to take InterfeRx licenses, subject to certain conditions. We also license key aspects of our intellectual property to companies active in the research products and services market. As of February 28, 2007, we had granted such licenses to eighteen companies. Our InterfeRx and research product licenses aim to generate modest near-term revenues that we can re-invest in the development of our proprietary RNAi therapeutics pipeline.

We also seek funding for the development of our proprietary RNAi therapeutics pipeline from foundations and government sources. We have obtained initial government support for our pandemic flu program from the Defense Advanced Research Projects Agency of the United States Department of Defense, or DARPA, and the NIAID. Further, the NIAID, awarded us a contract for up to $23.0 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus. We have also obtained funding for pre-clinical discovery programs from the Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, and the Michael J. Fox Foundation.

Alnylam Product Platform

To realize the potential of RNAi therapeutics as a broad new class of drugs, we are developing capabilities that we can apply to any specific siRNA in a relatively standard fashion to endow it with drug-like properties. We use the term product platform to describe these capabilities because we believe they will enable us to develop many products across a variety of therapeutic areas. The concept for our product platform is that it will provide a systematic approach to identifying RNAi drug candidates with the following steps:

Sequence selection. Using sophisticated bioinformatics tools, we scan through the entire sequence of a target mRNA to identify sequences that are unique to that mRNA and have few closely similar sequences in other mRNAs. From these unique sequences we derive a list of potential siRNAs that would match up exactly with the target mRNA and not with any other mRNAs. We narrow this list down further by applying filters for other important properties, such as the identity of sequences in mRNAs across multiple species to facilitate pre-clinical and clinical testing. This provides us with a shorter list of siRNAs, each of which we then synthesize for experimental evaluation.

Potency selection. The siRNAs synthesized in the sequence selection step are tested in cell culture systems to compare their potencies in suppressing production of the target protein.

Stabilization by chemical modification. Each of the most potent siRNAs is assessed to identify the sites within its structure where it is most vulnerable to attack by enzymes known as ribonucleases that could degrade the siRNA. A minimal set of chemical modifications is then introduced into the siRNA to protect these vulnerable sites, and the modified siRNA is tested to confirm its stability and that it has retained activity against the target mRNA.

Improvement of biodistribution by conjugation of additional chemical groups. The stabilized siRNA is further modified by the addition, or conjugation, of one or more chemical groups designed to improve uptake of the siRNA into cells and, if desired, to prolong the time it circulates in the blood.

Formulation with appropriate delivery reagents. In addition to, or instead of, introducing chemical modifications into candidate siRNAs, we may also investigate the effect of different formulation reagents on the stability and biodistribution of these candidate siRNAs. Examples of such formulation reagents include lipids that can be used to form very small particles, known as liposomes or lipoplexes, that contain the siRNAs of interest.

We expect this process to generate RNAi drug candidates that are potent against and specific to a particular target, are appropriately stable and are able to penetrate cells of target tissues. Moreover, we expect this process for finding suitable drug candidates to be simpler, faster and more productive than the corresponding process for small molecule

and protein drug candidates. Therefore, we believe that with the progress we have made and expect to make in the future in developing our product platform, we will be well positioned to pursue multiple therapeutic opportunities.

We believe that we have made considerable progress in developing our product platform, as documented in a number of publications, including papers in *Nature*, *Nature Medicine* and *Nature Chemical Biology*. This progress has enabled us to initiate and advance a number of discovery and development programs for RNAi

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therapeutics that will be administered directly to diseased parts of the body, which we refer to as Direct RNAi[tm] therapeutics. Our progress in achieving delivery of RNAi therapeutics following injection into the bloodstream, which we call Systemic RNAi[tm], has enabled the initiation of pre-clinical development programs for these applications as well. We recognize, however, that considerable challenges remain with respect to delivery of siRNAs to target cells and tissues, and we therefore regard further development of our product platform as a continuing high priority.

Product Pipeline

The following is a summary of our product pipeline as of February 28, 2007:

We consider a program to be a discovery program while we are still at the stage of identifying and comparing potential drug candidates but have not yet established the timing for human clinical trials. Once such timing has been established, we consider a program to have advanced to the development stage, and to be a development program.

Two of our current development programs are focused on viruses that infect the respiratory tract. The more advanced of these programs is focused on RSV. We initiated Phase I human clinical trials of ALN-RSV01, an RNAi therapeutic for the treatment of RSV infection, in December 2005. Our second development program, ALN-FLU01, which we are developing with Novartis, is focused on pandemic flu. A third development program, ALN-PCS01, is focused on the treatment of hypercholesterolemia with an RNAi therapeutic that targets a gene called proprotein convertase subtilisn/kexin type 9, or PCSK9.

We have spent substantial funds over the past three years to develop our product pipeline and expect to continue to do so in the future. We incurred approximately $49.8 million in 2006, $35.3 million in 2005 and $24.6 million in 2004 in research and development costs.

Development Programs

Respiratory Syncytial Virus Infection

Market Opportunity. RSV is a highly contagious virus that causes infections in both the upper and lower respiratory tract. RSV infects nearly every child by the age of two years and is responsible for a significant percentage of hospitalizations of infants, children with lung or congenital heart disease, the elderly and adults with immune-compromised systems. RSV infection typically results in cold-like symptoms, but can lead to more serious respiratory illnesses such as croup, pneumonia and bronchiolitis, and in extreme cases, severe illness and death. According to the Centers for Disease Control and Prevention, or CDC, RSV is responsible for up to an estimated

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100,000 pediatric hospitalizations each year in the United States. As a result, there is a significant need for novel therapeutics to treat patients who become infected with RSV.

Current Treatments. The only product currently approved for the treatment of RSV infection is Ribavirin, which is marketed as Virazole® by Valeant Pharmaceuticals International, or Valeant. This product has limited utilization, as it is approved only for treatment of hospitalized infants and young children with severe lower respiratory tract infections due to RSV. Moreover, administration of the drug is cumbersome and requires elaborate environmental reclamation devices because of potential harmful effects on healthcare personnel exposed to the drug.

Two products, a monoclonal antibody known as Synagis® and an immune globulin called Respigam®, have been approved for the prevention of severe lower respiratory tract disease caused by RSV in infants at high risk of such disease. Neither of these products is approved for *treatment* of an existing RSV infection.

Alnylam Program. In our pre-clinical testing, ALN-RSV01 was shown to be an RSV-specific siRNA that is effective in both preventing and treating RSV infection in mice when administered intranasally, or through the nose. ALN-RSV01 also showed no significant toxicities in IND-enabling toxicology studies. We submitted an IND for ALN-RSV01 to the United States Food and Drug Administration, or FDA, in November 2005, and initiated Phase I clinical trials on this experimental drug in December 2005 in both the United States and Europe and presented results from these trials in April 2006. ALN-RSV01 was found to be safe and well tolerated when administered intranasally in these two Phase I clinical studies. In October 2006, we initiated a Phase I study with an inhaled formulation of ALN-RSV01, and in November 2006, we initiated a human experimental infection study with an RSV strain designed to establish a safe and reliable RSV infection of the upper respiratory tract in adult volunteers.

Pandemic Flu

Market Opportunity. An influenza pandemic is a global outbreak that occurs when a new flu virus appears in the human population, causes serious illness and spreads easily from person to person. Over the last several years, a highly virulent new strain of avian flu known as H5N1 has become prevalent in the poultry population in Southeast Asia and caused significant mortality in humans that have been infected. Over the last year, H5N1 avian flu has also been detected in bird populations in Europe and Africa. The World Health Organization and CDC have expressed concern about the potential for this virus to mutate into a form that could cause a global pandemic of human disease. The market for pandemic flu therapies is expected to consist primarily of stockpiling by governments in preparation for possible future influenza pandemics.

Current Treatments. Current pharmaceutical products for the control of influenza infection fall into two main categories: vaccines and anti-viral drugs. Experts believe that current vaccines and existing anti-viral agents may not be sufficient to protect against newly emerging strains of influenza virus.

Effective flu vaccines are difficult to manufacture for two main reasons. First, the virus mutates constantly over time, undergoing sufficient change between one flu season and the next that a new vaccine must be manufactured each year. Second, the manufacturing process is very labor-intensive and time-consuming, requiring incubation of the virus in fertilized chick eggs into which it has been injected. For both of these reasons, experts are concerned that if a pandemic virus were to emerge, a new vaccine would be required and there would not be enough time to manufacture it.

There are four anti-viral flu drugs currently approved in the United States for the treatment of influenza. Two of these drugs, Symmetrel® (amantadine) and Flumadine® (rimantadine), are older drugs that belong to a class known as ion channel inhibitors, and resistance is widespread. The other two drugs, Relenza® (zanamivir) and Tamiflu® (oseltamivir), are newer drugs that are approved to prevent, as well as to treat, influenza. Both function by blocking

the activity of the viral protein known as neuraminidase, whose role is to promote release of newly replicated viruses from cells. Resistance to Tamiflu has been reported, and it cannot be known until a pandemic virus emerges how effective the current neuraminidase inhibitors will be in controlling this virus due to virus mutations.

Alnylam Program. The focus of our pandemic flu program is to develop an RNAi therapeutic targeting gene sequences that are highly conserved across known flu viruses. Our lead RNAi therapeutic is called ALN-FLU01 and is comprised of two siRNAs that target two distinct genes in the flu virus genome. We anticipate that the sequences

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targeted by ALN-FLU01 would remain largely unchanged in any newly emerging flu virus, so that our RNAi therapeutic could be effective in preventing and treating infection by a pandemic virus. We expect that ALN-FLU01 could be stockpiled by governments as part of their preparations for a flu pandemic. In December 2005, we were awarded initial funding for our pandemic flu program from DARPA. In connection with this program, in February 2006, we entered into a new collaboration with Novartis to develop RNAi therapeutics for pandemic flu.

Hypercholesterolemia

Market Opportunity. Coronary artery disease, or CAD, is the leading cause of mortality in the United States, responsible for 40% of all deaths annually. Hypercholesterolemia, measured as a high level of LDL cholesterol (LDL-c) in the blood, is one of the major risk factors for CAD. Although current therapies are effective in many patients, a large number of patients do not achieve adequate control of their high cholesterol level with existing treatments such as a statin. Studies have shown that this occurs in as many as 45% of patients. Currently in the United States there are almost 500,000 patients with high cholesterol levels not controlled by the use of existing lipid lowering therapies. These patients are said to have refractory or poorly controlled hypercholesterolemia and may constitute the target population for our product candidate ALN-PCS01.

Current Treatments. The current standard of care for patients with hypercholesterolemia includes the use of several agents. The first treatment often prescribed is a drug from the statin family. Commonly prescribed statins include Lipitor® (Atorvastatin), Zocor® (Simvastatin), Crestor® (Rosuvastatin) and Pravachol® (Pravastatin). A different type of drug such as Zetia® (Ezetimibe), which reduces dietary cholesterol uptake from the gut is increasingly being used on its own or in combination with a statin. Despite these therapies, there are many patients who have refractory or poorly controlled hypercholesterolemia and require more intensive treatment. In addition, some patients do not tolerate current treatments and at least 5% of those treated with a statin have to stop because of side-effects. In patients with very high uncontrolled cholesterol levels, a procedure called lipid apheresis is used that effectively removes cholesterol from the blood using a machine specifically designed for this process. However, this procedure is inconvenient and uncomfortable, requiring regular weekly visits to a doctor s office.

Alnylam Program. Pro-protein convertase subtilisn/kexin 9, otherwise known as PCSK9, is a widely acknowledged target for the treatment of hypercholesterolemia by lowering of LDL-c levels. PCSK9 is a protein that is produced by the liver but circulates in the bloodstream. The liver determines cholesterol levels, in part by taking up or absorbing LDL-c from the bloodstream. PCSK9 reduces the liver capacity to absorb LDL-c. Recent evidence indicates that if PCSK9 activity could be reduced then the liver should increase its uptake of LDL-c and blood cholesterol levels should decrease. In fact, some individuals have been shown to have a genetic mutation in PCSK9 that lowers its activity and results in increased liver LDL-c uptake and lowered blood cholesterol levels. In turn, these individuals have been shown to have a dramatically reduced risk of CAD (e.g., myocardial infarction or heart attack). In July 2006, we announced a collaboration with the University of Texas Southwestern to develop RNAi therapeutics targeting PCSK9. In mouse models, our RNAi therapeutic ALN-PCS01, directed against PCSK9, has been shown to be effective at silencing the human and mouse PCSK9 genes, as well as, blood cholesterol levels.

Discovery Programs

In addition to our development efforts on RSV, pandemic flu and hypercholesterolemia, we are conducting research activities to discover RNAi therapeutics to treat various diseases of the respiratory system and the nervous system. The diseases for which we have discovery programs include:

Progressive Multifocal Leukoencephalopathy, or PML. PML is caused by infection of the central nervous system, or CNS, with a virus called JC virus and can occur in certain immune-suppressed patients, including those receiving immunomodulatory therapies. Under our collaboration with Biogen Idec, we will initially

conduct investigative research into the potential of using RNAi technology to discover and develop therapeutics to treat PML. The goal of the program is to design and optimize an RNAi therapeutic toward conserved regions of the JC viral genome to harness the cell s own capabilities to achieve an anti-viral therapeutic effect.

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Ebola Virus. The Ebola virus is a type of hemorrhagic fever virus that can cause severe, often fatal, infection and poses a potential biological safety risk and bioterrorism threat. Under our contract with the NIAID, we are seeking to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus.

Cystic fibrosis, or CF. CF is an inherited respiratory disorder caused by mutations in the gene for a protein known as the cystic fibrosis transmembrane conductance regulator, or CFTR. In most CF patients, potentially functional CFTR protein is produced but does not reach the cell surface. We are attempting to redirect this CFTR protein to the cell surface using RNAi therapeutics to silence specific genes involved in protein processing within the cell. We are conducting this work in collaboration with, and with funding from, CFFT, the drug discovery and development affiliate of the Cystic Fibrosis Foundation.

Spinal cord injury, or SCI. Our SCI program is focused on a cellular system known as the Nogo pathway that appears to play a key role in blocking the regeneration of nerves in the spinal cord and brain after injury. In collaboration with Merck, we are seeking to develop an RNAi therapeutic that inhibits this pathway, thereby allowing nerves to regenerate, and potentially reducing or treating paralysis, after SCI.

Huntington s disease, or HD. HD is a fatal, inherited and progressive brain disease that results in uncontrolled movements, loss of intellectual faculties and emotional disturbance. HD patients produce an altered form of a protein known as huntingtin whose presence is believed to trigger the death of important cells in the brain. In collaboration with Medtronic, we are seeking to develop a novel drug-device product incorporating an RNAi therapeutic that will protect these cells by suppressing production of huntingtin.

Parkinson s disease, or PD. PD is a progressive brain disease characterized by uncontrollable tremor, and in some cases, may result in dementia. Like HD, PD is believed to result from the death of certain cells in the brain, which in some cases is triggered by the presence of abnormally large amounts of a protein called alpha-synuclein. Our goal is to develop an RNAi therapeutic that will protect these cells by suppressing production of alpha-synuclein.

Neuropathic pain. Neuropathic pain is chronic pain that results from injury or dysfunction of the nervous system. A protein called NaV1.8 is believed to play an important role in causing neuropathic pain. The goal of our program is to develop an RNAi therapeutic that will suppress the production of NaV1.8 and thereby alleviate neuropathic pain.

In addition to these programs, as part of our collaborations with Merck and Novartis, we have research activities to discover RNAi therapeutics directed to a number of other undisclosed targets.

microRNA Technology Program

In addition to our efforts on siRNAs, we are adapting our product platform to address the therapeutic possibilities offered by microRNAs, a recently discovered class of small RNAs that use the RNAi pathway to regulate genes and have been implicated in various human diseases. In animal experiments published in *Nature* in December 2005, we and our collaborators demonstrated that we could silence microRNAs using antagomirs , a potential new class of drugs we designed for this purpose. We believe that antagomirs may become an important component of our longer-term product platform for the development of RNAi therapeutics.

Strategic Alliances and Licenses

Strategic Alliances

We have formed and intend to form strategic alliances to gain access to the financial, technical, clinical and commercial resources necessary to develop and market RNAi therapeutics. We expect these alliances to provide us with financial support in the form of upfront cash payments, equity investments, research and development funding, license fees, milestone payments and royalties or profit sharing based on sales of RNAi therapeutics.

Novartis. We have formed two alliances with Novartis. We refer to the first of these, which was initiated in September 2005, as the broad Novartis alliance, and to the second, which was initiated in February 2006, as the Novartis flu alliance.

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In connection with the broad Novartis alliance, we entered into a series of transactions with Novartis beginning in September 2005. At that time, we and Novartis executed a stock purchase agreement and an investor rights agreement. When the transactions contemplated by the stock purchase agreement closed in October 2005, the investor rights agreement became effective, and we and Novartis executed a research collaboration and license agreement. Under the terms of the stock purchase agreement, in October 2005, Novartis purchased approximately 5.3 million shares of our common stock at a purchase price of $11.11 per share for an aggregate purchase price of approximately $58.5 million, which, immediately after such issuance, represented 19.9% of our then outstanding common stock. Novartis owned approximately 14% of our common stock as of December 31, 2006.

Under the terms of the collaboration and license agreement, we agreed with Novartis to work together on selected targets, as defined in the collaboration and license agreement, to discover and develop therapeutics based on RNAi. The collaboration and license agreement has an initial term of three years and may be extended for two additional one-year terms at the election of Novartis. In addition, Novartis may terminate the collaboration and license agreement after a period of two years under specified circumstances or in the event that we materially breach our obligations. We may terminate the agreement with respect to particular programs, products and/or countries in the event of specified material breaches by Novartis of its obligations, or in its entirety under specified circumstances for multiple such breaches. In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an upfront payment of $10.0 million to us in October 2005, partly to reimburse prior costs incurred by us to develop *in vivo* RNAi technology. In addition, the collaboration and license agreement includes terms under which Novartis will provide us with research funding and milestone payments as well as royalties on annual net sales of products resulting from the collaboration. The collaboration and license agreement also provides Novartis with a non-exclusive option to integrate our intellectual property relating to RNAi technology into Novartis operations under specified circumstances. In connection with the exercise of the integration option, Novartis would be required to make additional payments to us. Under the terms of the collaboration and license agreement, we retain the right to discover, develop, commercialize or manufacture compounds that function through the mechanism of RNAi, or products that contain such compounds as an active ingredient, with respect to targets not selected by Novartis for inclusion in the collaboration, provided that Novartis has a right of first offer in the event that we propose to enter into an agreement with a third party with respect to any such target.

Under the terms of the investor rights agreement, we granted Novartis demand and piggyback registration rights under the Securities Act of 1933 for the shares of our common stock held by Novartis. We also granted to Novartis rights to acquire additional equity securities in the event that we propose to sell or issue any equity securities, subject to specified exceptions, as described in the investor rights agreement, such that Novartis would be able to maintain its ownership percentage in us. Novartis agreed, until the later of (1) October 12, 2008 and (2) the date of termination or expiration of the selection term, as defined in the collaboration and license agreement, not to acquire any of our securities, other than an acquisition resulting in Novartis and its affiliates beneficially owning less than 20% of our total outstanding voting securities, participate in any tender or exchange offer, merger or other business combination involving us or seek to control or influence our management, board of directors or policies, subject to specified exceptions described in the investor rights agreement.

In February 2006, we entered into the Novartis flu alliance. The agreement governing the flu alliance is structured as an addendum to the collaboration and license agreement for the broad Novartis alliance. This addendum supplements and, to the extent described therein, supersedes in relevant part the collaboration and license agreement for the broad Novartis alliance. Under the terms of the addendum, we and Novartis have joint responsibility for the development of RNAi therapeutics for pandemic flu. Novartis will have primary responsibility for commercialization of any such RNAi therapeutics worldwide, but we will be actively involved, and may in certain circumstances take the lead, in commercialization in the United States. We are eligible to receive significant funding from Novartis for our efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits.

Merck. In July 2006, we amended and restated our research collaboration and license agreement with Merck, dated September 8, 2003, as amended. Our collaboration with Merck is focused on developing RNAi therapeutics for targets associated with human diseases and, under the terms of the amended and restated license agreement, will focus on the nine targets that then remained to be nominated by Merck under the terms of the

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original license agreement. These nine programs are in addition to the existing program directed to the Nogo pathway on which we were already working with Merck under the terms of the original agreement. We may select three of the nine additional programs as joint development programs, which Merck will co-fund and participate in from the outset. In October 2006, we selected a co-development program from the first three targets presented by Merck under the amended and restated license agreement. The amended and restated license agreement provides funding from Merck immediately for programs selected by us for co-development, and provides that, in the United States, we will have the right to co-promote RNAi therapeutic products developed in these three co-development programs. Merck will assume primary responsibility for the remaining six programs and we are eligible to receive milestone payments and royalties on any RNAi therapeutic products developed and commercialized by Merck in these six programs. The initial term of the collaboration under the amended and restated license agreement ends in September 2008 and, unless earlier terminated, will continue until the date on which no product is being developed or commercialized under the agreement. Unless earlier terminated, the amended and restated license agreement shall continue in effect until the expiration of all royalty obligations and profit-sharing obligations under the agreement.

Also in July 2006, we and Merck agreed to terminate the collaboration and license agreement, effective as of June 29, 2004, pursuant to which we were collaborating in the research, development and commercialization of RNAi products directed to certain ocular targets, including but not limited to, vascular endothelial growth factor, or VEGF. In connection with the termination of the ocular collaboration agreement, and subject to certain royalty and other obligations, we have retained our rights to develop, manufacture and commercialize ophthalmic products directed to VEGF and Merck has granted us a license under certain of its technology solely to develop, manufacture and commercialize RNAi products directed to VEGF.

Medtronic. In February 2005, we entered into a collaboration with Medtronic to pursue the potential development of therapeutic products for the treatment of neurodegenerative disorders such as Parkinson s, Huntington s and Alzheimer s disease. The collaboration is focused on developing novel drug-device combinations incorporating RNAi therapeutic products. Currently, we are engaged in a joint technology development program with Medtronic through April 2007. This initial joint technology development program is focused on delivering candidate RNAi therapeutic products to specific areas of the brain using implantable infusion systems.

After successful completion of the initial joint technology development program, the parties must jointly determine whether to initiate product development. If the parties jointly decide to initiate product development, we would be responsible for the discovery and early development of candidate RNAi therapeutic products, and Medtronic would be responsible for late-stage development and commercialization of any drug-device products that result. Medtronic also would adapt or develop medical devices to deliver the candidate RNAi therapeutic products to targeted locations in the nervous system.

After successful completion of the initial joint technology development program and a joint decision to initiate product development, Medtronic would make an initial equity investment in us and could make additional investments upon successful completion of specified milestones. The aggregate amount of our common stock that Medtronic would purchase, if a joint decision were made to initiate product development and the specified milestones were successfully completed, would be $21.0 million. The amount of the investment to be made at the time of the joint decision to initiate product development would be between $1.0 million and $8.0 million, as determined by us, at the then-current market price, as determined under the agreement. The remaining investments of between $13.0 million and $20.0 million would be made upon the achievement of the specified milestones at a purchase price equal to 120% of the then-current market price, as determined under the agreement. If either party decides not to initiate product development under the collaboration agreement, Medtronic would not be required to make any equity investment in us. We would also be eligible to receive additional cash milestone payments for each product developed and royalties on sales of any RNAi therapeutic component of novel drug-device combinations that result from the collaboration.

Biogen Idec. In September 2006, we entered into a collaboration and license agreement with Biogen Idec. The collaboration is focused on the discovery and development of therapeutics based on RNAi for the potential treatment of PML. We and Biogen Idec will initially conduct investigative research into the potential of RNAi technology to develop therapeutics to treat PML. Under the terms of the collaboration agreement with Biogen Idec,

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we granted Biogen Idec an exclusive license to distribute, market and sell certain RNAi therapeutics to treat PML and Biogen Idec has agreed to fund all related research and development activities. We also received an upfront $5.0 million payment from Biogen Idec. In addition, upon the successful development and utilization of a product resulting from the collaboration, Biogen Idec would be required to pay us milestone and royalty payments.

NIH. In September 2006, we were awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus, with the NIAID, a component of the NIH. The federal contract will provide us with up to $23.0 million in funding over a four-year period to develop RNAi therapeutics as anti-viral drugs targeting the Ebola virus. The Ebola virus can cause a severe, often fatal infection, and poses a potential biological safety risk and bioterrorism threat. Of the $23.0 million in funding, the government has committed to pay us $14.2 million over the first two years of the contract and, subject to the progress of the program and budgetary considerations in future years, the remaining $8.8 million over the last two years of the contract.

Isis. In March 2004, we entered into a collaboration and license agreement with Isis, a leading developer of antisense oligonucleotide drugs that target RNA. The agreement enhanced our intellectual property position with respect to RNA-based therapeutic products and our ability to develop siRNAs for RNAi therapeutic products, and provided us with the opportunity to defer investment in manufacturing technology. Isis granted us licenses to its current and future patents and patent applications relating to chemistry and to RNA-targeting mechanisms for the research, development and commercialization of siRNA products. We have the right to use Isis technologies in our development programs or in collaborations, and Isis has agreed not to grant licenses under these patents to any other organization for any siRNA products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. We granted Isis non-exclusive licenses to our current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. We also granted Isis the exclusive or co-exclusive right to develop and commercialize siRNA products against a limited number of targets. In addition, we granted Isis non-exclusive rights to our patents and patent applications for research, development and commercialization of antisense RNA products.

Under the terms of our agreement, we agreed to pay Isis an upfront license fee of $5.0 million, milestone payments payable upon the occurrence of specified development and regulatory events and royalties for each product that we or a collaborator develop utilizing Isis intellectual property. In addition, we agreed to pay to Isis a percentage of specified fees from strategic collaborations we may enter into that include access to the Isis intellectual property. In conjunction with the agreement, Isis made a $10.0 million equity investment in us. Isis also agreed to pay us a license fee, milestone payments payable upon the occurrence of specified development and regulatory events and royalties for each product developed by Isis or a collaborator that utilizes our intellectual property. The agreement also gives us an option to use Isis manufacturing services for RNA-based therapeutic products.

Our agreement with Isis also gives us the exclusive right to grant sub-licenses for Isis technology to third parties with whom we are not collaborating. We may include these sub-licenses in our InterfeRx licenses. If a license includes rights to Isis intellectual property, we will share revenues from that license equally with Isis.

If, by January 1, 2008, we or a collaborator have not completed the studies required for an IND submission or similar foreign filing for at least one product candidate involving the patent rights covered by our agreement, Isis would have the right to grant licenses to third parties for the patents and patent applications licensed to us, thereby making our rights non-exclusive.

Inex. In January 2007, Inex granted us an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics. In addition, 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 certain intellectual property to develop oligonucleotide immune stimulatory drugs that do not

function through an RNAi mechanism.

In connection with Inex s license grant to us, we issued Inex 361,990 shares of our common stock, valued at $8.0 million, in a private placement in January 2007, and in February 2007 we paid them an additional $0.4 million.

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We have also agreed to make available to Inex a $5.0 million loan for capital equipment expenditures related to manufacturing services performed by Inex for us. In addition, we will be required to pay Inex up to $13.0 million in development and commercialization milestone payments for each product we develop utilizing technology Inex has licensed to us.

Licenses

To generate revenues from our intellectual property rights, we have established our InterfeRx program, and our research reagents and services licensing program.

InterfeRx Program. Our InterfeRx program consists of the licensing of our intellectual property to others for the development and commercialization of RNAi therapeutic products relating to specific targets outside our areas of strategic focus. We expect to receive license fees, annual maintenance fees, milestone payments and royalties on sales of any resulting RNAi therapeutic products. Generally, we do not expect to collaborate with our InterfeRx licensees in the development of RNAi therapeutic products, but may do so in appropriate circumstances. To date, we have granted InterfeRx licenses to four companies: GeneCare in January 2005, Nastech in July 2005, Calando in August 2006 and Quark in September 2006. In the case of GeneCare, the license allows GeneCare to discover, develop, and commercialize RNAi therapeutic products directed against two DNA helicase genes associated with cancer. We retained the right to negotiate co-development and co-promotion arrangements with GeneCare for such products in the United States. In the case of Nastech, the license allows Nastech to discover, develop and commercialize RNAi therapeutic products directed against tumor necrosis factor-alpha, or TNF-alpha, the target of several drugs approved for the treatment of rheumatoid arthritis and other conditions. In the case of Calando, the license allows Calando to discover, develop and commercialize RNAi therapeutic products directed against an undisclosed cancer-associated gene target. In the case of Quark, the license allows Quark to discover, develop and commercialize RNAi therapeutic products targeting the p53 gene for the treatment of renal failure and the RTP801 gene for the treatment of macular degeneration. In each case, we received an upfront cash payment, and expect to receive annual and milestone payments, all in cash, and royalties on sales of any products that result from the licensing agreement.

In April 2005, we entered into an agreement with Benitec, under which we granted Benitec options to take up to five InterfeRx exclusive licenses to pursue synthetic RNAi therapeutic products against mutually agreed, specific targets in return for license fees, milestone payments and royalties. Under the same agreement, we also granted Benitec options to non-exclusively license our intellectual property in the field of expressed RNAi, that is, RNAi mediated by siRNAs generated from DNA constructs introduced into cells. If Benitec were to exercise any of these options, we would receive license fees and be entitled to receive milestone payments and royalties on any expressed RNAi products developed by Benitec or its licensees.

Research Reagents and Services. We have granted licenses to our intellectual property for the development and commercialization of research reagents and services, and intend to enter into additional licenses on an ongoing basis. Our target licensees are vendors that provide siRNAs and related products and services for use in biological research. We offer these licenses in return for an initial license fee, annual renewal fees and royalties from sales of siRNA research reagents and services. No single research reagent or research services license is material to our business.

Patents and Proprietary Rights

We have devoted considerable effort and resources to establish what we believe to be a strong position in intellectual property relevant to RNAi therapeutic products and delivery technologies. In this regard, we have focused on patents, patent applications and other intellectual property covering:

fundamental aspects of the structure and uses of siRNAs, including their use as therapeutics, and RNAi-related mechanisms;

chemical modifications to siRNAs that improve their suitability for therapeutic uses;

siRNAs directed to specific targets as treatments for particular diseases; and

delivery technologies, such as in the field of cationic liposomes.

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Intellectual Property Related to Fundamental Aspects and Uses of siRNA and RNAi-related Mechanisms

In this category, we include patents and patent applications that claim key aspects of siRNA architecture and RNAi-related mechanisms. Specifically, we include patents and patent applications relating to targeted cleavage of mRNA directed by RNAi-like oligonucleotides, double-stranded RNAs of particular lengths and particular structural features of these dsRNAs, such as overhanging ends and uses of these dsRNAs. Our strategy has been to secure rights to the potentially key patents and patent applications covering the fundamental aspects of siRNAs on an exclusive basis where possible or appropriate. The following table lists patents or patent applications to which we have secured rights that we regard as being potentially fundamental for the use of siRNAs as therapeutics.

Licensor/Patent Owner	Subject Matter	First Priority Date	Inventors	Status*	Alnylam Rights
Isis Pharmaceuticals	Inactivation of target mRNA	6/6/1996 and 6/6/1997	S. Crooke	Issued in the U.S. (U.S. Patent Nos. 5,898,031 & 6,107,094), pending in the rest of world	Exclusive rights for therapeutic purposes related to siRNAs**
Carnegie Institution of Washington	Double-stranded RNAs to induce RNAi	12/23/1997	A. Fire, C. Mello	Issued in the U.S. (U.S. Patent No. 6,506,559), pending in the rest of world	Non-exclusive rights for therapeutic purposes
Alnylam	Small double-stranded RNAs as therapeutic products	1/30/1999	R. Kreutzer, S. Limmer	Granted in the EU (EP 1144623 & EP 1214945) and Australia (AU 778474), granted in Germany (DE 20023125 U1) pending in the rest of world	Owned
Cancer Research Technology Limited	RNAi uses in mammalian cells	11/19/1999	M. Zernicka-Goetz, M.J. Evans, D.M. Glover	Granted in the EU (EP 1230375), Singapore (89569) Australia (AU 774285) pending in the rest of world	Exclusive rights for therapeutic purposes
Massachusetts Institute of Technology, Whitehead Institute, Max Planck Gesellschaft***	Mediation of RNAi by siRNAs containing 21-23 base pairs	3/30/2000	D.P. Bartel, P.A. Sharp, T. Tuschl, P.D. Zamore	Pending worldwide	Non-exclusive rights for therapeutic purposes***
Max Planck Gesellschaft	Synthetic siRNAs as therapeutic products	12/01/2000 04/24/2004 and 04/27/2004	T. Tuschl, S. Elbashir, W. Lendeckel	Issued in the U.S. (U.S. Patent Nos. 7,056,704 & 7,078,196), additional	Exclusive rights for therapeutic purposes

				pending in the U.S. and rest of the world	
Cold Spring Harbor Laboratory	RNAi uses in mammalian cells	3/16/2001	D. Beach, G. Hannon	Pending worldwide	Non-exclusive rights for therapeutic purposes
Stanford University	RNAi uses *in vivo*	7/23/2001	M.A. Kay, A.P. McCaffrey	Pending worldwide	Co-exclusive rights for therapeutic purposes

* The patent term generally is 20 years from the earliest application filing date. However, under the Drug Price Competition and Patent Term Extension Act of 1984, known as the Hatch-Waxman Act, we may be able to apply for patent term extensions for our U.S. patents. We cannot predict whether or not any patent term extensions will be granted or the length of any patent term extension that might be granted.

** We hold co-exclusive therapeutic rights with Isis. However, Isis has agreed not to license such rights to any third party, except in the context of a collaboration in which Isis plays an active role.

*** We hold exclusive rights to the interest owned by three of four co-owners. The fourth co-owner, the University of Massachusetts, has licensed its interest separately to third parties.

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We believe we have a strong portfolio of broad and exclusive rights to fundamental siRNA patents and patent applications. In securing these rights, we have focused on obtaining the strongest rights for those intellectual property assets we believe will be most important in providing competitive advantage with respect to RNAi therapeutic products. We note in particular the first, third and sixth patents and patent applications listed in the table above, those covering inventions by Dr. Crooke, by Dr. Kreutzer and Dr. Limmer and by Dr. Tuschl and his colleagues. We believe that the so-called Crooke patent, issued worldwide, is a broad patent covering the use of modified oligonucleotides to achieve enzyme-mediated cleavage of a target mRNA and, as such, has broad issued claims that cover RNAi. We have obtained rights to the Crooke patent through a license agreement with Isis. Under the terms of our license agreement, Isis agreed not to grant licenses under this patent to any other organization for siRNA products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. We believe the so-called Kreutzer-Limmer European patent was the first patent granted that specifically covers the use of small dsRNAs as therapeutics. Through our acquisition of Ribopharma AG, now known as Alnylam Europe AG, we own this patent, as well as corresponding patent applications in other countries, including the United States. The patent applications filed by Max Planck Gesellschaft zur Förderung der Wissenschaften e.V, which we refer to as Max Planck Gesellschaft, on the invention by Dr. Tuschl and his colleagues, or the Tuschl II patent application, cover what we believe are key structural features of siRNAs, namely the presence of overhangs at the 3 -end of each of the two strands and the use of chemical modifications to stabilize siRNAs. On June 6, 2006, the USPTO issued U.S. Patent No. 7,056,704 and then on July 18, 2006 the USPTO issued U.S. Patent No. 7,078,196, covering methods of making dsRNAs having a 3 overhang structure. We have obtained an exclusive license to claims in the Tuschl II patent series uniquely covering the use of RNAi for therapeutic purposes.

The Fire and Mello patent owned by the Carnegie Institution covers the use of dsRNAs to induce RNAi. The Carnegie Institution has made this patent broadly available for licensing and we, like many companies, have taken a non-exclusive license to the patent for therapeutic purposes. We believe, however, that the Fire and Mello patent does not claim specific structural features of dsRNAs that are important for the biological activity of siRNAs in mammalian cells. These specific features are the subjects of the Crooke patent, the Kreutzer-Limmer patent and the Tuschl II patent application for which we have secured exclusive rights.

A first Kreutzer-Limmer European patent, EP 1144623, was granted by the EPO in 2002, by Australia IP in December 2004 (AU 778474) and is pending in other countries, including the United States. In addition, a German Utility Model covering RNAi composition was branched off the European patent application, and was registered by the German Patent and Trademark Office in 2003. A German Utility Model is a form of patent that is directed only to physical matter, such as medicines, and does not cover methods.

The grant of a second European patent from the Kreutzer-Limmer series, EP 1214945, originating from a divisional application of EP 1144623, was published by the EPO on June 8, 2005. This patent further extends the coverage of the first granted EP patent covering critical aspects of dsRNA structure. Sirna, which was acquired by Merck in December 2006, and SR Pharma appealed the September 2006 decision of the Opposition Division of the European Patent Office to uphold the Kreutzer-Limmer patent (EP 1144623).

The other pending patent applications listed in the table above either provide further coverage for structural features of siRNAs or relate to the use of siRNAs in mammalian cells. For some of these, we have exclusive rights, and for others, we have non-exclusive rights. While we believe these pending patent applications are important, we also believe that access to the Crooke patent, the Kreutzer-Limmer patent and the Tuschl II patent application will be of particular importance for development and commercialization of RNAi therapeutic products, which is why we have secured exclusive rights with respect to these assets.

Intellectual Property Related to Chemical Modifications

Our collaboration and license agreement with Isis provides us with rights to use over 150 issued patents relating to chemical modifications we may wish to incorporate into our RNAi therapeutic products and rights based on future chemistry patent applications filed in the next five years to which it has rights. Under the terms of our license agreement, Isis agreed not to grant licenses under these patents to any other organization for dsRNA

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products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role.

In addition to licensing these intellectual property rights from Isis, we are also working to develop our own proprietary modifications that we can apply to siRNAs to endow them with drug-like properties. We have filed a number of patent applications relating to novel chemical modifications that we may apply to siRNAs.

In addition, a patent in the Tuschl II patent series (U.S. Patent No. 7,078,196) recently issued in the United States includes claims that cover methods of making siRNAs that incorporate any of various chemical modifications, including the use of phosphorothioates, 2 -O-methyl, and/or 2 -fluoro modifications, without any limitation on the number of such modifications. These internal and backbone modifications are believed to be important for achievement of drug-like properties for RNAi therapeutics. We hold exclusive worldwide rights to these claims for RNAi therapeutics.

Intellectual Property Related to siRNAs Directed to Specific Targets

We have also filed a number of patent applications claiming specific siRNAs directed to a large number of targets as treatments for specific diseases. We recognize, however, that there may be a significant number of competing applications filed by other organizations on similar siRNAs. Because our subsidiaries, Alnylam Europe and Alnylam U.S., were among the first companies to focus on RNAi therapeutics, we believe that a number of our patent applications may predate competing applications that others may have filed. Reflecting this, in August 2005, the EPO granted a broad patent, which we call the Kreutzer-Limmer II patent, with 103 allowed claims on therapeutic compositions, methods and uses comprising siRNAs that are complementary to all mRNA sequences in over 125 disease target genes. These genes include targets that are part of our development and pre-clinical programs, such as those expressed by viral pathogens including RSV and influenza virus. In addition, the claimed targets include oncogenes, cytokines, cell adhesion receptors, angiogenesis targets, apoptosis and cell cycle targets, and additional viral disease targets, such as hepatitis C virus and HIV. Moreover, a patent in the Tuschl II patent series (U.S. Patent No. 7,078,196) recently issued in the United States claims methods for preparing siRNAs which mediate cleavage of an mRNA in mammalian cells, and therefore cover siRNAs directed toward any and all target genes, including those derived from viruses, expressed in mammalian cells. We hold exclusive worldwide rights to these claims for RNAi therapeutics.

With respect to specific siRNAs, we believe that the most important patent coverage will ultimately result from demonstrating that particular compositions exert suitable biological and therapeutic effects. Accordingly, we are focused on achieving such demonstrations for siRNAs in key therapeutic programs.

Intellectual Property Related to the Delivery of siRNAs to Cells

Recently, we have expanded our areas of focus to encompass more aspects of the delivery of siRNAs to cells within a mammal. To achieve this we have obtained an exclusive license from the University of British Columbia and Inex in the field of RNAi therapeutics to intellectual property covering cationic liposomes and their use to deliver nucleic acid to cells. The issued U.S. and foreign patents, including U.S. Patent Nos. 5,976,567, 6,815,432 and 6,858,225, cover compositions, methods of making and methods of using cationic liposomes to deliver agents, such as nucleic acid molecules to cells.

Competition

The pharmaceutical marketplace is extremely competitive, with hundreds of companies competing to discover, develop and market new drugs. We face a broad spectrum of current and potential competitors, ranging from very

large, global pharmaceutical companies with significant resources to other biotechnology companies with resources and expertise comparable to our own. We believe that for most or all of our drug development programs, there will be one or more competing programs in other companies. In many cases, the companies with competing programs will have access to greater resources and expertise than we do and may be more advanced.

The competition we face can be grouped into three broad categories:

- other companies working to develop RNAi therapeutic products;

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companies developing technology known as antisense, which, like RNAi, attempts to silence the activity of specific genes by targeting the mRNAs copied from them; and

marketed products and development programs that compete with the drugs we may try to develop.

Other Companies Working to Develop RNAi Therapeutic Products

We are aware of several other companies that are working to develop RNAi therapeutic products. Some of these companies are seeking, as we are, to develop chemically synthesized siRNAs as drugs. Others are following a gene therapy approach, with the goal of treating patients not with synthetic siRNAs but with genes designed to produce siRNA-like molecules within cells.

Companies working on chemically synthesized siRNAs include Sirna, a subsidiary of Merck, Acuity Pharmaceuticals, Inc., or Acuity, Nastech, Calando, Quark, Nucleonics, SR Pharma, RXi Pharmaceuticals Corporation, or RXi, a subsidiary of CytRx Corporation, or CytRx, Protiva Biotherapeutics, Inc., or Protiva, and Intradigm, Inc., or Intradigm. Many of these companies have taken licenses to Alnylam intellectual property on a target-by-target basis.

Sirna, which was acquired by Merck in December 2006, has approximately ten years prior experience working to develop RNA molecules as drugs. This experience was largely gained with a different class of RNA molecules known as ribozymes, but could potentially be relevant for siRNAs. During 2004, Sirna initiated Phase I human clinical trials related to the development of Sirna-027, a candidate RNAi therapeutic designed to treat age-related macular degeneration, or AMD, by blocking VEGF activity. In September 2005, Sirna announced an alliance with Allergan, Inc. to develop Sirna-027 and to discover and develop other novel RNAi therapeutics against select gene targets in ophthalmic diseases. In December 2005, Sirna announced that it had selected a development candidate in its program to develop RNAi therapeutics for the treatment of hepatitis C infection. In April 2006, Sirna announced a multi-year alliance with GlaxoSmithKline to discover, develop and commercialize RNAi-based therapeutics for respiratory diseases, such as asthma, COPD and viral infections, including RSV.

Acuity initiated a Phase II human clinical trial in 2005 for a candidate RNAi therapeutic designed to treat AMD, formerly called Cand5 and now termed bevasiranib, by blocking VEGF activity. In June 2006, Acuity reported Phase II data claiming bevasiranib appeared safe and well tolerated in human subjects. Acuity has announced plans to initiate Phase III studies.

Nastech is developing an RNAi therapeutic directed against TNF-alpha under license from us. Separately, Nastech announced in February 2006 a program to develop RNAi therapeutics for pandemic flu and its acquisition of a flu RNAi program from Galenea Corporation. Nastech has received federal grants from the NIH to support further development of their flu program.

Calando, which is focused on RNAi therapeutics for the treatment of cancer, announced in February 2006 that it has established a collaborative development program relating to RNAi therapeutics with the National Cancer Institute of the NIH, with the goal of developing RNAi therapeutic products to target neuroblastoma. In October 2006, Calando announced preclinical data from an anti-cancer program targeting M2 subunit of ribonucleotide reductase. Calando has a license from us to develop and commercialize RNAi therapeutic products directed against an undisclosed cancer-associated gene target.

Quark is working on discovering and developing RNAi therapeutic products targeting the p53 gene for the treatment of renal failure and the RTP801 gene for the treatment of macular degeneration. Quark has licenses from us to develop and commercialize these RNAi therapeutic programs.

RXi, a subsidiary of CytRx, is focusing on developing RNAi therapeutics for various diseases including neurodegenerative disease, type 2 diabetes and obesity. In January of 2007, CytRx contributed all of its RNAi assets to RXi including licenses to RNAi intellectual property from the University of Massachusetts Medical School.

SR Pharma and its Atugen AG subsidiary are working on synthetic siRNA molecules as therapeutics for oncology. SR Pharma announced in January 2007 preclinical toxicology data on its lead program, Atu027, for systemic cancer indications.

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Protiva is developing RNAi therapeutics using a cationic liposome delivery technology called SNALP (stable nucleic acid-lipid particles). Alnylam and Protiva have collaborated on delivery technologies for RNAi therapeutics. Protiva is involved in a legal dispute with Inex regarding ownership rights to certain Protiva intellectual property for delivery of RNAi therapeutics with cationic liposomes.

Intradigm is developing RNAi therapeutics using a polymer delivery technology. In November 2006, Intradigm announced that it raised $16.0 million in a Series A financing.

Companies working on gene therapy approaches to RNAi therapeutics include Nucleonics, Inc., Benitec and Cequent, Inc.

Other Companies Working to Develop Antisense Technology

Antisense technology uses short, single-stranded, DNA-like molecules known as oligonucleotides to block mRNAs encoding specific proteins. An antisense oligonucleotide, or ASO, contains a sequence of bases complementary to a sequence within its target mRNA, enabling it to attach to the mRNA by base-pairing. The attachment of the ASO may lead to breakdown of the mRNA, or may physically block the mRNA from associating with the protein synthesis machinery of the cell. In either case, production of the protein encoded by the mRNA may be reduced. Typically, the backbone of an ASO, the linkages that hold its constituent bases together, will carry a number of chemical modifications that do not exist in naturally occurring DNA. These modifications are intended to improve the stability and pharmaceutical properties of the ASO.

While we believe that RNAi drugs may potentially have significant advantages over ASOs, including greater potency and specificity, others are developing ASO drugs that are currently at a more advanced stage of development than RNAi drugs. For example, Isis has developed an ASO drug, Vitravene®, which is currently on the market, and has several ASO drug candidates in clinical trials. This includes ISIS 301012, which targets a gene called apolipoprotein B and is in Phase II clinical testing for hypercholesterolemia. Isis also has a pre-clinical program with ASOs targeting PCSK9 for hypercholesterolemia. In addition, a number of other companies have product candidates in various stages of pre-clinical and clinical development. Included in these companies is Genta Incorporated, which has a drug candidate known as Genasense®, a potential treatment for various forms of cancer. AVI BioPharma, Inc. is developing ASOs based on a type of chemistry called Morpholinos and is currently working on a program targeting Ebola and influenza. Because of their later stage of development, ASOs, rather than siRNAs, may become the preferred technology for drugs that target mRNAs in order to turn off the activity of specific genes.

Competing Drugs for RSV

The only product currently approved for the treatment of RSV infection is Ribavirin, which is marketed as Virazole® by Valeant. This is approved only for treatment of hospitalized infants and young children with severe lower respiratory tract infections due to RSV. However, Ribavirin has been reported to have limited efficacy and limited anti-viral activity against RSV. Moreover, administration of the drug is cumbersome and requires elaborate environmental reclamation devices because of potential harmful effects on health care personnel exposed to the drug. According to published reports by Valeant, sales of Virazole were $16.6 million in 2006. Other current RSV therapies consist of primarily treating the symptoms or preventing the viral infection by using the prophylactic drug Synagis® (palivizumab), which is marketed by MedImmune, Inc. Synagis is a neutralizing monoclonal antibody that prevents the virus from infecting the cell by blocking the RSV F protein. Synagis is injected intramuscularly once a month during the RSV season to prevent infection. According to published reports by MedImmune, Synagis sales were $1.1 billion in 2006.

Competing Drugs for Pandemic Flu

Four drugs are currently approved in the U.S. for the treatment of influenza. Two of these drugs, Symmetrel® and Flumadine®, are older drugs that belong to a class known as ion channel inhibitors. The other two drugs, Relenza® and Tamiflu®, were approved relatively recently and function by blocking the activity of the viral neuraminidase protein. Flumadine, Relenza and Tamiflu are approved to prevent as well as to treat influenza.

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Symmetrel and Flumadine are effective only against influenza A viruses, and resistance is widespread. Tamiflu and Relenza are effective against both influenza A and the other main type that causes seasonal epidemics, influenza B. Resistance to Tamiflu has been reported.

The manufacturer of Tamiflu, F. Hoffman-LaRoche Ltd, or Roche, reported that 2005 sales of Tamiflu totaled 1.6 billion Swiss francs, or approximately $1.2 billion. Roche reported that these sales were driven by a severe influenza season in Japan early in the year and increased orders for pandemic readiness supplies, with over 60 countries having placed orders for pandemic stocks of Tamiflu, in some cases purchasing enough to cover 25% to 40% of their populations.

GlaxoSmithKline Plc, the manufacturer of Relenza, said in February 2006 that it expects production of Relenza in 2007 to exceed the 15 million dose output in 2006, all of which had already been sold out.

Competing Drugs for Hypercholesterolemia

The current standard of care for patients with hypercholesterolemia includes the use of several agents. Front line therapy consists of HMG CoA reductase inhibitors, commonly known as statins, which block production of cholesterol by the liver and increase clearance of LDL-c from the bloodstream. These include Lipitor®, Zocor®, Crestor® and Pravachol®. A different class of compounds such as Zetia, function by blocking cholesterol uptake from the diet and are utilized on their own or in combination with statins. All of these competing drugs had sales of greater than $1.0 billion during 2006, according to published reports.

Competing Drugs for Discovery Programs

For many of the diseases that are the subject of our RNAi therapeutics discovery programs, there are already drugs on the market or in development. These include:

For PML: Several treatments for PML have been tested without significant success. In HIV positive PML patients, the prognosis has been significantly changed by the advent of highly active anti-retroviral therapy, but 50% of cases are fatal and rarely do patients improve.

For Ebola Virus: No licensed vaccine, prophylactic therapy or treatment exists for Ebola infection. Multiple post-exposure treatments are under preclinical investigation including recombinant viral vectors, siRNA, antisense, and recombinant proteins. In the absence of effective vaccines and therapeutics, the response to Ebola infection is supportive patient care and case isolation to control disease spread.

For CF: Current pharmaceutical treatments for CF fall into two categories. The first category consists of antibiotics formulated to treat the lung infections to which CF patients are prone. This category includes TOBI®, a tobramycin solution for inhalation marketed by Chiron Corporation, a business of Novartis Vaccines and Diagnostics, and azithromycin. The second category contains one drug, Pulmozyme® (dornase alfa) marketed by Genentech, Inc., that reduces the viscosity of the mucus that builds up in the lungs of CF patients.

For SCI: There are currently no drugs approved in the United States to repair the neuronal damage associated with spinal cord injury. Patients are typically treated with methylprednisolone, an anti-inflammatory steroid that reduces the damage to neurons caused by activation of immune cells around the injury.

For Huntington s disease: While certain drugs are currently used to treat some of the symptoms of Huntington s, no drug has been approved in the United States for the treatment of the underlying disease.

For Parkinson s disease: Parkinson s disease is caused by the death in a specialized region of the brain of neurons that produce an important substance called dopamine. Most current drugs for Parkinson s disease work by boosting brain levels of dopamine or by mimicking its action. The primary drug for treating Parkinson s disease is typically carbidopa/levodopa, also sold as Sinemet® and Atamet®. Additional drugs include entacapone, seligiline, Mirapaz®, Perman® and Requip®. Modulation of the dopamine system only affects the symptoms of Parkinson s disease; there are no drugs approved for the treatment of the underlying disease.

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For neuropathic pain: A wide variety of drugs have been used to treat neuropathic pain. These include topical analgesics such as Lidoderm®, antidepressants such as amitryptyline, Paxil® and Effexor®, anticonvulsants such as carbamazepine, Neurontin® and most recently, Lyrica®, the muscle relaxant baclofen, anti-inflammatory drugs such as ibuprofen, and opioids such as oxycodone. More recently, the non-opioid drug ziconotide (Prialt®), which belongs to a new class of drugs known as N-type calcium channel blockers, was approved for treating severe chronic pain. Prialt must be administered directly into the spinal fluid using a special infusion device.

Regulatory Matters

The research, testing, manufacture and marketing of drug products and their delivery systems are extensively regulated in the United States and the rest of the world. In the United States, drugs are subject to rigorous regulation by the FDA. The Federal Food, Drug, and Cosmetic Act and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, record keeping, packaging, labeling, promotion and advertising, marketing and distribution of pharmaceutical products. The failure to comply with the applicable regulatory requirements may subject a company to a variety of administrative or judicially-imposed sanctions and the inability to obtain or maintain required approvals or to market approved drug products. These sanctions could include warning letters, product recalls, product seizures, total or partial suspension of production or distribution, clinical holds, injunctions, fines, civil penalties or criminal prosecution.

The steps ordinarily required before a new pharmaceutical product may be marketed in the United States include non-clinical laboratory tests, animal tests and formulation studies, the submission to the FDA of an IND, which must become effective prior to commencement of clinical testing in adequate and well-controlled clinical trials to establish that the drug product is safe and effective for the indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes several years and the actual time taken may vary substantially depending upon the complexity of the product and the nature of the disease. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures on a company s activities. Success in early stage clinical trials does not necessarily assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be subject to alternative interpretations that could delay, limit or even prevent regulatory approval. Even if a product receives regulatory approval, later discovery of previously unknown problems with a product, including new safety risks, may result in restrictions on the product or even complete withdrawal of the product from the market.

Non-clinical tests include laboratory evaluation of product chemistry and formulation, as well as animal testing to assess the potential safety and efficacy of the product. The conduct of the non-clinical tests and formulation of compounds for testing must comply with federal regulations and requirements. The results of non-clinical testing are submitted to the FDA as part of an IND, together with manufacturing information and analytical and stability data.

A 30-day waiting period after the filing of an IND is required prior to such application becoming effective and the commencement of clinical testing in humans. If the FDA has not commented on, or questioned, the application during this 30-day waiting period, clinical trials may begin. If the FDA has comments or questions, these must be resolved to the satisfaction of the FDA prior to commencement of clinical trials. The IND process can result in substantial delay and expense. The FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and

requirements, under protocols detailing the objectives of the trial and the safety and effectiveness criteria to be evaluated. Each protocol involving testing on human subjects in the United States, or in foreign countries if such tests are intended to support approval in the United States, must be submitted to the FDA as part of the IND. The study protocol and informed consent information for patients in clinical trials must be submitted to institutional review boards for approval prior to initiation of the trial.

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Clinical trials to support new drug applications, or NDAs, for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to primarily assess safety, tolerability, pharmacokinetics, pharmacological actions and metabolism associated with increasing doses. Phase II usually involves trials in a limited patient population, to assess the optimum dosage, identify possible adverse effects and safety risks, and provide preliminary support for the efficacy of the drug in the indication being studied.

If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II trials, Phase III trials are undertaken to further evaluate clinical efficacy and to further test for safety in an expanded patient population, typically at geographically dispersed clinical trial sites. Phase I, Phase II or Phase III testing of any product candidates may not be completed successfully within any specified time period, if at all. After successful completion of the required clinical testing, generally an NDA is prepared and submitted to the FDA.

We believe that any RNAi product candidate we develop, whether for RSV, pandemic flu, hypercholesterolemia, neuropathic pain, PD, SCI, Huntingtons, Ebola or CF will be regulated as a new drug by the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of extensive clinical and other testing, as described above, and a compilation of data relating to the product s pharmacology, chemistry, manufacture and controls. In addition, an NDA for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration must contain data assessing the safety and efficacy for the claimed indication in all relevant pediatric subpopulations. In some circumstances, the FDA may grant deferrals for the submission of pediatric data, or full or partial waivers. The cost of preparing and submitting an NDA is substantial. Under federal law, NDAs are subject to substantial application user fees and the sponsor of an approved NDA is also subject to annual product and establishment user fees.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. The FDA normally also will conduct a pre-approval inspection to ensure the manufacturing facility, methods and controls are adequate to preserve the drug s identity, strength, quality, purity and stability, and are in compliance with regulations governing current good manufacturing practices, or CGMPs.

If the FDA evaluation of the NDA and the inspection of manufacturing facilities are favorable, the FDA may issue an approval letter or an approvable letter followed by an approval letter. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for a specific indication. As a condition of NDA approval, the FDA may require post approval testing, including phase trials, and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling restrictions, which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

While we believe that any RNAi therapeutic we develop will be regulated as a new drug under the Federal Food, Drug, and Cosmetic Act, the FDA could decide to regulate certain RNAi therapeutic products as biologics under the Public Health Service Act. Biologics must have a biologics license application, or BLA, approved prior to commercialization. Like NDA, BLAs are subject to user fees. To obtain BLA approval, an applicant must provide non-clinical and clinical evidence and other information to demonstrate that the biologic product is safe, pure and potent, and like NDAs, must complete clinical trials that are typically conducted in three sequential phases (Phase I, II and III). Additionally, the applicant must demonstrate that the facilities in which the product is manufactured, processed, packed or held meet standards, including CGMPs and any additional standards in the

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license designed to ensure its continued safety, purity and potency. Biologics establishments are subject to pre-approval inspections. The review process for BLAs is also time consuming and uncertain, and BLA approval may be conditioned on post approval testing and surveillance. Once granted, BLA approvals may be suspended or revoked under certain circumstances, such as if the product fails to conform to the standards established in the license.

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements, including requirements for adverse event reporting and submission of periodic reports. Additionally, the FDA also strictly regulates the promotional claims that may be made about prescription drug products and biologics. In particular, a drug or biologic may not be promoted for uses that are not approved by the FDA as reflected in the product s approved labeling. In addition, the FDA requires substantiation of any claims of superiority of one product over another, including that such claims be proven by adequate and well-controlled head-to-head clinical trials. To the extent that market acceptance of our products may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively affect the sales of our products or our costs. We must also notify the FDA of any change in an approved product beyond variations already allowed in the approval. Certain changes to the product, its labeling or its manufacturing require prior FDA approval and may require the conduct of further clinical investigations to support the change. Such approvals may be expensive and time-consuming and, if not approved, the product will not be allowed to be marketed as modified.

If the FDA s evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter. The not approvable letter outlines the deficiencies in the submission and often requires additional testing or information in order for the FDA to reconsider the application. Even after submitting this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, the FDA may withhold approval of an NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

Some of our drug candidates may need to be administered using specialized drug delivery systems. We may rely on drug delivery systems that are already approved to deliver drugs like ours to similar physiological sites or, in some instances, we may need to modify the design or labeling of the legally available device for delivery of our product candidate. In such an event, the FDA may regulate the product as a combination product or require additional approvals or clearances for the modified device. In addition, to the extent the delivery device is owned by another company, we would need that company s cooperation to implement the necessary changes to the device and to obtain any additional approvals or clearances. Obtaining such additional approvals or clearances, and cooperation of other companies, when necessary, could significantly delay, and increase the cost of obtaining marketing approval, which could reduce the commercial viability of a drug candidate.

Once an NDA is approved, the product covered thereby becomes a listed drug that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An approved ANDA provides for marketing of a drug product that has the same active ingredients in the same strength, dosage form and route of administration as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. There is no requirement, other than the requirement for bioequivalence testing, for an ANDA applicant to conduct or submit results of non-clinical or clinical tests to prove the safety or effectiveness of its drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, are listed as such by the FDA, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, if the FDA deems that the approval of such drug was required to be supported by new clinical trials conducted by or for the sponsor. During such three-year exclusivity period, the FDA cannot grant

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approval of an abbreviated new drug application to commercially distribute a generic version of the drug based on that listed drug. However, the FDA can approve generic or other versions of that listed drug, such as a drug that is the same in every way but its indication for use, and thus the value of such exclusivity may be undermined. Federal law also provides a period of up to five years exclusively following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval.

Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an ANDA referencing that drug, are required to make one of four patent certifications, including certifying that it believes one or more listed patents are invalid or not infringed. If an applicant certifies invalidity or non-infringement, it is required to provide notice of its filing to the NDA sponsor and the patent holder. If the patent holder then initiates a suit for patent infringement against the ANDA sponsor within 45 days of receipt of the notice, the FDA cannot grant effective approval of the ANDA until either 30 months have passed or there has been a court decision holding that the patents in question are invalid, unenforceable or not infringed. If the patent holder does not initiate a suit for patent infringement within the 45 days, the ANDA may be approved immediately upon successful completion of FDA review, unless blocked by a regulatory exclusivity period. If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then the FDA cannot grant effective approval of the ANDA until those patents expire. The first of the ANDA applicants submitting substantially complete applications certifying that one or more listed patents for a particular product are invalid or not infringed may qualify for an exclusivity period of 180 days running from when the generic product is first marketed, during which subsequently submitted ANDAs cannot be granted effective approval. The 180-day generic exclusivity can be forfeited in various ways, including if the first applicant does not market its product within specified statutory timelines. If more than one applicant files a substantially complete ANDA on the same day, each such first applicant will be entitled to share the 180-day exclusivity period, but there will only be one such period, beginning on the date of first marketing by any of the first applicants.

From time to time legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of such changes, if any, may be.

Foreign Regulation of New Drug Compounds

Approval of a drug or biologic product by comparable regulatory authorities will be necessary in all or most foreign countries prior to the commencement of marketing of the product in those countries, whether or not FDA approval has been obtained. The approval procedure varies among countries and can involve requirements for additional testing. The time required may differ from that required for FDA approval. Although there are some procedures for unified filings in the European Union, in general, each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

In Europe, marketing authorizations may be submitted under a centralized or decentralized procedure. The centralized procedure is mandatory for the approval of biotechnology and many pharmaceutical products and provides for the grant of a single marketing authorization that is valid in all European Union member states. The decentralized procedure is a mutual recognition procedure that is available at the request of the applicant for medicinal products that are not subject to the centralized procedure. We will strive to choose the appropriate route of European regulatory filing to accomplish the most rapid regulatory approvals. However, our chosen regulatory strategy may not secure

regulatory approvals on a timely basis or at all.

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Hazardous Materials

Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material.

Manufacturing

We have no commercial manufacturing capabilities. We may manufacture material for use in IND-enabling toxicology studies in animals at our own facilities, but we do not anticipate manufacturing the substantial portion of material for human clinical use ourselves. We have contracted with several third party contract manufacturing organizations for the supply of certain amounts of material to meet our testing needs for preclinical toxicology and clinical testing. Commercial quantities of any drugs that we may seek to develop will have to be manufactured in facilities, and by processes, that comply with FDA regulations and other federal, state and local regulations. We plan to rely on third parties to manufacture commercial quantities of any product that we successfully develop. Under our agreement with Isis, at our request, we may negotiate a manufacturing services agreement with Isis for double-stranded RNA products designated to work through an RNAi mechanism.

Scientific Advisors

We seek advice from our scientific advisory board, which consists of a number of leading scientists and physicians, on scientific and medical matters. Our scientific advisory board meets regularly to assess:

our research and development programs;

the design and implementation of our clinical programs;

our patent and publication strategies;

new technologies relevant to our research and development programs; and

specific scientific and technical issues relevant to our business.

The current members of our scientific advisory board are:

Name	Position/Institutional Affiliation
David P. Bartel, Ph.D.	Professor/Whitehead Institute for Medical Research
Fritz Eckstein, Ph.D.	Professor/Max Planck Institute
Edward E. Harlow, Ph.D.	Professor/Harvard Medical School
Robert S. Langer, Ph.D.	Germeshausen Professor/Massachusetts Institute of Technology
Judy Lieberman, M.D., Ph.D.	Senior Investigator/CBR Institute for Biomedical Research
Paul R. Schimmel, Ph.D.	Ernest and Jean Hahn Professor/Skaggs Institute for Chemical Biology
Phillip A. Sharp, Ph.D.	Institute Professor/MIT Center for Cancer Research
Markus Stoffel, M.D., Ph.D.	Professor/ Institute of Molecular Systems Biology at the ETH Zurich
Thomas H. Tuschl, Ph.D.	Associate Professor/Rockefeller University

Phillip D. Zamore, Ph.D.	Professor/University of Massachusetts Medical School

Employees

As of February 28, 2007, we had 122 full-time equivalent employees, 101 of whom were engaged in research and development. None of our employees is represented by a labor union or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

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Financial Information About Geographic Areas

See Note 2 to our Consolidated Financial Statements, entitled Segment and Geographic Data, for financial information about geographic areas. The Notes to our Consolidated Financial Statements are contained herein in Item 8.

Corporate Information

Alnylam Pharmaceuticals, Inc. was incorporated in Delaware in May 2003. 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. Alnylam Pharmaceuticals, Inc. acquired Alnylam Europe AG in July 2003. Our principal executive office is located at 300 Third Street, Cambridge, Massachusetts 02142, and our telephone number is (617) 551-8200.

Investor Information

We maintain an internet website at www.alnylam.com. The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only. Our reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, including our annual reports on Form 10-K, our quarterly reports on Form 10-Q and our current reports on Form 8-K, and amendments to those reports, are accessible through our website, free of charge, as soon as reasonably practicable after these reports are filed electronically with, or otherwise furnished to, the Securities and Exchange Commission, or SEC. We also make available on our web site the charters of our audit committee, compensation committee and nominating and corporate governance committee, and our code of business conduct and ethics. In addition, we intend to disclose on our web site any amendments to, or waivers from, our code of business conduct and ethics that are required to be disclosed pursuant to the SEC rules.

Executive Officers of the Registrant

Name	Age	Position
John M. Maraganore, Ph.D.	44	President, Chief Executive Officer and Director
Barry E. Greene	43	Chief Operating Officer
Patricia L. Allen	45	Vice President of Finance and Treasurer

John M. Maraganore, Ph.D. has served as our President and Chief Executive Officer and as a member of our board of directors since December 2002. From April 2000 to December 2002, Dr. Maraganore served as Senior Vice President, Strategic Product Development for Millennium Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Maraganore serves as a member of the board of directors of the Biotechnology Industry Organization (BIO).

Barry E. Greene has served as our Chief Operating Officer since he joined us in October 2003 and served as our Treasurer from February 2004 through December 2005. From February 2001 to September 2003, Mr. Greene served as General Manager of Oncology at Millennium Pharmaceuticals, Inc., a biopharmaceutical company. Mr. Greene serves as a member of the board of directors of Acorda Therapeutics, Inc., a biotechnology company.

Patricia L. Allen has served as our Vice President of Finance since she joined us in May 2004 and as our Treasurer since January 2006. From March 1992 to May 2004, Ms. Allen held various positions at Alkermes, Inc., a

biopharmaceutical company, most recently as the Director of Finance. Ms. Allen is a certified public accountant.

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ITEM 1A. RISK FACTORS.

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

Risks Related to Our Business

Risks Related to Being an Early Stage Company

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

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

- execute product development activities using an unproven technology;
- build and maintain a strong intellectual property portfolio;
- gain acceptance for the development and commercialization of our products;
- develop and maintain successful strategic relationships; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

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

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

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

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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 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 December 31, 2006, we had an accumulated deficit of $140.5 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;

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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;

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.

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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 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 and the NIAID, a component of the NIH. 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

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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.

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 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 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 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 all applicable 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.

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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, including those related to quality control and quality assurance. The failure of a third-party manufacturer to perform its obligations as expected could adversely affect our business in a number of ways, including:

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

If a third-party manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different third-party manufacturer, which we may not be able to do 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.

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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 122 full time equivalent employees as of February 28, 2007, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. This rapid and substantial growth, and the geographical separation of our sites, has placed a strain on our administrative and operational infrastructure, and we anticipate that our continued growth will have a similar impact. If drug candidates we develop enter and advance through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with other organizations to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various collaborators, suppliers and other organizations. Our ability to manage our operations and growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures in at least two different countries. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

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

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

- fluctuations in foreign currency exchange rates that may increase the U.S. dollar cost of our international operations;
- difficulty managing operations in multiple locations, which could adversely affect the progress of our product candidate development program and business prospects;
- local regulations that may restrict or impair our ability to conduct biotechnology-based research and development;
- foreign protectionist laws and business practices that favor local competition; and
- failure of local laws to provide the same degree of protection against infringement of our intellectual property, which could adversely affect our ability to develop product candidates or reduce future product or royalty revenues, if any, from product candidates we may develop.

Risks Related to Our Industry

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

Any drug candidates we develop may fail in development or be delayed 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 are developing our most advanced product candidate, ALN-RSV01, for the treatment of respiratory syncytial virus, or RSV, infection. We recently completed two Phase I clinical trials of ALN-RSV01 and began an additional Phase I clinical trial in October 2006. In addition, in November 2006, we announced that we had initiated a human experimental infection study with RSV. We may not be able to further advance this or any other product candidate 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, or an institutional review board, or IRB, may suspend clinical trials of a drug candidate at any time for various reasons, including if we or they believe the subjects

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or patients participating in such trials are being exposed to unacceptable health risks. 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 IRBs, which approve and continually review clinical investigations and protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or delay the initiation and completion of clinical trials, and the FDA may decide not to consider any data or information derived from a clinical investigation not subject to initial and continuing IRB review and approval in support of a marketing application.

Our drug candidates that we develop may encounter problems during clinical trials that will cause us or regulatory authorities to delay, suspend or terminate 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;
- conditions imposed on us by 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 or maintaining 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 or inconclusive 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 HD, 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

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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.

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, among other things, research, testing, development, manufacturing, safety, efficacy, recordkeeping, labeling, marketing and distribution of drugs. 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 takes many 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 and affect reimbursement by third-party payors.

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

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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;
- 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;
- IRBs or regulators, including the FDA, 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
- 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 new or 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,

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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 prosecution.

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 product, or to provide favorable reimbursement.

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

- the timing of our receipt of any marketing approvals, the terms of any approvals and the countries in which approvals are obtained;
- the safety, efficacy and ease of administration of our product candidates;
- 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
- 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 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 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,

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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;

product recalls or public notification or medical product safety alerts to healthcare professionals;

restrictions on, or prohibitions against, marketing our products;

restrictions on importation or exportation 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,

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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, required 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, however, retained the discretion not to implement a drug reimportation plan if he finds that the benefits do not outweigh the costs, and has so far declined to approve a reimportation plan. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, 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, and federal drug import legislation has been introduced in Congress. The FDA has warned that imported drugs may be unsafe or illegal. If such programs become more widespread or the federal government changes its position against drug importation, prices we receive for any products that we may develop may decrease, 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, limitations on the indications for which they may be used, or suspension or withdrawal of approvals. 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.

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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 are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Cambridge 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 successfully any drugs that we develop.

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

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing 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, hypercholesterolemia, PML, Ebola, HD, PD, neuropathic pain, 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

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Pulmozyme®, are currently marketed for the treatment of CF. These drugs, or other of our competitors products, may be more effective, safer, less expensive 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 Sirna, a subsidiary of Merck, Acuity, Nastech, Calando, Quark, Nucleonics, SR Pharma, RXi, a subsidiary of CytRx, Inc., Protiva and Intradigm. In addition, we granted licenses to Isis, GeneCare, Benitec, Nastech, Calando, Quark 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, as a result of its acquisition of Sirna in December 2006, Merck, which has substantially more resources and experience in developing drugs 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

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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 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.

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, Idera Pharmaceuticals, Inc., Carnegie Institution of Washington, Cancer Research Technology Limited, the Massachusetts Institute of Technology, the Whitehead Institute for Biomedical Research, Max Planck Innovation GmbH, which was formerly known as Garching Innovation GmbH, which we refer to as Max Planck Innovation, Stanford University, Cold Spring Harbor Laboratory, the University of South Alabama, CBR Institute for Biomedical Research, University of British Columbia and Inex. 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

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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 of the opponents, including Sirna, which was recently acquired by Merck and SR Pharma. Based on the appeal, 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.

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.

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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 Max Planck Gesellschaft, our amended licenses with Max Planck Innovation, representing Max Planck Gesellschaft, 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.

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.

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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

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

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person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

We have not received written comments from the staff of the SEC regarding our periodic or current reports that remain unresolved.

ITEM 2. PROPERTIES

Our operations are based primarily in Cambridge, Massachusetts and Kulmbach, Germany. As of February 28, 2007, the properties we lease are listed below:

Location	Square Feet	Type	Lease Expires
Cambridge, MA	62,000	Office & laboratory	September 2011
Kulmbach, Germany	18,000	Office & laboratory	June 2008

We believe that the total space available to us under our current leases and options will meet our needs for the foreseeable future, and that additional space would be available to us on commercially reasonable terms if it were required.

ITEM 3. LEGAL PROCEEDINGS

We are currently not a party to any material legal proceedings.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

No matters were submitted to a vote of our security holders during the fourth quarter of 2006.

PART II

ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock began trading on the NASDAQ Global Market on May 28, 2004 under the symbol ALNY . Prior to that time, there was no established public trading market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on the NASDAQ Global Market for the period indicated:

Year Ended December 31, 2005:	High	Low
First Quarter	$ 11.00	$ 6.76
Second Quarter	$ 9.00	$ 6.90

Third Quarter	$ 15.22	$ 6.90
Fourth Quarter	$ 14.85	$ 9.06

Year Ended December 31, 2006:	**High**	**Low**
First Quarter	$ 18.39	$ 11.48
Second Quarter	$ 17.63	$ 12.82
Third Quarter	$ 15.52	$ 11.29
Fourth Quarter	$ 24.46	$ 13.77

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Holders of record

As of February 28, 2007, there were approximately 72 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of individual stockholders represented by these record holders.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

Information relating to our equity compensation plans will be included in our proxy statement in connection with our 2007 Annual Meeting of Stockholders, under the caption Equity Compensation Plan Information. That portion of our proxy statement is incorporated herein by reference.

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Stock Performance Graph

The following performance graph and related information shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

The comparative stock performance graph below compares the cumulative total stockholder return (assuming reinvestment of dividends, if any) from investing $100 on May 28, 2004, the date on which our common stock was first publicly traded, to the close of the last trading day of 2006, in each of (i) our common stock, (ii) the NASDAQ Stock Market (U.S.) Index and (iii) the NASDAQ Pharmaceutical Index.

Comparison of Cumulative Total Return*
Among Alnylam Pharmaceuticals, Inc.,
NASDAQ Stock Market (U.S.) Index and NASDAQ Pharmaceuticals Index

	5/28/2004	12/31/2004	12/31/2005	12/31/2006
Alnylam Pharmaceuticals, Inc.	$ 100.00	$ 124.29	$ 222.30	$ 356.07
Nasdaq Stock Market (U.S.) Index	$ 100.00	$ 109.70	$ 112.03	$ 123.08
Nasdaq Pharmaceutical Index	$ 100.00	$ 103.32	$ 113.77	$ 111.36

* $100 invested on May 28, 2004, the date on which Alnylam common stock was first publicly traded, in Alnylam common stock, the NASDAQ Stock Market (U.S.) Index or the NASDAQ Pharmaceutical Index, including reinvestment of dividends.

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ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data are derived from our financial statements. The historical results presented are not necessarily indicative of future results. The consolidated statement of operations data for the years ended December 31, 2006, 2005 and 2004 and the consolidated balance sheet data as of December 31, 2006 and 2005 have been derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data set forth below should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and the financial statements, and the related Notes, included elsewhere in this Annual Report on Form 10-K.

In July 2003, we acquired Ribopharma AG, now called Alnylam Europe AG, an RNAi company based in Kulmbach, Germany. As a result, the operations of Alnylam Europe AG were consolidated beginning with the quarter ended September 30, 2003.

Selected Consolidated Financial Data
(In thousands, except per share data)

	Year Ended December 31,				Period from Inception (June 14, 2002) through December 31,
	2006	2005	2004	2003	2002
Statement of Operations Data:					
Net revenues	$ 26,930	$ 5,716	$ 4,278	$ 176	$
Operating expenses(1)	66,431	49,188	36,542	25,233	4,222
Loss from operations	(39,501)	(43,472)	(32,264)	(25,057)	(4,222)
Net loss	(34,608)	(42,914)	(32,654)	(25,033)	(4,136)
Net loss attributable to common stockholders	$ (34,608)	$ (42,914)	$ (35,367)	$ (27,939)	$ (4,884)
Net loss per common share basic and diluted	$ (1.09)	$ (1.96)	$ (2.98)	$ (29.64)	$ (14.74)
Weighted average shares outstanding basic and diluted	31,890	21,949	11,886	943	331
(1) Non-cash stock-based compensation included in operating expenses	$ 8,304	$ 4,597	$ 4,106	$ 3,455	$ 172

	December 31,				
	2006	2005	2004	2003	2002
Balance Sheet Data:					

Cash, cash equivalents and marketable securities	$ 217,260	$ 80,002	$ 46,046	$ 23,193	$ 15,477
Working capital	199,859	63,930	41,606	20,345	12,846
Total assets	240,006	98,348	66,107	35,183	16,111
Notes payable	9,136	7,395	7,201	1,859	
Redeemable convertible preferred stock				55,189	18,084
Total stockholders equity (deficit)	201,174	61,779	46,142	(26,707)	(4,646)

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ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We are a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. RNAi is a naturally occurring biological pathway 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 are building a pipeline of RNAi therapeutics. Our lead program is in Phase I clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which we believe is the leading cause of hospitalization in infants in the United States and occurs in the elderly and in immune compromised adults.

In pre-clinical development programs, we are also working on another respiratory infection, influenza, with Novartis and an RNAi therapeutic targeting a gene called PCSK9 for the treatment of hypercholesterolemia. We have pre-clinical discovery programs focused on central nervous system, or CNS, diseases including Parkinson s disease, Huntington s disease, neuropathic pain, spinal cord injury and progressive multifocal leukoencephalopathy, or PML, a CNS disease caused by viral infection in immune compromised patients. We also have a program to treat the inherited respiratory disease known as cystic fibrosis, or CF, as well as a program for Ebola virus infection. We are also working to extend our capabilities to enable the development of RNAi therapeutics that travel through the bloodstream to reach diseased parts of the body, which we refer to as Systemic RNAi[tm], and are developing technology to achieve efficient and safe systemic delivery. In addition, we have formed alliances with leading companies, including Novartis, Merck, Biogen Idec and Medtronic.

We commenced operations in June 2002. We have focused our efforts since inception primarily on business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff, and raising capital. Since our inception, we have generated significant losses. As of December 31, 2006, we had an accumulated deficit of $140.5 million. Through December 31, 2006, we have funded our operations primarily through the net proceeds from the sale of equity securities. Through December 31, 2006, a substantial portion of our total net revenues have been collaboration revenue derived from our strategic alliances with Novartis and Merck. We expect our revenues to continue to be derived primarily from strategic alliances, such as our collaborations with Novartis, Merck and Biogen Idec, government and foundation funding and license fee revenues.

We currently have programs focused in a number of therapeutic areas, however, we are unable to predict when, if ever, we will be able to commence sales of any product. We have not achieved profitability on a quarterly or annual basis and we expect to incur significant additional losses over the next several years. We expect our net losses to increase primarily due to research and development activities relating to our collaborations, drug development programs and other general corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods. Our sources of potential funding for the next several years are expected to include proceeds from the sale of equity, license and other fees, funded research and development payments, proceeds from equipment lines of credit and milestone payments under existing and future collaborative arrangements.

Research and Development

Since our inception, we have focused on drug discovery and development programs. Research and development expenses represent a substantial percentage of our total operating expenses. We have initiated programs to identify specific RNAi therapeutics that will be administered directly to diseased parts of the body, which we refer to as direct RNAi therapeutics, and we expect to initiate additional programs as the capabilities of our product platform evolve. Included in our current programs are development programs, those programs for which we have

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established targeted timing for human clinical trials, and discovery programs, those programs for which we have yet to establish programs for targeted timing for human clinical trials. Our most advanced development program is focused on RSV. In November 2005, we filed an IND related to our RSV program and initiated human clinical trials of ALN-RSV01 in December 2005. Our other development programs are focused on another lung infection, influenza, or flu and on the treatment of hypercholesterolemia. We also have discovery programs to develop direct RNAi therapeutics for the treatment of the genetic respiratory disease CF, central nervous system disorders such as spinal cord injury, Parkinson s disease, Huntington s disease, neuropathic pain; viral disease such as Ebola; PML and several other diseases that are the subject of collaborations with Merck and Novartis.

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

- our ability to progress any product candidates into pre-clinical and clinical trials;
- the scope, rate and progress of our pre-clinical trials and other research and development activities;
- the scope, rate of progress and cost of any clinical trials we commence;
- clinical trial results;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the cost and timing of regulatory approvals;
- the cost and timing of establishing sales, marketing and distribution capabilities;
- the cost of establishing clinical and commercial supplies of any products that we may develop; and
- the effect of competing technological and market developments.

Any failure to complete any stage of the development of any potential products in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with completing our projects on schedule, or at all, and the potential consequences of failing to do so, are set forth in Item 1A above under the heading Risk Factors .

Strategic Alliances

A significant component of our business strategy is to enter into strategic alliances and collaborations with pharmaceutical and biotechnology companies, academic institutions, research foundations and others, as appropriate, to gain access to funding, technical resources and intellectual property to further our development efforts and to generate revenues. We have entered into license agreements with Max Planck Innovation and Isis, as well as a number of other entities, to obtain rights to important intellectual property in the field of RNAi. We have entered into collaborations with (1) Novartis to discover and develop therapeutics based on RNAi and to develop an RNAi

therapeutic for pandemic flu, (2) Merck to develop RNAi technology and therapeutics, (3) Medtronic to develop novel drug-device products incorporating RNAi therapeutics to treat diseases caused by degeneration of the nervous system and (4) Biogen Idec to perform investigative research into the potential of using RNAi technology to discover and develop therapeutics to treat PML. We have also entered into contracts with government agencies, such as the NIAID. In addition, we have entered into an agreement with CFFT to obtain funding and technical resources for our CF program.

Novartis. We have formed two alliances with Novartis. We refer to the first of these, which was initiated in September 2005, as the broad Novartis alliance, and to the second, which was initiated in February 2006, as the

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Novartis flu alliance. In October 2005, Novartis purchased approximately 5.3 million shares of our common stock at a purchase price of $11.11 per share for an aggregate purchase price of approximately $58.5 million, which, immediately after such issuance, represented 19.9% of our then outstanding common stock. Novartis owned approximately 14% of our common stock as of December 31, 2006.

Under the terms of the collaboration and license agreement, the parties agreed to work together on selected targets, as defined in the collaboration and license agreement, to discover and develop therapeutics based on RNAi. In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an upfront payment of $10.0 million to us in October 2005, partly to reimburse prior costs incurred by us to develop *in vivo* RNAi technology. In addition, the collaboration and license agreement includes terms under which Novartis agreed to provide us with research funding and milestone payments as well as royalties on annual net sales of products resulting from the collaboration. The collaboration and license agreement also provides Novartis with a non-exclusive option to integrate our intellectual property relating to RNAi technology into Novartis operations under specified circumstances. In connection with the exercise of the integration option, Novartis will be required to make additional payments to us.

In February 2006, we entered into the Novartis flu alliance. The agreement governing the flu alliance is structured as an addendum to the collaboration and license agreement for the broad Novartis alliance. We are eligible to receive significant funding from Novartis for our efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits.

Merck. In July 2006, we amended and restated our research collaboration and license agreement with Merck, from September 2003, as amended. Our collaboration with Merck is focused on developing RNAi therapeutics for targets associated with human diseases and, under the terms of the amended and restated license agreement, will focus on the nine targets that then remained to be nominated by Merck under the terms of the original license agreement. These nine programs are in addition to the existing program directed to the NOGO pathway on which we were already collaborating with Merck under the original agreement. We may select three of the nine additional programs as joint development programs, which Merck will co-fund and participate in from the outset. In October 2006, we selected a co-development program from the first three targets presented by Merck under the amended and restated license agreement. Under the original license agreement, the collaboration was structured such that co-funding by Merck would not begin until after the completion of defined pre-clinical work. The amended and restated license agreement provides funding from Merck immediately for programs selected by us for co-development, and provides that, in the United States, we will have the right to co-promote RNAi therapeutic products developed in these three co-development programs. Merck will assume primary responsibility for the remaining six programs and we are eligible to receive milestone payments and royalties on any RNAi therapeutic products developed and commercialized by Merck in these six programs.

Also in July 2006, we and Merck agreed to terminate our collaboration and license agreement, effective as of June 29, 2004, pursuant to which we were collaborating in the research, development and commercialization of RNAi products directed to certain targets, including but not limited to, vascular endothelial growth factor or VEGF.

Medtronic. In February 2005, we entered into a collaboration with Medtronic to pursue the potential development of therapeutic products for the treatment of neurodegenerative disorders such as Parkinson s, Huntington s and Alzheimer s disease. The collaboration is focused on developing novel drug-device combinations incorporating RNAi therapeutic products. Currently, we are engaged in a joint technology development program with Medtronic through April 2007. This initial joint technology development program is focused on delivering candidate RNAi therapeutic products to specific areas of the brain using implantable infusion systems.

After successful completion of the initial joint technology development program, the parties must jointly determine whether to initiate product development. If we make a joint decision to initiate product development, Medtronic would make an initial equity investment in us and could make additional investments upon successful completion of specified milestones. The aggregate amount of our common stock that Medtronic would purchase, if a joint decision were made to initiate product development and the specified milestones were successfully

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completed, would be $21.0 million. The amount of the investment to be made at the time of the joint decision to initiate product development would be between $1.0 million and $8.0 million, as determined by us, at the then-current market price. For the purpose of this investment, the then-current market price would be equal to the twenty-day trailing average of the closing price of our common stock on the Nasdaq Global Market at the end of the trading day two trading days prior to the date of the decision to initiate product development. The remaining investments of between $13.0 million and $20.0 million would be made upon the achievement of the specified milestones at a purchase price equal to 120% of the then-current market price, calculated in the same manner as described above. If either party decides not to initiate product development under the collaboration agreement, Medtronic would not be required to make any equity investment in us. We would also be eligible to receive additional cash milestone payments for each product developed and royalties on sales of any RNAi therapeutic component of novel drug-device combinations that result from the collaboration.

Biogen Idec. In September 2006, we entered into a collaboration and license agreement with Biogen Idec focused on the discovery and development of therapeutics based on RNAi for the potential treatment of PML. Under the terms of the collaboration agreement with Biogen Idec, we granted an exclusive license to distribute, market and sell certain RNAi therapeutics to treat PML and Biogen Idec has agreed to fund all related research and development activities. We also received an upfront $5.0 million payment from Biogen Idec. In addition, upon the successful development and utilization of a product resulting from the collaboration, Biogen Idec would be required to pay us milestone and royalty payments.

NIH. In September 2006, we were awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus, with the National Institute of Allergy and Infectious Diseases, or NIAID, a component of the National Institutes of Health, or NIH. The federal contract will provide us with up to $23.0 million in funding over a four-year period to develop, as anti-viral drugs targeting the Ebola virus. The Ebola virus can cause a severe, often fatal infection, and poses a potential biological safety risk and bioterrorism threat. Of the $23.0 million, the government has committed to pay us $14.2 million over the first two years of the contract and, subject to the progress of the program and budgetary considerations in future years, the remaining $8.8 million over the last two years of the contract.

Isis. In March 2004, we entered into a collaboration and license agreement with Isis, a leading developer of single-stranded antisense oligonucleotide drugs that target RNA. The agreement enhanced our intellectual property position with respect to RNA-based therapeutic products and our ability to develop double-stranded RNA for RNAi therapeutic products, and provided us with the opportunity to defer investment in manufacturing technology. Under the terms of our agreement, we agreed to pay Isis an upfront license fee of $5.0 million, $3.0 million of which was paid upon signing of the agreement and the remaining $2.0 million of which was paid in January 2005. We also agreed to pay milestone payments, payable upon the occurrence of specified development and regulatory events, and royalties to Isis for each product that we or a collaborator develop utilizing Isis intellectual property. In addition, we agreed to pay to Isis a percentage of specified fees from strategic collaborations we may enter into that include access to the Isis intellectual property. In conjunction with the agreement, Isis made a $10.0 million equity investment in us. Isis also agreed to pay us a license fee, milestone payments, payable upon the occurrence of specified development and regulatory events, and royalties for each product developed by Isis or a collaborator that utilizes our intellectual property. The agreement also gives us an option to use Isis manufacturing services for RNA-based therapeutic products.

Our agreement with Isis also gives us the exclusive right to grant sub-licenses for Isis technology to third parties with whom we are not collaborating. We may include these sub-licenses in our InterfeRx licenses. If a license includes rights to Isis intellectual property, we will share revenues from that license equally with Isis.

If, by January 1, 2008, we or a collaborator have not completed the studies required for an IND submission 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 the patents and patent applications licensed to us, thereby making our rights non-exclusive.

Inex. In January 2007, Inex granted us an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics. We granted Inex an option for three InterfeRx^{tm} licenses, subject to our review and third party obligations, to develop their own RNAi therapeutic

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products and exclusive access to our intellectual property to develop oligonucleotide drugs that do not function through an RNAi mechanism. In connection with Inex s license grant to us, we issued Inex 361,990 shares of our common stock, valued at $8.0 million, in a private placement on January 16, 2007 and on February 23, 2007, we paid them an additional $0.4 million. We have also agreed to make available to Inex a $5.0 million loan for capital equipment expenditures related to manufacturing services performed by Inex for us. In addition, we will be required to pay Inex up to $13.0 million in milestone payments for each product we develop utilizing technology Inex has licensed to us.

Critical Accounting Policies and Estimates

While our significant accounting policies are more fully described in the notes to our consolidated financial statements included in this Annual Report on Form 10-K, we believe the following accounting policies to be the most critical in understanding the judgments and estimates we use in preparing our consolidated financial statements:

Use of Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of our consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, stock based compensation and accrued expenses. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions and could have a material impact on our reported results.

Revenue Recognition

We recognize revenue in accordance with the Securities and Exchange Commission s Staff Accounting Bulletin No. 104, Revenue Recognition in Financial Statements. Revenues from our collaboration agreements with Merck and Novartis may include nonrefundable license fees, milestones, cost reimbursements research and development funding and royalties. When evaluating multiple element arrangements, we consider whether the components of the arrangement represent separate units of accounting as defined in EITF Issue No. 00-21, Revenue Arrangements with Multiple Deliverables, or EITF 00-21. Application of these standards requires subjective determinations and requires management to make judgments about the value of the individual elements and whether it is separable from the other aspects of the contractual relationship. To date, we have determined that our upfront non-refundable license fees cannot be separated from our ongoing collaborative activities, and accordingly, do not treat them as a separate element. Nonrefundable license fees are recognized as revenue as we perform under the collaboration agreement. Where our level of effort is relatively constant over the performance period, we recognize revenues on a straight-line basis over the estimated period of performance under the contract, unless evidence suggests that revenue is earned in a different pattern, in which case that pattern is followed.

We recognize milestone payments as revenue upon achievement of the milestone only if (1) the milestone payments are nonrefundable; (2) substantive effort is involved in achieving the milestone; and (3) the amount of the milestone is reasonable in relation to the effort expended or the risk associated with achievement of the milestone. If

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any of these conditions are not met, we defer the milestone payments and recognize them as revenue over the term of the contract as we complete our performance obligations.

Novartis. In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an up-front payment of $10.0 million to us in October 2005 to partly reimburse costs previously incurred by us to develop *in vivo* RNAi technology. In addition, the collaboration and license agreement includes terms under which Novartis agreed to provide us with research funding and milestone payments as well as royalties on annual net sales of products resulting from the collaboration and license agreement. We initially recorded as deferred revenue the non-refundable $10.0 million up-front payment and $6.4 million premium that represents the difference between the purchase price and the closing price of our common stock on the date of the stock purchase from Novartis. In addition to these payments, research funding and certain milestone payments will be amortized into revenue using the proportional performance method over the estimated duration of the Novartis agreement or ten years. Under this method, we estimate the level of effort to be expended over the term of the agreement and recognize revenue based on the lesser of the amount calculated based on the proportional performance of total expected revenue or the amount of non-refundable payments earned.

We believe the estimated term of the Novartis agreement includes the three-year term of the agreement, two one-year extensions at the election of Novartis and limited support as part of a technology transfer until the fifth anniversary of the termination of the agreement. Therefore, an expected term of ten years is used in the proportional performance model. We will evaluate the expected term when new information is known that could affect our estimate. In the event our period of involvement is different than we estimated, revenue recognition will be adjusted on a prospective basis.

Merck. We recognize revenues from reimbursable research and development activities at the time these activities are performed under the terms of the related agreement, when the collaborator is obligated to pay and when no future performance obligations exist. In revenue arrangements where both parties reimburse each other for research costs, such as our prior collaboration agreement with Merck for the co-development of RNAi therapeutics for the treatment of ocular diseases, in which both parties reimbursed each other for 50% of the costs incurred, as defined by the agreement, we followed EITF Issue No. 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products), or EITF 01-9, in determining the proper accounting for amounts owed to Merck in reimbursement for our portion of Merck s costs under the agreement. In accordance with EITF 01-9, we recorded revenues equal to the amount we were due to receive for costs incurred under the agreement less amounts reimbursable to the other party during the same accounting period unless we received a separable and identifiable benefit in exchange for the payments made to the other party under the arrangement and we could reasonably estimate the fair value of the benefit received.

Accounting for Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of Financial Accounting Standards Board, or FASB, Statement of Financial Accounting Standards, or SFAS, No. 123R, Share-Based Payment, or SFAS 123R, using the modified prospective transition method. Under that transition method, stock-based compensation expense is recognized beginning in 2006 for all stock-based payments granted prior to, but not yet vested as of, January 1, 2006, based on the grant-date fair value estimated in accordance with the original provisions of SFAS No. 123, Accounting for Stock Based Compensation, or SFAS 123, and compensation cost for all stock-based payments granted subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R. Such amounts are reduced by our estimate of forfeitures of all unvested awards. Results for prior periods have not been restated.

Prior to January 1, 2006, we accounted for employee stock awards granted under our compensation plans in accordance with Accounting Principles Board, or APB, Opinion No. 25, Accounting for Stock Issued to Employees,

or APB 25, and related interpretations. Under APB 25, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation expense is recorded. When the exercise price of options granted to employees under these plans is less than the market price of the common stock on the date of grant, compensation expense is recognized on a straight-line basis over the vesting period. All stock-based awards granted to non-employees are accounted for at their fair value in

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accordance with SFAS 123, as amended, and Emerging Issues Task Force, or EITF, Issue No. 96-18, Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, or EITF 96-18, under which compensation expense is generally recognized over the vesting period of the award.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. We calculate the grant date fair values using the Black-Scholes valuation model. Our expected stock price volatility assumption is based on a combination of implied volatilities of similar entities whose share or option prices are publicly available as well as the historical volatility of our publicly traded stock. For stock option grants issued during the year ended December 31, 2006, we used a weighted-average expected stock-price volatility assumption of 67%. Due to our short history of being a public company, we estimated the expected life of option grants made during the year ended December 31, 2006 using the simplified method prescribed under Staff Accounting Bulletin No. 107 since the grants qualify as plain-vanilla options, which averages the contractual term of the stock options (10 years) with the vesting term (2.2 years) for an average of 6.1 years for most stock options. The dividend yield of zero is based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

As of December 31, 2006, the estimated fair value of unvested employee awards was $17.1 million, net of estimated forfeitures. This amount will be recognized over the weighted average remaining vesting period of approximately 1.5 years for these awards. Stock-based employee compensation was $6.1 million for the year ended December 31, 2006. However, the total amount of stock-compensation expense recognized in any future period cannot be predicted at this time because it will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. SFAS 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term forfeitures is distinct from cancellations or expirations and represents only the unvested portion of the surrendered option. We currently expect, based on an analysis of our historical forfeitures, that approximately 84% of our options will actually vest, and therefore have applied an annual forfeiture rate of 4.35% to all unvested options as of December 31, 2006. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest.

Results of Operations

The following data summarizes the results of our operations for the periods indicated, in thousands:

	Year Ended December 31,		
	2006	**2005**	**2004**
Net revenues	$ 26,930	$ 5,716	$ 4,278
Operating expenses	66,431	49,188	36,542
Loss from operations	(39,501)	(43,472)	(32,264)
Net loss	$ (34,608)	$ (42,914)	$ (32,654)

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Discussion of Results of Operations for 2006 and 2005

The following table summarizes our total consolidated net revenues for the periods indicated, in thousands:

	Year Ended December 31,	
	2006	2005
Novartis	$ 21,775	$ 746
Other research collaborators	3,294	4,423
InterfeRx program and research reagent licenses	1,439	422
Other	422	125
Total net revenues	$ 26,930	$ 5,716

Novartis. The increase in revenues relates to a full year of activity for our main collaboration with Novartis compared to only one quarter of activity during 2005. In addition, the increase also resulted from our February 2006 alliance with Novartis for the development of RNAi therapeutics for pandemic flu which provides for the reimbursement of research costs incurred under this agreement as well as a share of any future profits.

Other research collaborators. Other research collaborators revenues consist of revenues from Biogen Idec, Merck, the NIH and other government and foundation revenues. The decrease in revenues from other research collaborators was related to a $2.7 million decrease in revenues primarily related to our Merck ocular disease collaboration, for which development was suspended in September 2005 based on portfolio management and commercial factors. The decrease in other research collaborator revenues was partially offset by NIH revenues as well as Biogen Idec revenues during 2006, which consisted of research and development funding and amortization revenues of the $5.0 million up-front payment.

InterfeRx. In addition to our collaboration agreements, we have an InterfeRx program under which we have licensed our intellectual property to others for the development and commercialization of RNAi therapeutics in narrowly defined therapeutic areas in which we are not currently engaged. We have also granted licenses to our intellectual property to others for the development and commercialization of research reagents and services. We expect these programs to provide revenues from license fees and royalties on sales by the licensees, subject to limitations under our agreements with Novartis. The increase in InterfeRx revenues and research reagent licenses revenue was due primarily to $0.8 million payment from Quark during 2006.

Deferred Revenue. Total deferred revenue of $17.9 million at December 31, 2006 consists of payments received from our collaborators pursuant to our license agreements that we have yet to earn pursuant to our revenue recognition policy.

For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances, collaborations and licensing activities.

Operating Expenses

The following tables summarize our operating expenses for the periods indicated, in thousands:

	2006	% of Total Operating Expenses	2005	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 49,798	75%	$ 35,319	72%	$ 14,479	41%
General and administrative	16,633	25%	13,869	28%	2,764	20%
Total operating expenses	$ 66,431	100%	$ 49,188	100%	$ 17,243	35%

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Research and development. The following table summarizes the components of our research and development expenses for the periods indicated, in thousands and as a percentage of total research and development expenses, together with the changes in thousands and percentages:

	2006	% of Expense Category	2005	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Research and development						
Compensation and related	$ 10,666	21%	$ 6,895	20%	$ 3,771	55%
Clinical trial and manufacturing expenses	10,019	20%	537	2%	9,482	1766%
Facilities-related expenses	6,315	13%	4,668	13%	1,647	35%
External services	6,001	12%	8,924	25%	(2,923)	(33)%
Lab supplies and materials	5,462	11%	3,672	10%	1,790	49%
Non-cash stock-based compensation	5,006	10%	2,431	7%	2,575	106%
License fees	4,040	8%	6,904	20%	(2,864)	(41)%
Other	2,289	5%	1,288	3%	1,001	78%
Total research and development expenses	$ 49,798	100%	$ 35,319	100%	$ 14,479	41%

During the year ended December 31, 2006, our research and development expenses increased primarily due to the expansion of our research and development organization in support of the growth of our programs.

As indicated in the table above, the increase in research and development expenses in 2006 as compared to the previous year was primarily due to clinical trial and manufacturing related expenses in support of our RSV clinical program, which began in December 2005. The increase in compensation related expenses and lab supplies and materials expenses was due to additional research and development headcount over the past year to support our alliances and expanding product pipeline. The increase in stock-based compensation for the year ended December 31, 2006 was primarily due to our adoption of SFAS 123R on January 1, 2006. We expect to continue to devote a substantial portion of our resources to research and development expenses and that research and development expenses will increase as we continue development of our and our collaborators product candidates and technologies.

We do not track most of our research and development costs or our personnel and personnel-related costs on a project-by-project basis, because all of our programs are in the early stages of development. However, our collaboration agreements contain cost sharing arrangements whereby certain costs incurred under the project are reimbursed. Costs reimbursed under the agreements typically include certain direct external costs and a negotiated full-time equivalent labor rate for the actual time worked on the project. As a result, although a significant portion of our research and development expenses are not tracked on a project-by-project basis, we do track direct external costs attributable to, and the actual time our employees worked on, our collaborations.

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General and administrative. The following table summarizes the components of our general and administrative expenses for the periods indicated, in thousands:

	2006	% of Expense Category	2005	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 4,624	28%	$ 3,780	27%	$ 844	22%
Compensation and related	3,546	21%	3,339	24%	207	6%
Non-cash stock-based compensation	3,298	20%	2,166	16%	1,132	52%
Facilities related	2,736	16%	1,893	14%	843	45%
Insurance	652	4%	616	4%	36	6%
Other	1,777	11%	2,075	15%	(298)	(14)%
Total general and administrative expenses	$ 16,633	100%	$ 13,869	100%	$ 2,764	20%

As indicated in the table above, the increase in general and administrative expenses in 2006 was primarily due to higher stock-based compensation expenses related to our adoption of SFAS No. 123R on January 1, 2006, higher facilities related costs due to the expansion of our facilities during 2006, as well as an increase in legal and professional service fees due to increased business activities during 2006.

Interest income was $6.2 million in 2006 compared to $1.5 million in 2005. The increase was due to our higher average cash, cash equivalent and marketable securities balances, primarily from our January and December 2006 public offerings of common stock, as well as higher average interest rates during 2006.

Interest expense was $1.0 million in each of 2006 and 2005. Interest expense in each year related to borrowings under our lines of credit used to finance capital equipment purchases. We expect that our interest expense will increase as we finance additional capital expenditures.

Discussion of Results of Operations for 2005 and 2004

Net revenues from research collaborators

The following table summarizes our total consolidated net revenues for the periods indicated, in thousands:

	Year Ended December 31, 2005	2004
Merck	$ 3,579	$ 4,066
CFFT	800	
Novartis	746	
InterfeRx	350	

Other	241	212
Total net revenues	$ 5,716	$ 4,278

Merck. Under our September 2003 collaboration and license agreement with Merck, we have received upfront and license payments which have been deferred and are being recognized as revenue over six years, the estimated period of performance under this agreement. In September 2003, we received a $2.0 million payment and, in both September 2004 and September 2005, we received additional payments of $1.0 million. We recognized revenues of $0.9 million and $0.6 million from the amortization of these payments in 2005 and 2004.

In December 2004, we achieved a scientific milestone, as defined by this agreement, resulting in a $2.0 million milestone payment from Merck. In connection with the achievement of this scientific milestone, Merck made a $5.0 million equity investment in our common stock. The purchase price of this common stock, as defined by the agreement, was determined based on the average trading price of our common stock during the twenty days prior to

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the purchase, which was $7.04. The price of our common stock on the date of the purchase was $7.40 and resulted in an actual value of $5.3 million for the common stock issued to Merck. As a result, we recorded a reduction of $0.3 million to the revenue recorded from Merck during 2004.

Under the terms of our agreement with Merck relating to ocular targets, in 2004 we received a $2.0 million license fee, as well as $1.0 million representing reimbursement of prior research and development costs, which we incurred on our pre-existing ocular disease program. Prior to the termination of this agreement in July 2006, these amounts were being amortized into revenues over the then-estimated period of performance under the collaboration agreement of eight years. As such, we recorded revenues of $0.5 million in 2005 and $0.2 million in 2004 from the amortization of these payments. In addition to upfront and milestone payments, this agreement provided for the sharing of research costs incurred under this agreement. We recorded net revenues of $2.2 million in 2005 and $1.5 million in 2004 from these cost sharing activities.

CFFT. Under the collaboration agreement we entered into with CFFT in March 2005, CFFT provided us with an initial payment of $0.5 million and a milestone payment of $0.3 million, which we recorded as revenue.

Novartis. Under our October 2005 collaboration and license agreement with Novartis, we received an upfront payment totaling $10.0 million in consideration for rights granted to Novartis under our collaboration and to partly reimburse costs previously incurred by us to develop *in vivo* RNAi technology. In addition, in October 2005, Novartis purchased approximately 5.3 million shares at a purchase price of $11.11 per share for an aggregate purchase price of approximately $58.5 million. The closing price of our common stock on the date of purchase was $9.90. We recorded the difference between the purchase price and the closing price of $6.4 million as deferred revenue. We recognized revenues of $0.7 million under our Novartis collaboration during 2005.

InterfeRx Licenses. In 2005, we began licensing our intellectual property to others under our InterfeRx program. Under existing programs, we recognized revenues of $0.4 million in 2005.

Deferred Revenue. Deferred revenue of $20.8 million at December 31, 2005 represents payments received from our collaborators pursuant to our license agreements with them which we have yet to earn pursuant to our revenue recognition policy.

Operating Expenses

The following tables summarize our operating expenses for the periods indicated, in thousands and as a percentage of total expenses, together with the changes in thousands and percentages:

	2005	% of Total Operating Expenses	2004	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 35,319	72%	$ 24,603	67%	$ 10,716	44%
General and administrative	13,869	28%	11,939	33%	1,930	16%
Total operating expenses	$ 49,188	100%	$ 36,542	100%	$ 12,646	35%

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Research and development. The following table summarizes the components of our research and development expenses for the periods indicated, in thousands and as a percentage of total research and development expenses, together with the changes in thousands and percentages:

	2005	% of Expense Category	2004	% of Expense Category	Increase $	Increase %
Research and development						
External services	$ 9,461	27%	$ 3,489	14%	$ 5,972	171%
License and patent fees	6,904	20%	5,833	24%	1,071	18%
Compensation and related	6,895	20%	5,925	24%	970	16%
Facilities-related expenses	4,668	13%	3,055	12%	1,613	53%
Lab supplies and materials	3,672	10%	3,057	12%	615	20%
Stock-based compensation	2,431	7%	2,087	9%	344	16%
Other	1,288	3%	1,157	5%	131	11%
Total research and development expenses	$ 35,319	100%	$ 24,603	100%	$ 10,716	44%

During the year ended December 31, 2005, our research and development expenses increased due to the expansion of our research and development organization in support of the growth of our programs.

As indicated by the table above, the most significant increase in our research and development expenses in 2005 was external services. External services includes pre-clinical expenses, clinical expenses and consulting expenses related to the development of our RSV program, which began in December 2005, and our ocular disease program, for which development was suspended in September 2005 based on changing clinical development and commercial factors. License and patent fees for 2005 included $3.7 million in payments to certain entities as a result of the Novartis agreement, as well as a $2.1 million non-cash charge in the second quarter of 2005 resulting from the issuance of 270,000 shares of our common stock in connection with the June 2005 amendment to our license agreements with Max Planck Innovation. Our facilities-related research and development expenses increased in 2005 due to the occupation of our new facility for all of 2005 compared to only half of 2004.

General and administrative. The following tables summarize the components of our general and administrative expenses for the periods indicated, in thousands and as a percentage of total general and administrative expenses, together with the changes in thousands and percentages:

	2005	% of Expense Category	2004	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 3,780	27%	$ 2,891	24%	$ 889	31%
Compensation and related	3,339	24%	3,316	28%	23	1%
Stock-based compensation	2,166	16%	2,019	17%	147	7%
Facilities related	1,893	14%	2,135	18%	(242)	(11)%

Insurance	616	4%	388	3%	228	59%
Other	2,075	15%	1,190	10%	885	74%
Total general and administrative expenses	$ 13,869	100%	$ 11,939	100%	$ 1,930	16%

As indicated in the table above, the most significant increase in general and administrative expenses in 2005 was an increase in consulting and professional services, which was due primarily to increases in expenses associated with business development activities and Sarbanes-Oxley compliance efforts. Increased insurance costs in 2005 were a result of our operation for a full year as a publicly traded company.

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Interest income was $1.5 million in 2005 compared to $0.5 million in 2004. The increase was due to our higher average cash, cash equivalent and marketable securities balances in 2005, as well as higher average interest rates.

Interest expense was $1.0 million in 2005 compared to $0.7 million in 2004. Interest expense for 2005 is the result of increased borrowings under our line of credit with Lighthouse used to finance capital equipment purchases.

Liquidity and Capital Resources

The following table summarizes our cash flow activities for the periods indicated, in thousands:

	Year Ended December 31,		
	2006	2005	2004
Net loss	$ (34,608)	$ (42,914)	$ (32,654)
Adjustments to reconcile net loss to net cash used in operating activities	12,633	9,672	6,599
Changes in operating assets and liabilities	(2,655)	16,757	6,485
Net cash used in operating activities	(24,630)	(16,485)	(19,570)
Net cash used in investing activities	(30,046)	(40,418)	(34,222)
Net cash provided by financing activities	166,631	52,617	50,604
Effect of exchange rate on cash	243	(229)	267
Net (decrease) increase in cash and cash equivalents	112,198	(4,515)	(2,921)
Cash and cash equivalents, beginning of period	15,757	20,272	23,193
Cash and cash equivalents, end of period	$ 127,955	$ 15,757	$ 20,272

Since we commenced operations in June 2002, we have generated significant losses. As of December 31, 2006, we had an accumulated deficit of $140.5 million. As of December 31, 2006, we had cash, cash equivalents and marketable securities of $217.3 million, compared to cash, cash equivalents and marketable securities of $80.0 million as of December 31, 2005. This cash balance includes approximately $163.3 million of net proceeds from our follow-on public offerings in January and December 2006. We invest primarily in cash equivalents, U.S. government obligations, high-grade corporate notes and commercial paper. Our investment objectives are primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available for sale. Fair value is determined based on quoted market prices.

Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception. This trend continued in 2006 as our use of cash in our operating activities increased as compared to the year ended December 31, 2005. The main components of our use of cash in operating activities are the net loss and changes in our operating assets and liabilities. Cash used in operating activities is adjusted for non-cash items to reconcile net loss to net cash used in operating activities. These non-cash adjustments primarily consist of stock-based compensation, depreciation and amortization. Non-cash stock-based compensation increased due primarily to our adoption of SFAS 123R on January 1, 2006 as well as to a lesser extent the increase of the fair value of non-employee stock options. In addition, we received $1.1 million in proceeds from our landlord for tenant improvements at our

Cambridge facility. These increases were offset by a net accounts receivable increase of $3.2 million and amortization of deferred revenue of $2.9 million for the year ended December 31, 2006. Our cash utilization is expected to continue throughout 2007 and thereafter as we continue to develop and advance our research and development initiatives. The actual amount of overall expenditures will depend on numerous factors, including the timing of expenses, the timing and terms of collaboration agreements or other strategic transactions, if any, and the timing and progress of our research and development efforts.

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Investing activities

For the year ended December 31, 2006, net cash used in investing activities of approximately $30.0 million resulted from net purchases of marketable securities of $25.1 million as well as purchases of property and equipment of $5.0 million related to the expansion of our Cambridge facility. For the year ended December 31, 2005, net cash provided by investing activities resulted from net sales of marketable securities of approximately $38.5 million, partially offset by purchases of property and equipment of approximately $1.9 million.

Financing activities

Since our inception, we have funded our operations primarily through the sale of equity securities. Through 2006, we raised approximately $54.8 million in net proceeds from the sale of redeemable convertible preferred stock and approximately $256.8 million from the sale of common stock, including $29.9 million from the sale of 5.75 million shares of our common stock in our initial public offering, which was completed in June 2004, $58.4 million from the sale of approximately 5.3 million shares of our common stock to Novartis, which was completed in October 2005, and $163.3 million of net proceeds from our follow-on public offerings in January and December 2006.

In addition to sales of equity securities, we have financed a portion of our property and equipment purchases through the establishment of equipment lines of credit. In March 2006, we entered into an agreement with Oxford Finance Corporation to establish an equipment line of credit for up to $7.0 million to help support capital expansion of our facility in Cambridge, Massachusetts and capital equipment purchases. During 2006, we borrowed an aggregate of $4.2 million from Oxford pursuant to the agreement. Of such amount, $1.3 million bears interest at fixed rates ranging from 10.1% to 10.4% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, approximately $2.9 million, bears interest at fixed rates ranging from 10.0% to 10.4% and is being repaid in 36 monthly installments of principal and interest.

In March 2004, we entered into an equipment line of credit with Lighthouse Capital Partners to finance leasehold improvements and equipment purchases of up to $10.0 million. The outstanding principal bears interest at a fixed rate of 9.25%, except for the drawdown made in December 2005 which bears interest at a fixed rate of 10.25%, maturing at various dates through December 2009. We were required to make interest-only payments on all draw-downs made during the period from March 26, 2004 through June 30, 2005, at which point all draw-downs began to be repaid over 48 months. On the maturity of each equipment advance under the line of credit, we are required to pay, in addition to the paid principal and interest, an additional amount of 11.5% of the original principal. This amount is being accrued over the applicable borrowing period as additional interest expense.

At December 31, 2006, we had an aggregate outstanding principal balance of $9.1 million under all of our loan agreements.

Based on our current operating plan, we believe that our existing resources, together with the cash we expect to generate under our collaborations, will be sufficient to fund our planned operations for at least the next several years, during which time we expect to extend the capabilities of our technology platform, further the development of our products, conduct clinical trials and continue to prosecute patent applications and otherwise build and maintain our patent portfolio. However, we may require significant additional funds earlier than we currently expect in order to develop, and commence clinical trials for, any product candidates.

We may seek additional funding through collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity

securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue.

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

our progress in demonstrating that siRNAs can be active as drugs;

our ability to develop relatively standard procedures for selecting and modifying siRNA drug candidates;

progress in our research and development programs, as well as the magnitude of these programs;

the timing, receipt, and amount of milestone and other payments, if any, from present and future collaborators, if any;

our ability to establish and maintain additional collaborative arrangements;

the resources, time and costs required to successfully initiate and complete our pre-clinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property;

the cost of preparing, filing, prosecuting, maintaining, and enforcing patent claims; and

the timing, receipt and amount of sales and royalties, if any, from our potential products.

Off-Balance Sheet Arrangements

In connection with certain license agreements, we are required to indemnify the licensor for certain damages arising under the agreement. In addition, we are a party to a number of agreements entered into in the ordinary course of business, which contain typical provisions, which obligate us to indemnify the other parties to such agreements upon the occurrence of certain events. These indemnification obligations are considered off-balance sheet arrangements in accordance with FASB Interpretation 45, Guarantor s Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others. To date, we have not encountered material costs as a result of such obligations and have not accrued any liabilities related to such obligations and have not accrued any liabilities related to such obligations in our financial statements. See Note 6 to our consolidated financial statements included in this Annual Report on Form 10-K for further discussion of these indemnification agreements.

Contractual Obligations

Set forth below is a description of our contractual cash obligations as of December 31, 2006, in thousands.

	Payments Due by Period				
Contractual Obligations	**2007**	**2008 and 2009**	**2010 and 2011**	**After 2011**	**Total**
Operating lease obligations(1)	$ 2,675	$ 4,757	$ 3,881	$	$ 11,313
Short and long-term debt(2)	3,942	7,129	234		11,305
Purchase obligations(3)	495				495
Fixed license payments(4)	488	991	1,045	5,630	8,154

Total contractual cash obligations	$ 7,600	$ 12,877	$ 5,160	$ 5,630	$ 31,267

(1) Operating lease obligations include our Cambridge, Massachusetts and Kulmbach, Germany non-cancelable operating lease agreements

(2) Relates to our line of credit with Oxford Financial Corporation, entered into in March 2006, and our line of credit with Lighthouse Capital Partners V, LP., entered into in March 2004

(3) Relates primarily to non-cancellable purchase orders

(4) Fixed license payments relates to our payment commitments for the rights to use certain technologies in our research and in any products we may develop that include these technologies

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We in-license technology from a number of sources. Pursuant to these in-license agreements, we will be required to make additional payments if and when we achieve specified development and regulatory milestones.

Recent Accounting Pronouncements

In February 2006, the FASB issued SFAS No. 155, Accounting for Certain Hybrid Instruments, or SFAS 155, which is an amendment to SFAS No. 133 and SFAS No. 140. SFAS 155 allows financial instruments which have embedded derivatives to be accounted for as a whole (eliminating the need to bifurcate the derivative from its host) if the holder elects to account for the instrument as a whole instrument on a fair value basis. This statement is effective for all financial instruments acquired or issued after the beginning of an entity s first fiscal year that begins after September 15, 2006. We do not believe the adoption of this statement will have a material impact on our consolidated financial statements.

In July 2006, the FASB issued FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes, or FIN 48, which clarifies the accounting for uncertainty in income taxes recognized in a company s financial statements in accordance with FASB Statement No. 109, Accounting for Income Taxes. FIN 48 requires a company to recognize, in its financial statements, the impact of a tax position only if that position is more likely than not of being sustained on an audit basis solely on the technical merit of the position. In addition, FIN 48 requires qualitative and quantitative disclosures including a discussion of reasonably possible changes that might occur in the recognized tax benefits over the next 12 months as well as a roll-forward of all unrecognized tax benefits. FIN 48 is effective for fiscal years beginning after December 15, 2006. We intend to adopt FIN 48 beginning January 2007 and are currently evaluating the impact FIN 48 might have on our consolidated financial statements.

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements, or SFAS 157, which addresses how companies should measure fair value when they are required to do so for recognition or disclosure purposes. The standard provides a common definition of fair value and is intended to make the measurement of fair value more consistent and comparable as well as improving disclosures about those measures. The standard is effective for financial statements for fiscal years beginning after November 15, 2007. This standard formalizes the measurement principles to be utilized in determining fair value for purposes such as derivative valuation and impairment analysis. We are still evaluating the implications of SFAS 157, but do not currently expect it to have a significant impact on our consolidated financial statements.

In February 2007, the FASB issued FAS No. 159, The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of FAS 115 (FAS No. 159). The new statement allows entities to choose, at specified election dates, to measure eligible financial assets and liabilities at fair value that are not otherwise required to be measured at fair value. If a company elects the fair value option for an eligible item, changes in that item s fair value in subsequent reporting periods must be recognized in current earnings. FAS No. 159 is effective for fiscal years beginning after November 15, 2007. We are currently evaluating the potential impact of FAS No. 159 on our financial position and results of operations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. Our marketable securities consist of U.S. government obligations, corporate debt and commercial paper. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments are sensitive to changes in interest rates. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market

interest rate at the date of purchase of the financial instrument. A 10% decrease in market interest rates at December 31, 2006 would impact the net fair value of such interest-sensitive financial instruments by approximately $0.2 million.

Foreign Currency Exchange Rate Risk

We are exposed to foreign currency exchange rate risk. Our European operations are based in Kulmbach, Germany and the functional currency of these operations is the Euro. We provide funding to our European

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operations to pay for obligations denominated in Euros. The effect that fluctuations in the exchange rate between the Euro and the United States Dollar have on the amounts payable to fund our European operations are recorded in our consolidated statements of operations as other income or expense. We do not enter into any foreign exchange hedge contracts.

Assuming the amount of expenditures by our European operations were consistent with 2006 and the timing of the funding of these operations were to remain consistent during the remainder of 2007, a constant increase or decrease in the exchange rate between the Euro and the United States Dollar during the remainder of 2007 of 10% would result in a foreign exchange gain or loss of approximately $0.1 million.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Management s Annual Report on Internal Control Over Financial Reporting

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of, the company s principal executive and principal financial officers and effected by the company s board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;

Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The Company s management assessed the effectiveness of the Company s internal control over financial reporting as of December 31, 2006. In making this assessment, the Company s management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on our assessment, management concluded that, as of December 31, 2006, the Company s internal control over financial reporting is effective based on those criteria.

The Company s independent registered public accounting firm has issued an audit report on our assessment of the Company s internal control over financial reporting. This report appears on page 70.

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Alnylam Pharmaceuticals, Inc:

We have completed integrated audits of Alnylam Pharmaceuticals, Inc s. 2006 and 2005 consolidated financial statements and of its internal control over financial reporting as of December 31, 2006 and an audit of its 2004 consolidated financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

Consolidated financial statements and financial statement schedule:

In our opinion, the consolidated financial statements listed in the accompanying index appearing under Item 15(a)(1) present fairly, in all material respects, the financial position of Alnylam Pharmaceuticals, Inc. and its subsidiaries at December 31, 2006 and 2005 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2006 in conformity with accounting principles generally accepted in the United States of America. In addition, in our opinion, the financial statement schedule listed in the index appearing under Item 15(a)(2) presents fairly, in all material respects, the information set forth therein when read in conjunction with the related consolidated financial statements. These financial statements and financial statement schedule are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements and financial statement schedule based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit of financial statements includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 8 to the consolidated financial statements, the Company changed the manner in which it accounts for share-based compensation in 2006.

Internal control over financial reporting:

Also, in our opinion, management s assessment, included in Management s Annual Report on Internal Control over Financial Reporting appearing under Item 8, that the Company maintained effective internal control over financial reporting as of December 31, 2006 based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2006, based on criteria established in *Internal Control Integrated Framework* issued by the COSO. The Company s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express opinions on management s assessment and on the effectiveness of the Company s internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. An audit of internal control over financial reporting includes obtaining an understanding of internal control over financial reporting, evaluating management s assessment, testing and evaluating the design and operating effectiveness of internal control, and

performing such other procedures as we consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable

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assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

PricewaterhouseCoopers LLP

Boston, Massachusetts
March 9, 2007

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2006	2005
ASSETS		
Current assets:		
Cash and cash equivalents	$ 127,955	$ 15,757
Marketable securities	89,305	64,245
Collaboration receivables	3,829	609
Related party notes receivable		146
Prepaid expenses and other current assets	1,695	1,657
Total current assets	222,784	82,414
Property and equipment, net	12,173	10,580
Intangible assets, net	1,933	2,491
Restricted cash	2,313	2,313
Other assets	803	550
Total assets	$ 240,006	$ 98,348
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 4,085	$ 1,975
Accrued expenses	4,479	3,899
Current portion of notes payable	3,217	1,876
Deferred revenue	11,144	10,734
Total current liabilities	22,925	18,484
Deferred revenue, net of current portion	6,786	10,099
Deferred rent	3,202	2,467
Notes payable, net of current portion	5,919	5,519
Total liabilities	38,832	36,569
Commitments and contingencies (Note 6)		
Stockholders equity:		
Preferred stock, $0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at December 31, 2006 and December 31, 2005		
Common stock, $0.01 par value, 125,000,000 shares authorized; 37,050,631 shares issued and outstanding at December 31, 2006; 26,721,149 shares issued and 26,638,255 shares outstanding at December 31, 2005	371	267

Additional paid-in capital	340,779	170,033
Deferred stock compensation	(89)	(2,460)
Accumulated other comprehensive income (loss)	640	(142)
Accumulated deficit	(140,527)	(105,919)
Total stockholders equity	201,174	61,779
Total liabilities and stockholders equity	$ 240,006	$ 98,348

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

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share amounts)

	Year Ended December 31,		
	2006	2005	2004
Net revenues from research collaborators	$ 26,930	$ 5,716	$ 4,278
Operating expenses:			
Research and development(1)	49,798	35,319	24,603
General and administrative(1)	16,633	13,869	11,939
Total operating expenses	66,431	49,188	36,542
Loss from operations	(39,501)	(43,472)	(32,264)
Other income (expense):			
Interest income	6,177	1,549	504
Interest expense	(1,029)	(969)	(661)
Other expense	(255)	(22)	(233)
Total other income (expense)	4,893	558	(390)
Net loss	(34,608)	(42,914)	(32,654)
Accretion of redeemable convertible preferred stock			(2,713)
Net loss attributable to common stockholders	$ (34,608)	$ (42,914)	$ (35,367)
Comprehensive loss:			
Net loss	$ (34,608)	$ (42,914)	$ (32,654)
Foreign currency translation	665	(534)	399
Unrealized gain (loss) on marketable securities	117	(28)	(55)
Comprehensive loss	$ (33,826)	$ (43,476)	$ (32,310)
Net loss per common share basic and diluted	$ (1.09)	$ (1.96)	$ (2.98)
Weighted average common shares used to compute basic and diluted net loss per common share	31,890	21,949	11,886

(1) Non-cash stock-based compensation expense included in these amounts are as follows:

Research and development	$ 5,006	$ 2,431	$ 2,087
General and administrative	3,298	2,166	2,019

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

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS EQUITY (DEFICIT)
(In thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in	Deferred Stock	Accumulated Other Comprehensive (Loss)	Accumulated	Total Stockholde Equity
	Shares	Amount	Shares	Amount	Capital	Compensation	Income	Deficit	(Deficit)
lance at cember 31, 03	21,066,680	$ 55,189	2,251,482	$	$ 7,416	$ (4,681)	$ 76	$ (29,518)	$ (26,70
justment to lect change par value of mmon stock ote 8.)				22	(22)				
ercise of mmon stock ions			255,075	3	165				16
uance of nvertible ferred stock	1,666,667	10,557			833			(833)	
cretion of ferred stock		1,880			(1,880)				(1,88
purchase of tricted stock ferred mpensation ated to stock ions and tricted stock nortization deferred mpensation pense ated to stock ions and tricted stock			(82,890)	(1)	1				
					3,056	(3,056)			
					65	4,040			4,10
nversion of eemable nvertible ferred stock	(22,733,347)	(67,626)	11,964,908	120	67,506				67,62

o common ck upon ial public ering uance of mmon stock on initial blic ering, net of ering costs $4,616	5,750,000	57	29,827				29,88
uance of mmon stock rsuant to laboration eement	710,273	7	5,249				5,25
reign rency nslation					399		39
realized s on rketable urities					(55)		(5
t loss						(32,654)	(32,65
lance at cember 31, 04	20,848,848	208	112,216	(3,697)	420	(63,005)	46,14
ercise of mmon and tricted stock ions and rrants	199,750	2	184				18
uance of mmon stock	5,589,657	57	54,273				54,33
ferred mpensation ated to stock ions and tricted stock			2,661	(2,661)			
nortization deferred mpensation pense ated to stock ions and tricted stock			699	3,898			4,59
reign rency nslation					(534)		(53
					(28)		(2

realized s on rketable urities t loss						(42,914)	(42,91
lance at cember 31, 05	26,638,255	267	170,033	(2,460)	(142)	(105,919)	61,77
ercise of mmon stock ions and rrants	539,425	5	998				1,00
uance of mmon stock	56,990	1	591				59
ferred mpensation ated to stock ions and tricted stock			1,614	(467)			1,14
nortization deferred mpensation pense ated to stock ions and tricted stock			4,318	2,838			7,15
uance of mmon stock on public erings, net offering ts of $6,586	9,815,961	98	163,225				163,32
reign rency nslation					665		66
realized n on rketable urities					117		11
t loss						(34,608)	(34,60
lance at cember 31, 06	$ 37,050,631	$ 371	$ 340,779	$ (89)	$ 640	$ (140,527)	$ 201,17

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

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2006	2005	2004
Cash flows from operating activities:			
Net loss	$ (34,608)	$ (42,914)	$ (32,654)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,815	3,119	2,444
Loss on disposal of equipment			49
Non-cash stock-based compensation	8,304	4,597	4,106
Realized foreign currency losses (gains)	255	(137)	
Non-cash license expense	130	2,093	
Charge for 401(k) company stock match	129		
Changes in operating assets and liabilities, net of effects of acquisition:			
Proceeds from landlord tenant improvements	1,106		3,003
Collaboration receivables	(3,220)	243	(859)
Prepaid expenses and other assets	(336)	(256)	(637)
Accounts payable	2,088	1,025	(615)
Accrued expenses	611	(12)	2,399
Deferred revenue	(2,904)	15,757	3,194
Net cash used in operating activities	(24,630)	(16,485)	(19,570)
Cash flows from investing activities:			
Purchases of property and equipment	(4,986)	(1,947)	(9,006)
Increase in restricted cash			373
Proceeds from sale of equipment			185
Purchases of marketable securities	(172,303)	(70,882)	(33,499)
Sales of marketable securities	147,243	32,411	7,725
Net cash used in investing activities	(30,046)	(40,418)	(34,222)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of issuance costs	164,890	52,423	35,308
Proceeds from issuance of preferred stock, net of issuance costs			10,000
Proceeds from notes payable	4,000	1,037	7,201
Repayments of notes payable	(2,259)	(843)	(1,859)
Deferred financing costs incurred in connection with the equipment line of credit			(46)
Net cash provided by financing activities	166,631	52,617	50,604
Effect of exchange rate on cash	243	(229)	267

Net increase (decrease) in cash and cash equivalents	112,198	(4,515)	(2,921)
Cash and cash equivalents, beginning of period	15,757	20,272	23,193
Cash and cash equivalents, end of period	$ 127,955	$ 15,757	$ 20,272
Supplemental disclosure of cash flows			
Cash paid for interest	$ 726	$ 633	$ 487
Supplemental disclosure of non-cash financing activities			
Common stock issued to Max Planck Innovation	$ 130	$ 2,093	$
Fair value of warrant issued in connection with equipment line of credit included as deferred financing costs			557
Conversion of redeemable convertible preferred stock into common stock			67,626
Accretion of redeemable convertible preferred stock			2,713

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

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. NATURE OF BUSINESS

Alnylam Pharmaceuticals, Inc. (the Company or Alnylam) commenced operations on June 14, 2002 as a biopharmaceutical company seeking to develop and commercialize new drugs that work through a recently discovered system in cells known as RNA interference, or RNAi. Alnylam is focused on discovering, developing and commercializing RNAi therapeutics by establishing strategic alliances with leading pharmaceutical and biotechnology companies, establishing and maintaining a strong intellectual property position in the RNAi field and generating revenues through licensing agreements. The Company has devoted substantially all of its efforts to business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff, and raising capital.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The Company comprises four entities, Alnylam Pharmaceuticals, Inc. (the parent company) and three subsidiaries (Alnylam U.S., Inc., Alnylam Europe AG and Alnylam Securities Corporation). Alnylam Pharmaceuticals, Inc. is a Delaware corporation that was formed on May 8, 2003. Alnylam U.S. is also a Delaware corporation that was formed on June 14, 2002. Alnylam Securities Corporation is a Massachusetts corporation that was formed on December 19, 2006.

The accompanying consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries Alnylam U.S., Inc., Alnylam Europe AG and Alnylam Securities Corporation. All significant intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Concentrations of Credit Risk and Significant Customers

Financial instruments which potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. As of December 31, 2006 and 2005, substantially all of the Company s cash, cash equivalents and marketable securities were invested in money market mutual funds, commercial paper, corporate notes and government securities through highly rated financial institutions.

To date, the Company s revenue has been generated from primarily Merck and Novartis. Novartis owned approximately 14% of the Company s outstanding common stock as of December 31, 2006. In 2006 the Company had revenue from Novartis and Merck, which accounted for 81% and 3%, respectively, of the Company s total revenue. In 2005 the Company had significant revenue from Merck and Novartis, which accounted for 63% and 13%, respectively, of the Company s total revenue. In 2004, the Company had significant revenue from only Merck, which

accounted for 95% of revenues recorded. Receivables from Novartis represented approximately 70% of the Company s collaboration receivables balance at December 31, 2006. Receivables from Novartis and Merck represented approximately 72% and 28%, respectively, of the Company s collaboration receivables balance at December 31, 2005. Deferred revenue from Novartis, Biogen Idec and Merck represented approximately 51%, 26% and 22%, respectively, of the Company s deferred revenue balance at December 31, 2006. Deferred revenue from Novartis and Merck represented approximately 77% and 23%, respectively, of the Company s deferred revenue balance at December 31, 2005.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Fair Value of Financial Instruments

The carrying amounts of the Company s financial instruments, which include cash equivalents, collaboration receivable, accounts payable, accrued expenses and notes payable, approximate their fair values at December 31, 2006 and 2005. At December 31, 2006, the Company had no investments with maturities of greater than one year classified as short-term in its balance sheet. Unrealized gains or losses are included as a component of accumulated other comprehensive income, included in stockholders equity in the consolidated balance sheets. The following table summarizes the Company s marketable securities at December 31, 2006 and 2005 in thousands:

	December 31, 2006			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 69,787	$ 33	$	$ 69,820
Corporate notes	19,483	2		19,485
Total	$ 89,270	$ 35	$	$ 89,305

	December 31, 2005			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 2,024	$ 1	$	$ 2,025
Asset backed securities	14,752		(16)	14,736
Corporate notes	47,552		(68)	47,484
Total	$ 64,328	$ 1	$ (84)	$ 64,245

Revenue Recognition

The Company recognizes revenue in accordance with the Securities and Exchange Commission s (SEC) Staff Accounting Bulletin No. 104, Revenue Recognition in Financial Statements. The Company has entered into collaboration agreements with Merck and Novartis Pharma and its affiliate, Novartis Institutes for BioMedical Research, Inc. (collectively Novartis) and Biogen Idec. Revenues from these collaboration agreements may include nonrefundable license fees, milestones, research and development funding, cost reimbursements and royalties. When evaluating multiple element arrangements, the Company considers whether the components of the arrangement represents separate units of accounting as defined in Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue*

Arrangements with Multiple Deliverables (EITF 00-21). Application of these standards requires subjective determinations and requires management to make judgments about the value of the individual elements and whether it is separable from the other aspects of the contractual relationship. Nonrefundable license fees are recognized as revenue as the Company performs under the collaboration agreements. Where the Company s level of effort is relatively constant over the performance period, the Company recognizes total fixed or determined contract revenues on a straight-line basis over the estimated period of performance under the contract unless evidence suggests that revenue is earned in a different pattern, in which case that pattern is followed.

The Company recognizes milestone payments as revenue upon achievement of the milestone only if (1) the milestone payments are nonrefundable; (2) substantive effort is involved in achieving the milestone; and (3) the amount of the milestone is reasonable in relation to the effort expended or the risk associated with achievement of the milestone. If any of these conditions are not met, the Company defers the milestone payments and recognizes them as revenue over the estimated period of performance under the contract as the Company completes its performance obligations.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Novartis

In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an upfront payment of $10.0 million to the Company in October 2005, to partly reimburse prior costs incurred by the Company to develop *in vivo* RNAi technology. In addition, the collaboration and license agreement includes terms under which Novartis agreed to provide the Company with research funding and milestone payments as well as royalties on annual net sales of products resulting from the collaboration and license agreement. The Company initially deferred the non-refundable $10.0 million upfront payment and the $6.4 million premium received that represents the difference between the purchase price and the closing price of the common stock of the Company on the date of the stock purchase from Novartis. These payments, in addition to research funding and certain milestone payments, are amortized into revenue using the proportional performance method over the estimated duration of the Novartis agreement or ten years. Under this model, the Company estimates the level of effort to be expended over the term of the agreement and recognize revenue based on the lesser of the amount calculated based on proportional performance of total expected revenue or the amount of non-refundable payments earned.

The Company believes the estimated term of the Novartis agreement includes the three-year term of the agreement, two one-year extensions at the election of Novartis and limited support as part of a technology transfer until the fifth anniversary of the termination of the agreement. Therefore, an expected term of ten years is used in the proportional performance model. The Company will evaluate the expected term when new information is known that could affect the Company s estimate. In the event the Company s period of performance is different than estimated, revenue recognition will be adjusted on a prospective basis.

Merck

The Company recognizes revenues from reimbursable research and development activities at the time these activities are performed under the terms of the related agreement, when the collaborator is obligated to pay and when no future performance obligations exist. In revenue arrangements where both parties reimburse each other for research costs, such as the Company s June 2004 collaboration agreement with Merck for the co-development of RNAi therapeutics for the treatment of ocular diseases, in which both parties reimbursed each other for 50% of the costs incurred, as set forth in the agreement, the Company followed EITF Issue No. 01-9, *Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products)* (EITF 01-9) in determining the proper accounting for these costs. In accordance with EITF 01-9, revenue recognized by the Company for costs reimbursed by the Company s customer were reduced by amounts reimbursable to the other party during the same accounting period unless the Company received a separable and identifiable benefit in exchange for the payments made to the other party under the arrangement and the Company could reasonably estimate the fair value of the benefit received.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under the liability method, deferred tax assets and liabilities reflect the impact of temporary differences between amounts of assets and liabilities for financial reporting purposes and such amounts as measured under enacted tax laws. A valuation allowance is required to offset any net deferred tax assets if, based upon the available evidence, it is more likely than not that some or all of the deferred tax asset will not be realized.

Research and Development Costs

Research and development costs are expensed as incurred. Included in research and development costs are wages, benefits and other operating costs such as legal expenses to secure and defend patents (which are expensed as incurred), facilities, supplies and overhead directly related to the Company s research and development department as well as costs to acquire technology licenses.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

During the years ended December 31, 2006, 2005 and 2004, the Company included approximately $0.6 million, $0.3 million and $1.3 million, respectively, of legal patent costs in research and development costs and expenses.

The Company has entered into several license agreements for rights to utilize certain technologies. The terms of the licenses may provide for upfront payments, annual maintenance payments, milestone payments based upon certain specified events being achieved and royalties on product sales. Costs to acquire and maintain licensed technology that has not reached technological feasibility and does not have alternative future use are charged to research and development expense as incurred. During the years ended December 31, 2006, 2005 and 2004, the Company charged to research and development expense $4.0 million, $6.1 million and $5.8 million, respectively, of costs associated with license fees.

Accounting for Stock-Based Compensation

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS 123R, *Share-Based Payment*, using the modified-prospective-transition method. Under that transition method, stock-based compensation expense recognized for the year ended December 31, 2006 includes compensation for all stock-based payments granted prior to, but not yet vested as of, January 1, 2006, based on the grant date fair value estimated in accordance with the original provisions of SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123), and compensation cost for all stock-based payments granted subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R. Such amounts have been reduced by the Company s estimate of forfeitures of all unvested awards. Results for prior periods have not been restated.

Prior to January 1, 2006, the Company accounted for its stock-based compensation plans under the recognition and measurement provisions of Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and related interpretations for all awards granted to employees. Under APB 25, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation expense is recorded. When the exercise price of options granted to employees under these plans is less than the market price of the common stock on the date of grant, compensation expense is recognized over the vesting period of the award.

For stock options granted to non-employees, the Company recognizes compensation expense in accordance with the requirements of SFAS 123 and Emerging Issues Task Force Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* under which compensation expense is generally recognized over the vesting period of the award, which is generally the period during which services are rendered by such non-employees. Stock options granted by the Company to non-employees, other than members of our Board of Directors, generally vest over a four-year service period. The Company has two equity instruments that are required to be evaluated under SFAS 123R, stock option plans and an employee stock purchase plan. The Company accounts for non-employee grants as an expense over the vesting period of the underlying stock options using the method prescribed by FASB Interpretation No. 28.

Foreign Currency

The Company s foreign subsidiary, Alnylam Europe AG (a German-based company), has designated its local currency, the Euro, as its functional currency. Financial statements of this foreign subsidiary are translated to United States

dollars for consolidation purposes using current rates of exchange for assets and liabilities; equity is translated using historical exchange rates; and revenue and expense amounts are translated using the average exchange rate for the period. Net unrealized gains and losses resulting from foreign currency translation are included in other comprehensive income (loss) which is a separate component of stockholders equity. The Company also records a charge or a credit to stockholders equity for exchange gains or losses on intercompany balances that are of a long-term nature. Net realized gains and losses from foreign currency transactions are

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

included in the consolidated statement of operations. The Company recognized a loss of $0.3 million during 2006, a gain of $0.1 million during 2005 and a loss of $0.2 million during 2004 from foreign currency transactions.

Comprehensive Loss

Comprehensive loss is comprised of net loss and certain changes in stockholders equity that are excluded from net loss. The Company includes foreign currency translation adjustments in other comprehensive loss for Alnylam Europe AG as the functional currency is not the United States dollar.

Net Loss Per Common Share

The Company accounts for and discloses net loss per common share in accordance with SFAS No. 128 *Earnings per Share* . Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options and warrants (using the treasury stock method), unvested restricted stock awards and the weighted average conversion of the preferred stock into shares of common stock (using the if-converted method) for periods prior to the Company s initial public offering, which was completed in June 2004. Because the inclusion of potential common stock would be anti-dilutive for all periods presented, diluted net loss per share is the same as basic net loss per share.

The following table sets forth the potential common stock excluded from the calculation of net loss per share because their inclusion would be anti-dilutive:

	December 31,		
	2006	**2005**	**2004**
Options to purchase common stock	4,649,959	3,907,127	2,851,967
Warrants to purchase common stock		52,630	52,630
Unvested restricted common stock		55,063	331,567
Options that were exercised before vesting	40,288	72,796	118,563
	4,690,247	4,087,616	3,354,727

Segment Information

The Company has two operating segments, United States and Germany, which management aggregates into one reporting segment in determining how to allocate resources and assess financial performance. The majority of the Company s net revenues from research collaborators was derived in the United States.

The following table presents total long-lived tangible assets by geographic area at December 31, 2006 and 2005, in thousands:

	December 31, 2006	2005
Long-lived tangible assets:		
United States	$ 10,077	$ 8,207
Germany	2,096	2,373
Total long-lived tangible assets	$ 12,173	$ 10,580

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Recent Accounting Pronouncements

In February 2006, the FASB issued SFAS No. 155, *Accounting for Certain Hybrid Instruments* (SFAS 155), which is an amendment to SFAS No. 133 and SFAS No. 140. SFAS 155 allows financial instruments which have embedded derivatives to be accounted for as a whole (eliminating the need to bifurcate the derivative from its host) if the holder elects to account for the instrument as a whole instrument on a fair value basis. This statement is effective for all financial instruments acquired or issued after the beginning of an entity s first fiscal year that begins after September 15, 2006. The Company does not believe the adoption of this statement will have a material impact on its consolidated financial statements.

In July 2006, the FASB issued FASB Interpretation No. 48, *Accounting for Uncertain Tax Provisions, an Interpretation of SFAS Statement 109* (FIN 48). FIN 48 clarifies the accounting for uncertain tax positions as described in SFAS No. 109, *Accounting for* Income *Taxes*, and requires a company to recognize, in its financial statements, the impact of a tax position only if that position is more likely than not of being sustained on an audit basis solely on the technical merit of the position. In addition, FIN 48 requires qualitative and quantitative disclosures including a discussion of reasonably possible changes that might occur in the recognized tax benefits over the next twelve months as well as a roll-forward of all unrecognized tax benefits. FIN 48 is effective for fiscal years beginning after December 15, 2006. The Company intends to adopt FIN 48 beginning January 2007 and is currently evaluating the impact of FIN 48 and does not expect that it will have a material impact on its consolidated financial statements.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements* , which addresses how companies should measure fair value when they are required to do so for recognition or disclosure purposes. The standard provides a common definition of fair value and is intended to make the measurement of fair value more consistent and comparable as well as improving disclosures about those measures. The standard is effective for financial statements for fiscal years beginning after November 15, 2007. This standard formalizes the measurement principles to be utilized in determining fair value for purposes such as derivative valuation and impairment analysis. The Company is still evaluating the implications of this standard, but does not currently expect it to have a significant impact on its consolidated financial statements.

In February 2007, the FASB issued FAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of FAS 115* (FAS No. 159). The new statement allows entities to choose, at specified election dates, to measure eligible financial assets and liabilities at fair value that are not otherwise required to be measured at fair value. If a company elects the fair value option for an eligible item, changes in that item s fair value in subsequent reporting periods must be recognized in current earnings. FAS No. 159 is effective for fiscal years beginning after November 15, 2007. The Company is currently evaluating the potential impact of FAS No. 159 on its consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

3. ACQUISITION OF RIBOPHARMA AG

Intangible assets at December 31, 2006 and 2005 are as follows, in thousands:

	December 31, 2006	2005
Core Technology	$ 3,054	$ 3,197
Workforce	437	437
	3,491	3,634
Less accumulated amortization:		
Core Technology	(1,185)	(879)
Workforce	(373)	(264)
Total accumulated amortization	(1,558)	(1,143)
	$ 1,933	$ 2,491

During the years ended December 31, 2006, 2005 and 2004, the Company recorded $0.4 million, $0.5 million and $0.5 million, respectively, of amortization expense related to the core technology and workforce intangibles, of which the entire amount is included in research and development expenses. The Company expects annual amortization expense related to the core technology intangible asset to be $0.3 million through 2012 and $0.2 million in 2013. Core technology and workforce are being amortized over their estimated useful lives of ten years and four years, respectively. During 2006, the Company reduced its intangible assets by $0.1 million related to the utilization of pre-acquisition deferred tax assets associated with net operating losses.

4. PROPERTY AND EQUIPMENT

Property and equipment consist of the following at December 31, 2006 and 2005, in thousands:

	Useful Life	December 31, 2006	2005
Laboratory equipment	5 years	$ 9,903	$ 7,799
Computer equipment and software	3 years	2,065	1,265
Furniture and fixtures	5 years	914	571
Leasehold improvements	*	7,056	6,010
Construction in progress		1,127	32

	21,065	15,677
Less: accumulated depreciation and amortization	(8,892)	(5,097)
	$ 12,173	$ 10,580

* shorter of asset life or lease term

Depreciation expense was $3.4 million, $2.6 million and $2.0 million for the years ended December 31, 2006, 2005 and 2004, respectively.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

5. NOTES PAYABLE

Equipment Lines of Credit

In March 2006, the Company entered into an agreement with Oxford Finance Corporation (Oxford) to establish an equipment line of credit for up to $7.0 million to help support capital expansion of the Company s facility in Cambridge, Massachusetts and capital equipment purchases. All borrowings under this line of credit are collateralized by the assets financed and the agreement contains certain provisions that restrict the Company s ability to dispose of or transfer these assets. During 2006, the Company borrowed an aggregate of approximately $4.2 million from Oxford pursuant to the agreement. Of such amount, approximately $1.3 million bears interest at fixed rates ranging from 10.1% to 10.4% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, approximately $2.9 million, bears interest at fixed rates ranging from 10.0% to 10.4% and is being repaid in 36 monthly installments of principal and interest.

In March 2004, the Company entered into an agreement with Lighthouse Capital Partners V, L.P. (Lighthouse) to establish an equipment line of credit for $10.0 million. In June 2005, the parties amended the agreement to allow the Company the ability to draw down amounts under the line of credit through December 31, 2005 upon adherence to certain conditions. All borrowings under the line of credit are collateralized by the assets financed and the agreement contains certain provisions that restrict the Company s ability to dispose of or transfer these assets. The outstanding principal bears interest at a fixed rate of 9.25%, except for the drawdown made in December 2005, which bears interest at a fixed rate of 10.25%, maturing at various dates through December 2009. On the maturity of each equipment advance under the line of credit, the Company is required to pay, in addition to the paid principal and interest, an additional amount of 11.5% of the original principal. This amount is being accrued over the applicable borrowing period as additional interest expense. As of December 31, 2006, there was $5.5 million outstanding under this line of credit with Lighthouse.

In connection with the agreement, the Company issued to Lighthouse and an affiliate of Lighthouse warrants to purchase redeemable convertible preferred stock, which were converted into warrants to purchase 52,630 shares of the Company s common stock at an exercise price of $9.50 per share upon the closing of the Company s initial public offering in June 2004. The Company recorded the fair value of these warrants of $0.6 million as a deferred financing cost which is being amortized to interest expense over the 63-month repayment term of the first advance. The fair value of the warrants was calculated using the Black-Scholes option pricing model with the following assumptions: 100% volatility, risk-free interest rate of 3.49%, no dividend yield and a seven-year term. Lighthouse and its affiliate net-exercised these warrants in full during the second quarter of 2006 and the Company issued an aggregate of 18,072 shares in connection with such exercises.

At December 31, 2006, future cash payments under the notes payable to Lighthouse and Oxford, including interest, are as follows, in thousands:

Year Ending December 31,	
2007	$ 3,942

2008	3,942
2009	3,187
2010	234
Total through 2010	11,305
Less: portion representing interest	2,169
Principal	9,136
Less: current portion	3,217
Long-term notes payable	$ 5,919

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

6. COMMITMENTS AND CONTINGENCIES

Indemnifications

Licensor indemnification In connection with a certain license agreement, the Company is required to indemnify the licensor for certain damages arising in connection with the intellectual property rights licensed under the agreement. The Company believes that the probability of receiving a claim is remote and, as such, no amounts have been accrued related to this indemnification at December 31, 2006 and 2005.

The Company is also a party to a number of agreements entered into in the ordinary course of business, which contain typical provisions, which obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain. Since its inception, the Company has not incurred any expenses as a result of such indemnification provisions. Accordingly, the Company has determined that the estimated aggregate fair value of its potential liabilities under such indemnification provisions is minimal and has not recorded any liability related to such indemnification provisions at December 31, 2006 and 2005.

Technology License Commitments

The Company has licensed the rights to use certain technologies in its research process as well as in any products the Company may develop including these licensed technologies. In accordance with the related license agreements, the Company is required to make certain fixed annual payments to the licensor or a designee of the licensor over various agreement terms. Many of these agreement terms are consistent with the remaining lives of the underlying intellectual property that the Company has licensed. At December 31, 2006, the Company was committed to make the following fixed license payments under existing license agreements, in thousands:

Year Ending December 31,	
2007	$ 488
2008	493
2009	498
2010	520
2011	525
Thereafter	5,630
Total	$ 8,154

Operating Leases

The Company leases office and laboratory space in Cambridge, Massachusetts and Kulmbach, Germany under non-cancelable operating lease agreements. Total rent expense, including operating expenses, under these operating

leases was $2.6 million, $1.9 million and $2.2 million, for the years ended December 31, 2006, 2005 and 2004, respectively.

In September 2003, the Company entered into an operating lease to rent 33,453 square feet of laboratory and office space in Cambridge, Massachusetts through September 2011. Rental payments began in April 2004. Under the original terms of the lease agreement, the Company began paying rent on an additional 10,605 square feet in this same facility in September 2005. In March 2006, the Company amended its lease agreement and began paying rent on an additional 17,823 square feet in this same facility on July 1, 2006, bringing the total square feet leased in Cambridge to 61,881 square feet. The Company has the option to extend the lease for two successive five-year extensions.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Pursuant to the terms of the lease agreement, the Company secured a $2.3 million letter of credit as security for its leased facility. The underlying cash securing this letter of credit has been classified as long-term restricted cash in the accompanying consolidated balance sheets.

The Company also leases 15,024 square feet of laboratory and office space in Kulmbach, Germany through June 2008 under a non-cancelable operating lease. The Company began paying rent on an additional 2,661 square feet in the same facility in July 2006. The Company has the option to extend its lease of this facility for two successive three-year extensions.

Future minimum lease payments under these non-cancelable leases are approximately as follows, in thousands:

Year Ending December 31,	
2007	$ 2,675
2008	2,539
2009	2,218
2010	2,218
2011	1,663
Total	$ 11,313

Related Party Notes Receivable

In connection with the acquisition of Ribopharma AG, the Company agreed to provide two shareholders of Ribopharma AG who received cash and common stock in the acquisition with non-recourse loans to cover any tax contingencies the shareholders may incur as a result of the acquisition. These loans bear interest at four percent per annum and are payable upon certain liquidity events. In addition to the loan commitment, the Company entered into an indemnity agreement whereby the Company has indemnified these shareholders for any taxes payable as a result of making the loan to the Ribopharma shareholders up to a maximum of approximately $0.2 million for each shareholder. With respect to the indemnity, the Company issued a letter of credit in 2003 to the two shareholders amounting to $0.4 million related to the potential indemnity that the Company has with the two shareholders. The required amount of the letter of credit is collateralized by restricted funds maintained by the Company at the bank issuing the letter of credit. As a result, the Company classified this amount as restricted cash in its consolidated balance sheet as of December 31, 2003. In June 2004, loans totaling approximately $0.3 million were provided to these shareholders and each shareholder subsequently released the Company from its indemnity obligation. As a result, the Company cancelled its letter of credit and removed this restriction of its cash. During December 2005, one of the notes for $0.1 million was paid in full. The remaining related party note receivable was paid in full in February 2006. At December 31, 2006, there were no amounts remaining under the related party note receivable.

In connection with the employment agreements of the same two Ribopharma AG employees, the Company has committed to paying a one-time payment to each employee of $0.3 million upon the issuance of a specific patent in

the United States of America. This contingent payment will be paid and expensed upon the issuance of the patent.

Legal Proceedings

The Company may periodically become subject to legal proceedings and claims arising in connection with on-going business activities, including being subject to claims or disputes related to patents that have been issued or are pending in the field of research the Company is focused on. The Company does not believe that there were any material claims against the Company at December 31, 2006.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

7. STOCKHOLDERS EQUITY

Preferred Stock

Prior to the Company s initial public offering in June 2004, the Company s primary source of funding was from sales of preferred stock, both convertible and redeemable convertible. During the year ended December 31, 2004, the Company recorded accretion of preferred stock of $2.7 million. In connection with the Company s initial public offering in June 2004, and in accordance with the preferred stock agreements, all outstanding shares of preferred stock converted into 11,964,908 of the Company s common stock. At December 31, 2006 there were no shares of preferred stock outstanding.

The Company has authorized up to 5,000,000 shares of preferred stock, $0.01 par value per share, for issuance. The preferred stock will have such rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be determined by the board of directors upon its issuance.

Stockholder Rights Agreement

On July 13, 2005, the Board of Directors of the Company declared a dividend of one right (collectively, the Rights) to buy one one-thousandth of a share of newly designated Series A Junior Participating Preferred Stock (Series A Junior Preferred Stock) for each outstanding share of the Company s common stock to stockholders of record at the close of business on July 26, 2005. Initially, the Rights are not exercisable and will be attached to all certificates representing outstanding shares of common stock, and no separate Rights Certificates will be distributed. The Rights will expire at the close of business on July 13, 2015 unless earlier redeemed or exchanged. Until a right is exercised, the holder thereof, as such, will have no rights as a stockholder of the Company, including the right to vote or to receive dividends. The rights are not immediately exercisable. Subject to the terms and conditions of the Rights Agreement entered into by the Company with Computershare (formerly EquiServe Trust Company, N.A.), as Rights Agent (the Rights Agreement), the Rights will become exercisable upon the earlier of (1) 10 business days following the later of (a) the first date of a public announcement that a person or group (an Acquiring Person) acquires, or obtained the right to acquire, beneficial ownership of 20 percent or more of the outstanding shares of common stock of the Company or (b) the first date on which an executive officer of the Company has actual knowledge that an Acquiring Person has become such or (2) 10 business days following the commencement of a tender offer or exchange offer that would result in a person or group beneficially owning more than 20 percent of the outstanding shares of common stock of the Company. Each right entitles the holder to purchase one one-thousandth of a share of Series A Junior Preferred Stock at an initial purchase price of $80.00 in cash, subject to adjustment. In the event that any person or group becomes an Acquiring Person, unless the event causing the 20% threshold to be crossed is a Permitted Offer (as defined in the Rights Agreement), each Right not owned by the Acquiring Person will entitle its holder to receive, upon exercise, that number of shares of common stock of the Company (or in certain circumstances, cash, property or other securities of the Company) which equals the exercise price of the Right divided by 50% of the current market price (as defined in the Rights Agreement) per share of such common stock at the date of the occurrence of the event. In the event that, at any time after any person or group becomes an Acquiring Person, (i) the Company is consolidated with, or merged with and into, another entity and the Company is not the surviving entity of such consolidation or merger (other than a consolidation or merger which follows a Permitted Offer) or if the Company is the surviving entity, but shares of its

outstanding common stock are changed or exchanged for stock or securities (of any other person) or cash or any other property, or (ii) more than 50% of the Company s assets or earning power is sold or transferred, each holder of a Right (except Rights which previously have been voided as set forth in the Rights Agreement) shall thereafter have the right to receive, upon exercise, that number of shares of common stock of the acquiring company which equals the exercise price of the Right divided by 50% of the current market price of such common stock at the date of the occurrence of the event.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Public Offerings of Common Stock

In June 2004, the Company completed the initial public offering of its common stock. The initial public offering consisted of the sale of 5,000,000 shares of common stock at a price of $6.00 per share. As part of the offering, the Company granted to the underwriters an option to purchase an additional 750,000 shares within 30 days of the initial public offering to cover over-allotments. This option was exercised in full in June 2004. Net proceeds from the initial public offering after deducting underwriters discounts and expenses were $29.9 million. Upon the closing of the initial public offering, the authorized number of shares of the Company s common stock increased to 125,000,000. In addition, upon the closing of the Company s initial public offering, the Company adopted certain stock incentive plans.

In January 2006, the Company completed a public offering of its common stock. The public offering consisted of the sale and issuance of 5,115,961 shares of the Company s common stock. The Company granted the underwriters an option to purchase up to an additional 767,394 shares of common stock within 30 days after the offering to cover over-allotments, which option was not exercised. The price to the public was $13.00 per share, and proceeds to the Company from the offering, net of expenses, were approximately $62.2 million. The shares of common stock were registered pursuant to registration statements filed with Securities and Exchange Commission in 2006 and 2005.

In December 2006, the Company completed a public offering of its common stock. The public offering consisted of the sale and issuance of 4,700,000 shares of the Company s common stock. The Company granted the underwriters an option to purchase up to an additional 705,000 shares of common stock within 30 days after the offering to cover over-allotments, which option was not exercised. The price to the public was $22.00 per share, and proceeds to the Company from the offering, net of expenses, were approximately $101.1 million. The shares of common stock were registered pursuant to registration statements filed with Securities and Exchange Commission in November 2006.

8. STOCK INCENTIVE PLANS

Stock Option Plans

Prior to the Company s initial public offering in June 2004, the Company had adopted stock incentive plans in 2002 and 2003. In June 2002, the Company adopted the 2002 Stock Incentive Plan (the 2002 Stock Plan), which was terminated in November 2002, and was replaced with the Alnylam U.S., Inc. 2002 Employee, Director and Consultant Stock Plan (the 2002 Plan). All options previously granted under the 2002 Stock Plan were cancelled and new options for the same number of shares, vesting provisions and exercise price were granted under the 2002 Plan. In September 2003, the Company adopted the Alnylam Pharmaceuticals, Inc. 2003 Employee, Director and Consultant Stock Plan (the 2003 Plan). Subsequent to the closing of the Company s initial public offering, no further stock options or other equity awards have been granted, or may be granted in the future, under the 2002 Plan or the 2003 Plan.

As of December 31, 2006, the Company s 2004 Stock Incentive Plan (the 2004 Plan) provides for the granting of stock options to purchase 6,404,615 shares of common stock. The 2004 Plan provides for an annual increase in the number of shares available for issuance under the plan equal to the lesser of 2,631,578 shares of common stock, 5% of the Company s outstanding shares or an amount determined by the board of directors. In addition, the 2004 Plan includes a non-employee director stock option program under which each eligible non-employee director will be entitled to a grant of options to purchase 25,000 shares of common stock upon his or her initial appointment to the board of

directors and a subsequent annual grant of an option to purchase 10,000 shares of common stock based on continued service. The chairman of the audit committee will receive an additional annual grant of an option to purchase 10,000 shares of common stock based on continued service.

On September 12, 2006, the board of directors amended the 2004 Plan: (1) to grant an eligible non-employee director options to purchase 30,000 shares of common stock upon his or her initial appointment to the board of

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

directors, and (2) commencing on the date of each annual meeting of stockholders beginning with the 2007 annual meeting, to grant to each eligible non-employee director who has served as a director for at least six months and who is serving as a director immediately prior to and following such annual meeting options to purchase 15,000 shares of common stock.

At December 31, 2006, an aggregate of 5,389,264 shares of common stock were reserved for issuance under the Company s stock plans, including outstanding options to purchase 4,649,959 shares of common stock and 739,305 shares were available for future grant under the 2004 Plan. Each option shall expire within ten years of issuance. Stock options granted by the Company to employees generally vest as to 25 percent of the shares on the first anniversary of the grant date and 6.25% of the shares at the end of each successive three-month period until fully vested.

In December 2004, the Financial Accounting Standards Board (FASB) issued Statement of Accounting Standard (SFAS) No. 123R, *Share-Based Payment,* an amendment of FASB Statements Nos. 123 and 95 (SFAS 123R), that addresses the accounting for stock-based payment transactions in which a company receives employee services in exchange for either equity instruments of the company or liabilities that are based on the fair value of the company s equity instruments or that may be settled by the issuance of such equity instruments. The statement eliminates the ability to account for employee stock-based compensation transactions using the intrinsic method and requires that such transactions be accounted for using a fair-value-based method and recognized as expense on a straight-line basis over the vesting period in the consolidated statements of operations. In March 2005, the SEC issued Staff Accounting Bulletin (SAB) No. 107 (SAB 107) regarding the SEC staff s interpretation of SFAS 123R. This interpretation provides the SEC staff s views regarding interactions between SFAS 123R and certain SEC rules and regulations and provides interpretations of the valuation of stock-based payments for public companies. The interpretive guidance is intended to assist companies in applying the provisions of SFAS 123R and investors and users of the financial statements in analyzing the information provided.

Since the Company s adoption of SFAS 123R, there have been no changes to the Company s equity plans or modifications to outstanding stock-based awards. Stock options granted by the Company to non-employee directors (i) upon their appointment to the board vest as to one-third of such shares on each of the first, second and third anniversaries of the date of grant and (ii) at each year s annual meeting at which they serve as a director vest in full on the first anniversary of the date of grant.

Upon the adoption of SFAS 123R, $0.8 million of the Company s deferred stock-based compensation balance of $2.5 million as of December 31, 2005, which was accounted for under APB 25, was reclassified against additional paid-in-capital. The remaining portion of deferred stock-based compensation balance at December 31, 2006 was composed of $0.1 million relating to the intrinsic value of stock options granted below fair market value that were accounted for under the minimum value method because the Company s stock was not publicly traded. The Company accounts for non-employee grants as an expense over the vesting period of the underlying stock options using the method prescribed by FASB Interpretation No. 28. At the end of each financial reporting period prior to vesting, the value of these options (as calculated using the Black-Scholes option-pricing model) is re-measured using the then-current fair value of the Company s common stock. The Company recognized approximately $2.2 million, $2.1 million and $1.0 million of non-employee stock-based compensation expense for the years ended December 31, 2006, 2005 and 2004, respectively. Total compensation cost for all stock-based payment arrangements for the years ended December 31, 2006, 2005 and 2004 was $8.3 million, $4.6 million and $4.1 million, respectively. Under the provisions of SFAS 123R, the Company recorded $6.1 million of stock-based compensation for the year ended

December 31, 2006, which represents an increase in basic and diluted net loss per share allocable to common stockholders of $0.19 per share for the year ended December 31, 2006. No amounts relating to the stock-based compensation have been capitalized.

The following table illustrates the effect on net loss and net loss per share if the Company had applied the fair value recognition provisions of SFAS 123 to options granted under the Company s stock option plans for the years ended December 31, 2005 and 2004, in thousands, except per share amounts. For purposes of this pro-forma

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

disclosure, the value of the options is estimated using a Black-Scholes option-pricing model and amortized to expense over the options vesting periods.

	2005	2004
Net loss, as reported	$ (42,914)	$ (35,367)
Add: Total stock-based compensation expense determined under the intrinsic value method for all employee awards	2,484	3,137
Deduct: Total stock-based compensation expense determined under the fair value method for all employee awards	(6,285)	(3,448)
Pro forma net loss	$ (46,715)	$ (35,678)
Basic and diluted net loss per common share, as reported	$ (1.96)	$ (2.98)
Basic and diluted net loss per common share, pro forma	$ (2.13)	$ (3.00)

The fair value of stock options at date of grant, based on the following assumptions, was estimated using the Black-Scholes option-pricing model. The Company s expected stock-price volatility assumption is based on a combination of implied volatilities of similar entities whose share or option prices are publicly available as well as the historical volatility of our publicly traded stock. The expected life assumption is based on the simplified method provided for under SAB 107, which averages the contractual term of the Company s options (10 years) with the ordinary vesting term (2.2 years). The dividend yield assumption is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends. The risk-free interest rate used for each grant is equal to the zero coupon rate in effect at the time of grant for instruments with a similar expected life. Based on historical experience, the Company has assumed an annualized forfeiture rate of 4.35% for its stock options. The Company will record additional expense if the actual forfeitures are lower than estimated and will record a recovery of prior expense if the actual forfeitures are higher than estimated.

	2006	2005	2004
Risk-free interest rate	4.70%	3.97%	3.60%
Expected dividend yield			
Expected option life	6.1 years	5 years	5 years
Expected volatility	67%	68%	88%

At December 31, 2006, there remained $17.1 million of unearned compensation expense related to unvested employee stock options to be recognized as expense over a weighted-average period of approximately 1.5 years.

The following table summarizes the activity of the Company s stock option plans:

	Weighted

	Number of Options	Average Exercise Price
Outstanding, December 31, 2005	3,907,127	$ 5.73
Granted	1,299,074	19.68
Exercised	(521,353)	1.92
Cancelled	(34,889)	8.26
Outstanding, December 31, 2006	4,649,959	$ 10.03
Exercisable at December 31, 2004	724,097	$ 0.57
Exercisable at December 31, 2005	1,550,510	$ 2.54
Exercisable at December 31, 2006	1,953,502	$ 4.44

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The weighted average remaining contractual life for options outstanding and exercisable at December 31, 2006 was 8.3 years and 7.4 years.

The aggregate intrinsic value of outstanding options at December 31, 2006 was $54.1 million, of which $33.3 million related to exercisable options. The aggregate intrinsic value was calculated based on the positive difference between the closing fair market value of the Company s common stock on December 31, 2006 ($21.40) and the exercise price of the underlying options. The intrinsic value of options exercised was $7.6 million, $1.6 million and $0.5 million for the years ended December 31, 2006, 2005 and 2004, respectively.

Employee Stock Purchase Plan

In 2004, the Company adopted the 2004 Employee Stock Purchase Plan (the 2004 Purchase Plan) with 315,789 shares authorized for issuance. Under the 2004 Purchase Plan, the Company makes one offering each year, at the end of which employees may purchase shares of common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of the offering is equal to the lesser of 85% of the closing price of the common stock at the beginning or end of the offering period. The annual offering period begins on the 1st day of November each year and ends on the 31st day of October each year. The Company issued 40,530 shares and 51,792 shares during 2006 and 2005, respectively, and as of December 31, 2006, 223,467 shares were available for issuance under the 2004 Purchase Plan.

The weighted average fair value of stock purchase rights granted as part of the 2004 Purchase Plan during the year ended December 31, 2006 was $8.16. The fair value was estimated using the Black-Scholes option-pricing model. The Company used a weighted-average stock-price volatility of 67%, option life assumption of one year and risk-free rate of 4.89%. The Company recorded $0.2 million of stock-based compensation for the year ended December 31, 2006 related to the 2004 Purchase Plan.

9. INCOME TAXES

Deferred income taxes reflect the tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting and income tax purposes. A valuation allowance is established when uncertainty exists as to whether all or a portion of the net deferred tax assets will be realized. Components of the net deferred tax asset as of December 31, 2006 and 2005 are as follows, in thousands:

	2006	2005
Deferred Tax Assets:		
Net operating loss carryforwards	$ 21,656	$ 10,248
Research and development credits	3,456	2,153
Capitalized research and development and start-up costs	13,674	15,931
Deferred revenue	7,211	8,390
Deferred compensation	1,731	
Intangible assets	3,100	1,529
Other	1,706	843

Total deferred tax assets	52,534	39,094
Deferred Tax Liabilities:		
Intangible assets	(1,004)	(1,104)
Deferred tax asset valuation allowance	(50,863)	(37,690)
Net deferred tax asset	$ 667	$ 300

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The Company s effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2006, 2005 and 2004:

	2006	2005	2004
At U.S. federal statutory rate	34.0%	34.0%	34.0%
State taxes, net of federal effect	5.3	5.6	5.4
Other permanent items	(5.4)	(3.4)	(3.8)
Purchased in-process research and development			(0.1)
Research credits	4.2	2.5	1.9
Valuation allowance	(38.0)	(38.4)	(37.4)
Effective income tax rate	0.1%	0.3%	0.0%

As required by SFAS No. 109, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Management has concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of its deferred tax assets, except for $0.7 million related to its subsidiary, Alnylam Europe AG at December 31, 2006. Accordingly, the deferred tax assets have been fully reserved except for $0.7 million at December 31, 2006 related to Alnylam Europe AG. Management reevaluates the positive and negative evidence on an annual basis.

At December 31, 2006, the Company had federal and state net operating loss carryforwards of $54.6 million and $53.6 million available, respectively, to reduce future taxable income and which will expire at various dates beginning in 2008 through 2026. At December 31, 2006, federal and state research and development and other credit carryforwards were $2.3 million and $1.7 million, respectively, available to reduce future tax liabilities, and, which expire at various dates beginning in 2018 through 2026. Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with the Company s public offerings, may limit the amount of net operating loss and tax credit carryforwards that can be utilized to offset future taxable income or tax liability. The amount of the limitation is determined in accordance with Section 382 of the Internal Revenue Code.

10. 401(K) SAVINGS PLAN

The Company sponsors a savings plan for its employees, who meet certain eligibility requirements, which is designed to be a qualified plan under section 401(k) of the Internal Revenue Code (the 401(k) Plan). The Company maintains a 401(k) plan in which all of its regular employees in the United States are eligible to participate. Participants may contribute up to 60% of their annual base salary to the plan, subject to certain limitations. Beginning in April 2006, the Company began matching in its common stock up to 3% of a participant s base salary. Employer common stock matches vest anywhere from immediately to two years, depending on years of service with the Company. Employees have the ability to transfer funds from the Company stock fund to other plan funds as they choose, subject to blackout periods. The Company issued 7,866 shares of common stock during the year ended December 31, 2006 in connection with matching contributions under the 401(k) plan.

11. SIGNIFICANT AGREEMENTS

Novartis Broad Alliance

Beginning in September 2005, the Company entered into a series of transactions with Novartis. In September 2005, the Company and Novartis executed a stock purchase agreement (the Stock Purchase Agreement) and an investor rights agreement (the Investor Rights Agreement). In October 2005, in connection with the closing of the transactions contemplated by the Stock Purchase Agreement, the Investor Rights Agreement became effective and the Company and Novartis executed a research collaboration and license agreement (the Collaboration and License Agreement) (collectively the Novartis Agreements).

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Under the terms of the Stock Purchase Agreement, in October 2005, Novartis purchased 5,267,865 shares of the Company s common stock at a purchase price of $11.11 per share for an aggregate purchase price of approximately $58.5 million, which, after such issuance, represented 19.9% of the Company s outstanding common stock as of the date of issuance. Novartis owned approximately 14% of the Company s outstanding common stock at December 31, 2006.

Under the terms of the Investor Rights Agreement, the Company granted Novartis demand and piggyback registration rights under the Securities Act of 1933, as amended, for the shares acquired by Novartis. The Company also granted to Novartis rights to acquire additional equity securities of the Company in the event that the Company proposes to sell or issue any equity securities of the Company, subject to specified exceptions, as described in the Investor Rights Agreement, such that Novartis would be able to maintain its ownership percentage in the Company. Novartis agreed, until the later of (1) three years from the date of the Investor Rights Agreement and (2) the date of termination or expiration of the Selection Term (as defined in the Collaboration and License Agreement), not to acquire any securities of the Company (other than an acquisition resulting in Novartis and its affiliates beneficially owning less than 20% of the total outstanding voting securities of the Company), participate in any tender or exchange offer, merger or other business combination involving the Company or seek to control or influence the management, Board of Directors or policies of the Company, subject to specified exceptions described in the Investor Rights Agreement.

Under the terms of the Collaboration and License Agreement, the parties will work together on a defined number of selected targets, as defined in the Collaboration and License Agreement, to discover and develop therapeutics based on RNA interference (RNAi). The Collaboration and License Agreement has an initial term of three years and may be extended for two additional one-year terms at the election of Novartis. In addition, Novartis may terminate the Collaboration and License Agreement after a period of two years under certain circumstances or in the event that the Company materially breaches its obligations. The Company may terminate the agreement with respect to particular programs, products and or countries in the event of certain material breaches of obligations by Novartis, or in its entirety under certain circumstances for multiple such breaches. Novartis made upfront payments totaling $10.0 million to the Company in October 2005 in consideration for the rights granted to Novartis under the Collaboration and License Agreement and to reimburse prior costs incurred by the Company to develop *in vivo* RNAi technology. In addition, the Collaboration and License Agreement includes terms under which Novartis will provide the Company with research funding and milestone payments as well as royalties on annual net sales of products resulting from the Collaboration and License Agreement. The Collaboration and License Agreement also provides Novartis with a non-exclusive option to integrate the Company s intellectual property relating to certain RNAi technology into Novartis operations under certain circumstances (the Integration Option). In connection with the exercise of the Integration Option, Novartis will be required to make certain additional payments to the Company. The terms of the Collaboration and License Agreement allow the Company to retain the right to discover, develop, commercialize or manufacture compounds that function through the mechanism of RNAi or products that contain such compounds as an active ingredient with respect to targets not selected by Novartis for inclusion in the Collaboration and License Agreement, provided that Novartis has a right of first offer in the event that the Company proposes to enter into an agreement with a third party with respect to any such target.

Novartis Pandemic Flu Alliance

In February 2006, the Company entered into an alliance with Novartis for the development of RNAi therapeutics for pandemic flu (Novartis Flu Agreement). The Novartis Flu Agreement supplements and, to the extent described

therein, supersedes in relevant part the collaboration and license agreement for the broad Novartis alliance. Under the terms of the Novartis Flu Agreement, the Company and Novartis have joint responsibility for development of RNAi therapeutics for pandemic flu. Novartis will have primary responsibility for commercialization of such RNAi therapeutics worldwide, but the Company will be actively involved, and may in certain circumstances take the lead, in commercialization in the United States. The Company is eligible to receive

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

significant funding from Novartis for its efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits.

Collaboration Agreement with Merck

In July 2006, the Company executed an Amended and Restated Research Collaboration and License Agreement (the Amended License Agreement) with Merck, which amends and restates the Research Collaboration and License Agreement, dated September 8, 2003, between the Company and Merck, as amended (the Original License Agreement). The collaboration between the Company and Merck is focused on developing RNAi therapeutics for targets associated with human diseases and, under the terms of the Amended License Agreement, will focus on the nine targets that then remained to be nominated by Merck under the terms of the Original License Agreement. These nine programs will be in addition to the existing program directed to the NOGO pathway on which the Company and Merck are already collaborating. The Company may select three of the nine additional programs as joint development programs, which Merck will co-fund and participate in from the outset. In October 2006, the Company selected a co-development program from the first three targets presented by Merck under the Amended License Agreement. Under the Original License Agreement, the collaboration was structured such that co-funding by Merck would not begin until after the completion of defined pre-clinical work. The Amended License Agreement provides funding from Merck immediately for programs selected by the Company for co-development, and provides that, in the United States, the Company will have the right to co-promote RNAi therapeutic products developed in these three co-development programs. Merck will assume primary responsibility for the remaining six programs and the Company is eligible to receive milestone payments and royalties on any RNAi therapeutic products developed and commercialized by Merck in these six programs. The initial term of the collaboration under the Amended License Agreement is five years from the date of the Original License Agreement and, unless earlier terminated, will continue until the date on which no product is being developed or commercialized under the agreement. Unless earlier terminated, the Amended License Agreement shall continue in effect until the expiration of all royalty obligations and profit-sharing obligations under the agreement.

Also in July 2006, the Company and Merck agreed to terminate their Collaboration and License Agreement, effective as of June 29, 2004 (the Ocular Collaboration Agreement), pursuant to which the Company and Merck were collaborating in the research, development and commercialization of RNAi products directed to certain targets, including but not limited to, vascular endothelial growth factor (VEGF). In connection with the termination of the Ocular Collaboration Agreement, and subject to certain royalty and other obligations, the Company has retained its rights to develop, manufacture and commercialize ophthalmic products directed to VEGF and Merck has granted the Company a license under certain of its technology solely to develop, manufacture and commercialize RNAi products directed to VEGF.

At December 31, 2006, the Company has deferred revenue on its balance sheet of $3.9 million related to upfront cash payments and additional license fee payments received from the Original License Agreement and the Ocular Collaboration Agreement. The Company is recognizing the remaining deferred revenue on a straight-line basis over the period of expected performance or five years.

Collaboration Agreement with Biogen Idec

In September 2006, the Company entered into a Collaboration and License Agreement (the Biogen Idec Collaboration Agreement) with Biogen Idec. The collaboration will focus on the discovery and development of therapeutics based

on RNAi for the potential treatment of progressive multifocal leukoencephalopathy (PML). The Company and Biogen Idec will initially conduct investigative research into the potential of RNAi technology to develop therapeutics to treat PML. Under the terms of the Biogen Idec Collaboration Agreement, the Company granted Biogen Idec an exclusive license to distribute, market and sell certain RNAi therapeutics to treat PML and Biogen Idec has agreed to fund all related research and development activities. The Company also received an upfront $5.0 million payment from Biogen Idec. In addition, assuming the successful development and utilization

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

of a product resulting from the collaboration, Biogen Idec will be required to pay Alnylam milestone and royalty payments.

Collaboration with Medtronic

In February 2005, the Company entered into a strategic alliance with Medtronic to pursue the development of therapeutics for the treatment of neurodegenerative disorders such as Huntington s, Alzheimer s and Parkinson s disease. The collaboration is focused on developing novel drug-device combinations incorporating RNAi therapeutics. Currently, we are engaged in a joint technology development program with Medtronic through April 2007. This initial joint technology development program is focused on delivering candidate RNAi therapeutics to specific areas of the brain using an implantable infusion system.

After successful completion of the initial joint technology development program and a joint decision to initiate product development, the Company would be responsible for the discovery and early development of candidate RNAi therapeutics, and Medtronic would be responsible for late-stage development and commercialization of any drug-device products that result. Medtronic also would adapt or develop medical devices to deliver the candidate RNAi therapeutics to targeted locations in the nervous system.

After successful completion of the initial joint technology development program and a joint decision to initiate product development, Medtronic would make an initial equity investment in the Company and could make additional investments upon successful completion of specified milestones. The aggregate amount of common stock of the Company that Medtronic would purchase if a joint decision were taken to initiate product development and the specified milestones were successfully completed would be $21.0 million. The amount of the investment to be made at the time of the joint decision to initiate product development would be between $1.0 million and $8.0 million, as determined by the Company, at the then-current market price. For the purpose of this investment, the then-current market price would be equal to the twenty-day trailing average of the closing price of common stock of the Company on the NASDAQ Global Market at the end of the trading day two trading days prior to the date of the decision to initiate product development. The remaining investments would be made upon the achievement of the specified milestones at a purchase price equal to 120% of the then-current market price, calculated as just described. If either Medtronic or the Company decides not to initiate product development under the collaboration agreement, Medtronic would not be required to make any equity investment in the Company.

After successful completion of the initial joint technology development program and a joint decision to initiate product development, the Company would also be eligible to receive additional cash milestone payments for each product developed and royalties on sales of any RNAi therapeutic component of novel drug-device combinations that result from the collaboration.

Max Planck Innovation GmbH License Agreement (formerly known as Garching Innovation GmbH)

In December 2002, the Company entered into a co-exclusive license with Max Planck Innovation (formerly known as Garching Innovation GmbH) for the worldwide rights to use and sublicense certain patented technology to develop and commercialize therapeutic products and related applications. The Company also obtained the rights to use, without the right to sublicense, the technology for all diagnostic uses other than for the purposes of therapeutic monitoring. In consideration for the rights to license this technology, the Company agreed to issue to Max Planck Innovation shares of Series B redeemable convertible preferred stock. As of December 31, 2002, the Company valued

this consideration at the Series B redeemable convertible preferred stock issuance price of $2.50 per share for total consideration of $1.8 million. The Company recorded the consideration as license fee expense during the period from inception (June 14, 2002) through December 31, 2002 as the technology had not reached technological feasibility and does not have any alternative future use. In July 2003, the Company formally issued the 723,240 shares of Series B redeemable preferred stock to Max Planck Innovation. The Company will also be required to pay future royalties on net sales of all therapeutic and prophylactic products developed with the technology.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The Company was also given the ability to acquire the remaining 50 percent exclusive rights to the technology that had not been previously granted to the Company by Max Planck Innovation upon the establishment of a German-based company with comparable operational work force and resources. The Company obtained the remaining 50 percent exclusive rights upon the acquisition of Ribopharma AG in July 2003 and in consideration for the remaining rights to this technology, issued 158,605 shares of Series B redeemable convertible preferred stock, which were converted into 83,476 shares of common stock upon the closing of the Company s initial public offering in June 2004. These shares were determined to have a fair value of $0.4 million and the value was recorded as license fee expense in 2003.

In June 2005, the Company entered into an amendment to its agreement with Max Planck Innovation. This amendment eliminated the requirement that the Company maintain operations in Germany that are comparable to its operations in the United States and replaced this provision with a requirement that the Company maintain a minimum level of employees in Germany until December 2007. This amendment secures the Company s exclusivity to use and sublicense certain patented technology to develop and commercialize therapeutic products and related applications. In connection with this amendment, the Company issued 270,000 shares of its common stock, which were valued at $2.1 million, to Max Planck Innovation and certain of its affiliated entities. The Company recorded the consideration as license fee expense for the year ended December 31, 2005, as the technology had not reached technological feasibility and does not have any alternative future uses. The Company also issued an aggregate of 8,594 shares of common stock in July 2006 pursuant to and in accordance with the terms of the license agreement under which the Company was required to issue these shares upon the issuance of U.S. Patent No. 7,056,704.

Isis Collaboration and License Agreement

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

Under the terms of the agreement, the Company agreed to pay Isis an upfront license fee of $5.0 million, $3.0 million of which was paid upon signing of the agreement and the remaining $2.0 million of which was paid in January 2005. The Company recorded the initial $5.0 million of consideration as license fee expense within research and development costs during the year ended December 31, 2004 as the technology had not reached technological feasibility and does not have any alternative future use. The Company also agreed to make milestone payments, payable upon the occurrence of specified development and regulatory events, and royalties to Isis for each product that the Company or a collaborator develops utilizing Isis intellectual property. In addition, the Company agreed to pay to Isis a percentage of certain fees earned from strategic collaborations it may enter into that include access to the Isis intellectual property. In conjunction with the agreement, Isis purchased 1,666,667 shares of Series D preferred stock

of the Company for $10.0 million, which were converted into 877,193 shares of common stock upon the closing of the Company s initial public offering in June 2004. Isis also agreed to pay the Company a license fee, milestone payments, payable upon the occurrence of specified development and regulatory events, and royalties for each product developed by Isis or a collaborator that utilizes the Company s intellectual property. The agreement also gives the Company an option to use Isis manufacturing services for RNA-based therapeutics. In connection with the Merck ocular collaboration signed in June 2004, which is discussed below, the Company

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

recorded $0.5 million in license fee expense related to payments due to Isis. In October 2005, as a result of certain payments received by the Company in connection with the Novartis Agreements, the Company made payments totaling approximately $3.7 million to Isis.

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

If, by January 1, 2008, the Company or a collaborator has 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 the patents and patent applications licensed to the Company, thereby making the Company s rights non-exclusive.

NIH Contract

In September 2006, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus, with the NIAID, a component of the NIH. The federal contract will provide the Company with up to $23.0 million in funding over a four-year period to develop RNAi therapeutics as anti-viral drugs targeting the Ebola virus. The Ebola virus can cause a severe, often fatal infection, and poses a potential biological safety risk and bioterrorism threat. Of the $23.0 million in funding, the government has committed to pay the Company up to $14.2 million over the first two years of the contract and, subject to the progress of the program and budgetary considerations in future years, the remaining $8.8 million over the last two years of the contract.

InterfeRx and Research Reagent Licenses

The Company has entered into agreements whereby it licenses its intellectual property to others for the development and commercialization of RNAi therapeutics relating to specific protein targets outside of the Company s strategic focus (InterfeRx Licenses). In addition to its InterfeRx Licenses, the Company has granted licenses to its intellectual property for the development and commercialization of research reagents and services.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

12. QUARTERLY FINANCIAL DATA (UNAUDITED)

The following information has been derived from unaudited consolidated financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair presentation of such information.

	Three Months Ended			
	March 31, 2006	June 30, 2006	September 30, 2006	December 31, 2006
	(In thousands, except per share data)			
Revenues	$ 5,717	$ 6,021	$ 8,211	$ 6,981
Operating expenses	15,514	17,130	16,815	16,972
Net loss	(8,860)	(9,910)	(7,400)	(8,438)
Net loss per common share basic and diluted	$ (0.30)	$ (0.31)	$ (0.23)	$ (0.26)
Weighted average shares basic and diluted	30,028	32,010	32,122	33,048

	Three Months Ended			
	March 31, 2005	June 30, 2005	September 30, 2005	December 31, 2005
	(In thousands, except per share data)			
Revenues	$ 1,643	$ 1,108	$ 1,413	$ 1,552
Operating expenses	8,324	12,312	12,083	16,469
Net loss	(6,600)	(11,145)	(10,678)	(14,491)
Net loss per common share basic and diluted	$ (0.32)	$ (0.54)	$ (0.51)	$ (0.56)
Weighted average shares basic and diluted	20,435	20,606	20,914	25,731

13. SUBSEQUENT EVENT

In January 2007, Inex granted the Company an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics. The Company 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 certain intellectual property to develop oligonucleotide drugs that do not function through an RNAi mechanism.

In connection with Inex s license grant to us, the Company issued Inex 361,990 shares of common stock in a private placement in January 2007, which was valued at $8.0 million, and in February 2007 paid them an additional $0.4 million. The Company has also agreed to make available to Inex a $5.0 million loan for capital equipment expenditures related to manufacturing services performed by Inex beginning in 2008. In addition, the Company will be required to pay Inex $13.0 million in milestone payments for each product that the Company develops utilizing technology Inex has licensed to the Company.

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ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Our management, with the participation of our chief executive officer and vice president of finance and treasurer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2006. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2006, the Company s chief executive officer and vice president of finance and treasurer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management s report on our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) and the independent registered public accounting firm s related audit report are included in Item 8 of this Form 10-K and are incorporated herein by reference.

No change in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2006 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We will file with the Securities and Exchange Commission a definitive Proxy Statement, which we refer to herein as the Proxy Statement, not later than 120 days after the close of the fiscal year ended December 31, 2006. The information required by this item is incorporated herein by reference to the information contained under the sections captioned Proposal One Election of Class III Directors, Section 16(a) Beneficial Ownership Reporting Compliance and Corporate Governance of the Proxy Statement. The information required by this item relating to executive officers is included in Part I, Item 1 Business- Executive Officers of the Registrant of this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Information about Executive Officer and Director Compensation, Compensation Committee Interlocks and Insider Participation , Employment Arrangements and Compensation Committee Report of the Proxy Statement.

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ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Security Ownership of Certain Beneficial Owners and Management Information about Executive Officer and Director Compensation and Securities Authorized for Issuance Under Equity Compensation Plans of the Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Corporate Governance, Employment Arrangements and Certain Relationships and Related Transactions of the Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Corporate Governance, Principal Accountant Fees and Services and Pre-Approval Policies and Procedures of the Proxy Statement.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) (1) Financial Statements

The following consolidated financial statements are filed as part of this report under Item 8 Financial Statements and Supplementary Data :

(a) (2) List of Schedules

Schedule II Valuation and Qualifying Accounts for the years ended December 31, 2006, 2005 and 2004.

All other schedules to the consolidated financial statements are omitted as the required information is either inapplicable or presented in the consolidated financial statements.

(a) (3) List of Exhibits

The exhibits which are filed with this report or which are incorporated herein by reference are set forth in the Exhibit Index hereto.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized, on March 9, 2007.

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ John M. Maraganore, Ph.D.

John M. Maraganore, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, the Report has been signed below by the following persons on behalf of the Registrant and in the capacities indicated as of March 9, 2007.

Name	Title
/s/ John M. Maraganore, Ph.D. John M. Maraganore, Ph.D.	Director and President and Chief Executive Officer (Principal Executive Officer)
/s/ Patricia L. Allen Patricia L. Allen	Vice President of Finance and Treasurer (Principal Financial and Accounting Officer)
/s/ Peter Barrett, Ph.D. Peter Barrett, Ph.D.	Director
/s/ John K. Clarke John K. Clarke	Director
/s/ Vicki L. Sato, Ph.D. Vicki L. Sato, Ph.D.	Director
/s/ Paul R. Schimmel, Ph.D. Paul R. Schimmel, Ph.D.	Director
/s/ Phillip A. Sharp, Ph.D. Phillip A. Sharp, Ph.D.	Director
/s/ Kevin P. Starr	Director

Kevin P. Starr	
/s/ James L. Vincent	Director
James L. Vincent	

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SCHEDULE II
ALNYLAM PHARMACEUTICALS, INC.
VALUATION AND QUALIFYING ACCOUNTS
(In thousands)

Year	Description	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
2006:	DEFERRED TAX ASSET VALUATION ALLOWANCE	$ 37,690	$ 13,540	$ 367	$ 50,863
2005:	DEFERRED TAX ASSET VALUATION ALLOWANCE	$ 21,135	$ 16,855	$ 300	$ 37,690
2004:	DEFERRED TAX ASSET VALUATION ALLOWANCE	$ 8,917	$ 12,218	$	$ 21,135

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EXHIBIT INDEX

Exhibit No.	Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (filed as Exhibit 3.1 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)
3.2	Amended and Restated Bylaws of the Registrant (filed as Exhibit 3.4 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
4.1	Specimen certificate evidencing shares of common stock (filed as Exhibit 4.1 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
4.2	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 (as Exhibit 4.1 to the Registrant s Current Report on Form 8-K filed on July 14, 2005 (File No. 000-50743) and incorporated herein by reference)
10.1*	2002 Employee, Director and Consultant Stock Plan, as amended, together with forms of Incentive Stock Option Agreement, Non-qualified Stock Option Agreement and Restricted Stock Agreement (filed as Exhibit 10.1 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.2*	2003 Employee, Director and Consultant Stock Plan, as amended, together with forms of Incentive Stock Option Agreement, Non-qualified Stock Option Agreement and Restricted Stock Agreement (filed as Exhibit 10.2 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.3*	2004 Stock Incentive Plan, as amended (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on June 10, 2005 (File No. 000-50743) and incorporated herein by reference)
10.4*	Forms of Incentive Stock Option Agreement and Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan, as amended (filed as Exhibit 10.3 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)
10.5*	

	Form of Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan granted to John M. Maraganore, Ph.D., on December 21, 2004 (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on December 28, 2004 (File No. 000-50743) and incorporated herein by reference)
10.6*	Form of Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan granted to James L. Vincent on July 12, 2005 (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on July 13, 2005 (File No. 000-50743) and incorporated herein by reference)
10.7*	Form of Restricted Stock Agreement under 2004 Stock Incentive Plan issued to James L. Vincent on July 12, 2005 (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on July 13, 2005 (File No. 000-50743) and incorporated herein by reference)
10.8*	2004 Employee Stock Purchase Plan (filed as Exhibit 10.4 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.9*	Summary of Cash Compensation For Directors (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on June 10, 2005 (File No. 000-50743)) and incorporated herein by reference)
10.10	Registration Rights Agreement dated as of July 31, 2003 and amended as of October 9, 2003 and February 26, 2004 by and among the Registrant and the parties listed on Schedule A thereto (filed as Exhibit 10.5 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.11	Investor Rights Agreement entered into as of March 11, 2004 by and between the Registrant and Isis Pharmaceuticals, Inc. (filed as Exhibit 10.25 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.12	Stock Purchase Agreement, dated as of September 6, 2005, by and between the Registrant and Novartis Pharma AG (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on September 12, 2005 (File No. 000-50743) and incorporated herein by reference)

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Exhibit No.	Exhibit
10.13	Investor Rights Agreement, dated as of September 6, 2005, by and between the Registrant. and Novartis Pharma AG (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on September 12, 2005 (File No. 000-50743) and incorporated herein by reference)
10.14*	Letter Agreement between the Registrant and John M. Maraganore, Ph.D. dated October 30, 2002 (filed as Exhibit 10.7 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.15*	Letter Agreement between the Registrant and Barry E. Greene dated September 29, 2003 (filed as Exhibit 10.10 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.16	Loan and Security Agreement by and between Lighthouse Capital Partners V, L.P. and the Registrant dated as of March 26, 2004, together with the Negative Pledge Agreement by and between Lighthouse Capital Partners V, L.P. and the Registrant dated as of March 26, 2004 (filed as Exhibit 10.11 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.17	Amendment No. 1 dated August 2, 2004 to Loan and Security Agreement dated as of March 26, 2004 by and between the Registrant and Lighthouse Capital Partners V, L.P. (filed as Exhibit 10.6 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)
10.18	Amendment No. 02 dated June 20, 2005 to Loan and Security Agreement dated as of March 26, 2004, as amended, by and between the Registrant and Lighthouse Capital Partners V, L.P. (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on June 24, 2005 (File No. 000-50743) and incorporated herein by reference)
10.19	Warrants to Purchase Preferred Stock effective as of March 30, 2004 issued to Lighthouse Capital Partners V, L.P. and Lighthouse Capital Partners IV, L.P. (filed as Exhibit 10.12 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.20	Lease, dated as of September 26, 2003 by and between the Registrant and Three Hundred Third Street LLC (filed as Exhibit 10.15 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.21	License Agreement between Cancer Research Technology Limited and Alnylam U.S., Inc. dated July 18, 2003 (filed as Exhibit 10.16 to the Registrant s Registration Statement on Form S-1 (File

No. 333-113162) and incorporated herein by reference)

10.22 License Agreement between the Carnegie Institution of Washington and Alnylam Europe, AG, effective March 1, 2002, as amended by letter agreements dated September 2, 2002 and October 28, 2003 (filed as Exhibit 10.17 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)

10.23 License Agreement by and between the Cold Spring Harbor Laboratory and Alnylam U.S., Inc. dated December 30, 2003 (filed as Exhibit 10.18 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)

10.24 Co-exclusive License Agreement between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam U.S., Inc. dated December 20, 2002, as amended by Amendment dated July 8, 2003 together with Indemnification Agreement by and between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam Pharmaceuticals, Inc. effective April 1, 2004 (filed as Exhibit 10.19 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)

10.25 Co-exclusive License Agreement between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam Europe, AG dated July 30, 2003 (filed as Exhibit 10.20 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)

10.26 Agreement between the Registrant, Garching Innovation GmbH (now known as Max Planck Innovation GmbH), Alnylam U.S., Inc. and Alnylam Europe AG dated June 14, 2005 (filed as Exhibit 10.8 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)

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Exhibit No.	Exhibit
10.27	Agreement between The Board of Trustees of the Leland Stanford Junior University and Alnylam U.S., Inc. effective as of September 17, 2003 (filed as Exhibit 10.21 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.28	Research Collaboration and License Agreement by and among Merck & Co., Inc., Alnylam U.S., Inc. and Registrant dated September 8, 2003 (filed as Exhibit 10.22 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.29	Sponsored Research Agreement among Mayo Foundation for Medical Education and Research, Mayo Clinic Jacksonville and Alnylam Pharmaceuticals, Inc. effective as of October 1, 2003 (filed as Exhibit 10.23 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.30	Strategic Collaboration and License Agreement effective as of March 11, 2004 between Isis Pharmaceuticals, Inc. and the Registrant (filed as Exhibit 10.24 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.31	Agreement between the Registrant and Perini Building Company, Inc. effective as of March 26, 2004 (filed as Exhibit 10.26 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.32	Collaboration Agreement by and among Medtronic, Inc. and the Registrant effective as of February 8, 2005 (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q (File No. 000-50743) for the quarterly period ended March 31, 2005 and incorporated herein by reference)
10.33	Research Collaboration and License Agreement effective as of October 12, 2005 by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on October 12, 2005 (File No. 000-50743) and incorporated herein by reference)
10.34	Addendum Re: Influenza Program to Research Collaboration and License Agreement, dated February 17, 2006, by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on February 24, 2006 (File No. 000-50743) and incorporated herein by reference)
10.35	First Amendment to Lease, dated March 16, 2006, by and between the Registrant and ARE-MA Region No. 28, LLC (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on March 16, 2006 (File No. 000-50743) and incorporated herein by reference)

10.36	Master Security Agreement by and between the Registrant and Oxford Finance Corporation, dated March 31, 2006 (filed as Exhibit 10.1 to the Registrant s Report on Form 8-K filed on March 31, 2006 (File No. 000-50743) and incorporated herein by reference)
10.37	Amendment No. 1 to Addendum Re: Influenza Program to Research Collaboration and License Agreement, effective as of March 14, 2006, by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (filed as Exhibit 10.39 to the Registrant s Annual Report on Form 10-K (File No. 000-50743) for the annual period ended December 31, 2005 and incorporated herein by reference)
10.38	Amendment No. 2 to Addendum Re: Influenza Program to Research Collaboration and License Agreement, effective as of May 5, 2006, by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on May 9, 2006 (File No. 000-50743) for the quarterly period ended March 31, 2006 and incorporated herein by reference)
10.39	Amended and Restated Research and Collaboration and License Agreement, effective as of July 3, 2006, by and between the Registrant and Merck & Co., Inc. (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on August 14, 2006 (File No. 000-50743) for the quarterly period ended June 30, 2006 and incorporated herein by reference)
10.40	Collaboration and License Agreement dated September 20, 2006, by and between the Registrant and Biogen Idec Inc. (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on November 9, 2006 (File No. 000-50743) for the quarterly period ended September 30, 2006 and incorporated herein by reference)

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Exhibit No.	Exhibit
10.41	Letter Agreement by and between the Registrant and Vincent J. Miles effective as of October 20, 2006 (filed as Exhibit 10.2 to the Registrant s Quarterly Report on Form 10-Q (File No. 000-50743) for the quarterly period ended September 30, 2006 and incorporated herein by reference)
21.1#	Subsidiaries of the Registrant
23.1#	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
31.1#	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13(a)- 14(a)/15d-14(a), by Chief Executive Officer
31.2#	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13(a)- 14(a)/15d-14(a), by Vice President of Finance and Treasurer
32.1#	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Chief Executive Officer
32.2#	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Vice President of Finance and Treasurer

* Management contracts or compensatory plans or arrangements required to be filed as an exhibit hereto pursuant to Item 15(a) of Form 10-K.

Indicates confidential treatment requested as to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Request.

Filed herewith