ALNYLAM PHARMACEUTICALS, INC.
Form 10-K
March 10, 2008

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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, 2007

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:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.01 par value per share	**The Nasdaq Global Market**

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 þ No o

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, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act:

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o (do not check if smaller reporting company)	Smaller reporting company 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 29, 2007, was $561,228,166.

As of February 29, 2008, the registrant had 40,802,423 shares of Common Stock, $0.01 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement for its 2008 annual meeting of stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant s fiscal year end of December 31, 2007, are incorporated by reference into Part III of this Form 10-K.

ALNYLAM PHARMACEUTICALS, INC.
ANNUAL REPORT ON FORM 10-K
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This annual report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and 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, similar expressions are intended to identify 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 explicitly disclaim any 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 the expression of 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 broad new 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 apply in a systematic way to develop RNAi therapeutics for a variety of diseases.

We are applying our technological expertise to build a pipeline of RNAi therapeutics to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Our lead RNAi therapeutic program, ALN-RSV01, is in Phase II clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which is reported to be the leading cause of hospitalization in infants in the United States and also occurs in the elderly and in immune compromised adults. In February 2008, we reported positive results from our Phase II experimental infection clinical trial, referred to as the GEMINI study. The GEMINI study was designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01. In this study, ALN-RSV01 was safe and well tolerated and demonstrated statistically significant anti-viral activity, including an approximately 40% reduction in viral infection and a 95% increase in infection-free patients ($p<0.01$).

We have three RNAi therapeutic programs in pre-clinical development, ALN-PCS, ALN-VSP and ALN-HTT, focused on the treatment of hypercholesterolemia, liver cancer and Huntington s disease, respectively. We have additional discovery programs for RNAi therapeutics for the treatment of a broad range of diseases, including viral hemorrhagic fever, including the Ebola virus, progressive multifocal leukoencephalopathy, or PML, pandemic flu, Parkinson s disease and cystic fibrosis, or CF, as well as other undisclosed programs.

We also are working internally and with third-party collaborators to develop capabilities to deliver our RNAi therapeutics directly to specific sites of disease, such as the delivery of ALN-RSV01 to the lungs, which we refer to as Direct RNAi^{tm}. In addition, we are working to extend our capabilities to advance the development of RNAi therapeutics that are administered by intravenous, subcutaneous or intramuscular approaches, which we refer to as Systemic RNAi^{tm}. During 2007, we obtained an exclusive worldwide license to the liposomal delivery formulation

technology of Tekmira Pharmaceuticals Corporation, or Tekmira, formerly know as Inex Pharmaceuticals Corporation, for the discovery, development and commercialization of lipid-based nanoparticle formulations for the delivery of RNAi therapeutics. We also signed an agreement with the Massachusetts Institute of Technology, or MIT, Center for Cancer Research to sponsor an exclusive five-year research program focused on the delivery of RNAi therapeutics. We have other RNAi therapeutic delivery collaborations and intend to continue to collaborate

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with academic and corporate third parties, to evaluate different delivery options, including with respect to Direct RNAi and Systemic RNAi.

We rely on the strength of our intellectual property portfolio relating to the development and commercialization of small interfering RNAs, or 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. We believe that no other company possesses a portfolio of such broad and exclusive rights to the fundamental RNAi patents and patent applications required for the development and commercialization of RNAi therapeutics.

In addition, our expertise in RNAi therapeutics and broad intellectual property estate have allowed us to form alliances with leading companies, including F. Hoffmann-La Roche Ltd, or Roche, Novartis Pharma AG, or Novartis, Medtronic, Inc., or Medtronic, 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 Institutes of Health, or NIH, and the Defense Threat Reduction Agency, or DTRA, an agency of the United States Department of Defense, or DoD. We have established collaborations and in some instances, received funding from a number of major medical and disease associations, including The University of Texas Southwestern Medical Center, or UTSW, the Mayo Clinic, The Michael J. Fox Foundation and the Cystic Fibrosis Foundation Therapeutics, or CFTT. Finally, to further enable the field and monetize our intellectual property rights, we have also entered into approximately 20 license agreements with other biotechnology companies interested in developing RNAi therapeutic products and research companies that commercialize RNAi reagents or services.

In 2007, we and Isis Pharmaceuticals, Inc., or Isis, established Regulus Therapeutics LLC, or Regulus Therapeutics, as a joint venture focused on the discovery, development and commercialization of microRNA, or miRNA, therapeutics. Because miRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, miRNA therapeutics represent a new approach to target the pathways of human disease. Regulus Therapeutics combines our and Isis technologies, know-how and intellectual property relating to miRNA therapeutics. In addition, we believe Regulus Therapeutics has assembled a strong leadership team, as well as leading authorities in the field of miRNA research to lead this new venture.

RNA Interference

RNAi is a 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 in 1998, and two of the scientists who made this discovery, Dr. Andrew Fire and Dr. Craig Mello, received the 2006 Nobel Prize for Physiology or Medicine.

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, 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 a 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.

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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 which 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 naturally 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, Thomas Tuschl, Ph.D., 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 segment 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 broad new 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.

For these potential benefits of RNAi therapeutics 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

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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*, *Cell, Nature Medicine and Nature Biotechnology.*

Our 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. Our product platform provides a systematic approach to identifying RNAi drug candidates. We believe that we have made considerable progress in developing our product platform, as documented in recent publications by our scientists in *Nature Chemical Biology* and *Nature Drug Discovery.* This progress has enabled us to initiate and advance a number of development programs for RNAi therapeutics that will be administered directly to diseased parts of the body. Our progress in achieving delivery of RNAi therapeutics through Systemic RNAi 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.

Our Product Pipeline

The following is a summary of our product pipeline as of February 29, 2008:

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.

Our most advanced program is focused on RSV, a virus that infects the respiratory tract. In January 2008, we completed a Phase II human clinical trial of ALN-RSV01, an RNAi therapeutic for the treatment of RSV infection, designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV. We intend to initiate a second Phase II human clinical trial of ALN-RSV01 in naturally infected adult patients during the first half of 2008.

Our ALN-PCS program is focused on the treatment of hypercholesterolemia with an RNAi therapeutic that targets a gene called proprotein convertase subtilisn/kexin type 9, or PCSK9. Other development programs include

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ALN-VSP, which is focused on the development of an RNAi therapeutic for the treatment of liver cancer and potentially other cancers designed to target both vascular endothelial growth factor, or VEGF, and kinesin spindle protein, or KSP, and ALN-HTT, a program targeting the huntingtin gene for the treatment of Huntington s disease.

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 research and development costs of $120.7 million in 2007, $49.3 million in 2006 and $35.0 million in 2005, respectively. The increase in research and development costs in 2007 was primarily the result of $27.5 million in payments due to certain entities, primarily Isis, in connection with the Roche alliance.

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 NIH, RSV is responsible for more than 125,000 pediatric hospitalizations and between 1,250 and 2,500 deaths each year. A study published in the *New England Journal of Medicine* estimates that over 170,000 elderly adults are hospitalized with RSV each year, resulting in more than 14,000 deaths each year. 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 complicated 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 June 2007, we initiated the GEMINI study, a double-blind, placebo-controlled, randomized Phase II trial designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV. In total, 88 subjects were randomized 1:1 to receive either ALN-RSV01 or placebo treatment prior to and after experimental infection with a wild type clinical strain of RSV. In February 2008, we reported positive results from the GEMINI study. ALN-RSV01 was found to be safe and well tolerated and demonstrated statistically significant anti-viral activity, including an approximately 40% reduction in viral infection and a 95% increase in infection-free patients ($p<0.01$).

We intend to initiate a second Phase II human clinical trial of ALN-RSV01 in naturally infected adult patients during the first half of 2008.

Prior to the GEMINI study, ALN-RSV01 was shown in pre-clinical testing to be 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 animal toxicology studies performed to enable the filing of an investigational new drug, or IND, application. We submitted an IND for ALN-RSV01 to the United States Food and Drug Administration, or FDA, in November 2005, and have completed a number of Phase I clinical trials on this experimental drug carried out

in both the United States and Europe. The results from these Phase I trials have been presented at medical conferences. ALN-RSV01 was found to be safe and well tolerated when administered intranasally or by nebulizer.

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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, defined as a high level of LDL cholesterol, or 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, which include drugs known as statins. 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 constitute a potential target population for our product candidate.

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 also 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 s 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, including myocardial infarction or heart attack. In addition, a recent study has shown that PCSK9 levels are increased by statin therapy while LDL-c levels are decreased, suggesting that the introduction of a PCSK9 inhibitor to statin therapy may result in even further reductions in LDL-c levels.

In July 2006, in collaboration with UTSW, we began our ALN-PCS program focused on the development of an RNAi therapeutic directed at PCSK9. As part of the UTSW collaboration, we and UTSW are testing RNAi therapeutics targeting PCSK9 in certain UTSW animal models. Non-human primate data for our ALN-PCS program has demonstrated efficient silencing of PCSK9 and rapid and durable reductions in LDL blood cholesterol levels by approximately 50%.

Liver Cancer

Market Opportunity. There are an estimated 600,000 to 700,000 patients worldwide with primary liver cancer and every year more than 600,000 patients die of liver cancer. Hepatocellular carcinoma, or HCC, is the most common form of liver cancer and is responsible for about 90% of primary malignant liver tumors in adults. HCC is the sixth most common cancer in the world and the third leading cause of cancer-related deaths globally. In addition to primary liver cancer patients, in whom the disease starts in the liver, there are another 500,000 patients identified each year with secondary liver cancer, whereby the primary tumor of another tissue, such as colorectal, stomach, pancreatic, breast, lung or skin, has metastasized to the liver.

Current Treatments. The treatment options are dependent on the stage of disease, site of tumor and condition of the patient, but can include surgical resection, radiation, chemotherapy, chemoembolism, liver transplantation and various combinations of these approaches. Even with relatively early diagnosis and resection, the prognosis remains very poor for liver cancer patients, who are often diagnosed late in their clinical course of disease. For primary liver cancer, with early diagnosis and a resectable tumor, the five-year disease free survival rate has been reported at approximately 20%. However, this applies only to about 15% of primary liver cancer patients.

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For most primary liver cancer patients, the disease is fatal within three to six months. The prognosis for secondary liver cancer is generally also very poor, due often to the late stage of the disease and metastatic nature of the neoplasm. For example, in the absence of treatment, the prognosis for patients with hepatic colorectal metastases is extremely poor, with five-year survival rates of 3% or less. Among patients that can be treated with complete resection of hepatic colorectal metastases, only 30 to 40% will survive for five years following resection.

Alnylam Program. The ALN-VSP program is focused on a dual targeting therapeutic drug candidate, which targets the genes for both kinesin spindle protein, or KSP, and vascular endothelial growth factor, or VEGF. KSP is a key component of the cellular machinery that mediates chromosome separation during cell division and this is critical for tumor proliferation. As such, it represents a potent target as an anti-tumor mechanism. VEGF is a potent angiogenic factor that drives the development of blood vessels that are critical to ensuring adequate blood supply to the growing tumor. Pre-clinical studies have demonstrated potent anti-tumor activity of our drug candidate. We believe that the dual targeting mechanism of this therapeutic drug candidate is a novel and potentially effective strategy.

Huntington s Disease

Market Opportunity. Huntington s disease, or HD, is a fatal, inherited and progressive brain disease that results in uncontrolled movements, loss of intellectual faculties, emotional disturbance and premature death. HD patients typically first start to develop the disease in their third or fourth decade of life and have an average survival of only 10 to 20 years after initial diagnosis. The disease is associated with the production of an altered form of a protein known as huntingtin whose presence is believed to trigger the death of important cells in the brain. This autosomal dominant, neurodegenerative disease afflicts approximately 30,000 patients in the United States. An estimated 150,000 additional people in the United States carry the mutant huntingtin gene and, therefore, have an approximate 50% risk of developing the disease in their lifetimes.

Current Treatments. The current treatment of this severe disease is only supportive care and symptomatic therapy, with no drugs or therapies available that can slow the underlying disease progress and the inexorable erosion of the patient s neuronal functionality.

Alnylam Program. In collaboration with Medtronic, we are seeking to develop a novel drug-device product incorporating an RNAi therapeutic targeting the huntingtin gene that will protect these cells by suppressing huntingtin mRNA and the disease causing protein. Alnylam scientists and collaborators have published and presented *in vivo* data demonstrating efficacy for an siRNA targeting the huntingtin gene in a mouse model of the disease. The program, ALN-HTT, is part of a 50:50 co-development/profit share relationship with Medtronic for the United States market. Outside the United States, Medtronic will be solely responsible for the development and commercialization of the drug-device.

Discovery Programs

In addition to our development efforts on RSV, hypercholesterolemia, liver cancer and Huntington s disease, we are conducting research activities to discover RNAi therapeutics to treat various diseases. The diseases for which we have discovery programs include: viral hemorrhagic fever, including the Ebola virus, which can cause severe, often fatal infection and poses a potential biological safety risk and bioterrorism threat; progressive multifocal leukoencephalopathy, or PML, which is a disease of the central nervous system caused by viral infection in immune compromised patients; pandemic flu; Parkinson s disease, a progressive brain disease which is characterized by uncontrollable tremor, and in some cases, may result in dementia; and cystic fibrosis, an inherited respiratory disease, or CF.

In addition to these programs, as part of our collaboration with Novartis, we have research activities to discover RNAi therapeutics directed to a number of other undisclosed targets. Our alliance with Roche also contemplates such research activities.

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microRNA Technology Program and Regulus Therapeutics LLC

In September 2007, we and Isis established Regulus Therapeutics, a joint venture focused on the discovery, development and commercialization of miRNA therapeutics. Regulus Therapeutics combines our and Isis technologies, know-how and intellectual property relating to miRNA therapeutics. In addition, we believe that Regulus Therapeutics has assembled a strong leadership team, as well as leading authorities in the field of miRNA research to lead this new venture. In December 2007, Kleanthis G. Xanthopoulos, Ph.D. was appointed as President and Chief Executive Officer of Regulus Therapeutics. Dr. Xanthopoulos was the co-founder and former President and Chief Executive Officer of Anadys Pharmaceuticals, Inc. In February 2008, Peter S. Linsley, Ph.D. was appointed as Chief Scientific Officer of Regulus Therapeutics. Dr. Linsley was an Executive Director of Cancer Biology at Merck Research Laboratories and the former Vice President of Research and Development at Rosetta Inpharmatics LLC.

Regulus Therapeutics is exploring therapeutic opportunities that arise from alterations in miRNA expression. Since miRNAs are believed to regulate the expression of broad networks of genes and biological pathways, miRNA therapeutics define a new and potentially high-impact strategy to target multiple points on disease pathways. Conventional messenger RNAs are genetically encoded and in turn instruct the creation of proteins through the process of translation. However, these small miRNAs do not instruct creation of proteins but instead regulate the expression of other genes. There are approximately 600 miRNAs that have been identified in the human genome, and these are believed to regulate the expression of up to 30% of all human genes. Thus, miRNAs may act as master regulators for physiological pathways or genetic networks to achieve integrated biological functions. This ability to affect the expression of multiple genes in the pathway of disease makes miRNAs an exciting new platform for drug discovery and development.

To date, miRNAs have been implicated in several disease areas such as cancer, viral infection, inflammatory diseases and metabolic disorders. Regulus Therapeutics most advanced program is an miRNA therapeutic that targets miR-122 for the treatment of hepatitis C virus, or HCV, infection, a significant disease worldwide, for which emerging therapies target viral genes and, therefore, are prone to viral resistance. Regulus Therapeutics is targeting miR-122, an endogenous host gene required for viral infection by HCV. In addition to the miR-122 program, Regulus Therapeutics is also actively exploring additional areas for development of miRNA therapeutics, including cancer, other viral diseases, metabolic disorders and inflammatory diseases.

We and Isis own 49% and 51%, respectively, of Regulus Therapeutics. Regulus Therapeutics is operated as an independent company with a separate board of directors, scientific advisory board and management team. In connection with the execution of the limited liability company agreement, we, Isis and Regulus Therapeutics entered into a license and collaboration agreement to pursue the discovery, development and commercialization of therapeutic products directed to miRNAs. Under the terms of the license and collaboration agreement, we and Isis assigned to Regulus Therapeutics specified patents and contracts covering miRNA-specific technology. In addition, each of us granted to Regulus Therapeutics an exclusive, worldwide license under our rights to other miRNA-related patents and know-how to develop and commercialize therapeutic products containing compounds that are designed to interfere with or inhibit a particular miRNA, subject to our and Isis existing contractual obligations to third parties. Regulus Therapeutics also has the right to request a license from us and Isis to develop and commercialize therapeutic products directed to other miRNA compounds, which license is subject to our and Isis approval and to each such party s existing contractual obligations to third parties. Regulus Therapeutics granted to us and Isis an exclusive license to technology developed or acquired by Regulus Therapeutics for use solely within our respective fields (as defined in the license and collaboration agreement), but specifically excluding the right to develop, manufacture or commercialize the therapeutic products for which we and Isis granted rights to Regulus Therapeutics. In addition, we made an initial cash contribution to Regulus Therapeutics of $10.0 million, resulting in us and Isis making initial capital contributions to Regulus Therapeutics of approximately equal aggregate value.

After a sufficient portfolio of data is obtained with respect to each miRNA drug candidate developed by Regulus Therapeutics, Regulus Therapeutics may elect to continue to pursue the development and commercialization of products directed to such miRNA compound and related miRNA compounds, in which event Regulus Therapeutics would be obligated to pay us and Isis a royalty on net sales of any such resulting products. If Regulus Therapeutics decides not to continue to pursue the development and commercialization of products directed to

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particular miRNA compounds, either we or Isis may pursue development and commercialization of such Regulus Therapeutics products. Development and commercialization of such products by either party would be subject to the payment to Regulus Therapeutics of a specified upfront fee, royalties on net sales, milestone payments upon achievement of specified regulatory events and a portion of income received from sublicensing rights.

In connection with the execution of the limited liability company agreement and the license and collaboration agreement, we also executed a services agreement with Isis and Regulus Therapeutics. Under the terms of the services agreement, we and Isis agreed to provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services, as set forth in an operating plan mutually agreed upon by us and Isis. Pursuant to this agreement, we and Isis generally will be paid by Regulus Therapeutics for these services.

Our Collaboration and Licensing Strategy

Our business plan is to develop and commercialize a pipeline of RNAi therapeutic products. As part of this business plan, we enter into collaboration and licensing agreements as a means of obtaining resources and funding to advance our RNAi therapeutics programs.

Our collaboration strategy is to form (1) non-exclusive platform alliances where our collaborators obtain access to our capabilities and intellectual property to develop their own RNAi therapeutic products; and (2) 50/50 co-development and/or ex-U.S. market geographic partnerships on specific RNAi therapeutic programs. We have entered into a broad, non-exclusive platform license agreement with Roche, under which we and Roche also will collaborate on RNAi drug discovery for one or more disease targets. We also have discovery and development alliances with Novartis and Medtronic. Two of the programs we are pursuing under our alliances with Novartis and Medtronic are 50/50 co-development programs.

One of the key factors in our ability to form significant alliances with pharmaceutical companies is the strength of our intellectual property 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, their use and manufacture. Our patent estate also includes access to a broad portfolio of intellectual property relating to chemical modifications of oligonucleotides and siRNAs, including access to a substantial patent estate licensed from Isis, and a number of issued patents related to the formulation and delivery of siRNAs, including patents licensed from MIT and Tekmira. Finally, our patent estate also includes patents and pending patent applications claiming siRNAs directed to specific targets as treatments for particular diseases.

To generate revenues from our intellectual property rights, we also grant licenses to biotechnology companies under 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 Pharmaceutical Company Inc., or Nastech. Tekmira 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, which includes the manufacture and sale of reagents. 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. As of February 29, 2008, we had granted such licenses, on both an exclusive and nonexclusive basis, to approximately 20 companies, and options to take such licenses to two additional companies.

We also seek opportunities to form new ventures in areas outside our core strategic interest. For example, our joint venture with Isis, Regulus Therapeutics, was formed to capitalize on our technology and intellectual property in the

field of miRNA therapeutics. Given the broad applications for RNAi technology, we believe additional opportunities exist for new ventures to be formed.

Since delivery of RNAi therapeutics remains a major objective of our research activities, we also look to form collaboration and licensing agreements with other companies and academic institutions to gain access to delivery technologies. During 2007, we formed agreements with Tekmira and MIT, among others.

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We also seek funding for the development of our proprietary RNAi therapeutics pipeline from foundations and government sources. In 2006, 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. In 2007, DTRA awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus. This federal contract is expected to provide us with up to $38.6 million through the first half of 2010. We have also obtained initial government support for our pandemic flu program from the Defense Advanced Research Projects Agency of the DoD. In addition, we have obtained funding for pre-clinical discovery programs from CFFT and The Michael J. Fox Foundation.

Strategic Alliances

We have formed, and intend to continue 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/or royalties or profit sharing based on sales of RNAi therapeutics.

Roche. In July 2007, we and, for limited purposes, Alnylam Europe AG, or Alnylam Europe, entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement, which became effective in August 2007, we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include other therapeutic areas upon payment of an additional specified amount.

In consideration for the rights granted to Roche under the license and collaboration agreement, Roche paid us $273.5 million in upfront cash payments. Roche is also required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees.

Under the license and collaboration agreement, we and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets, subject to our contractual obligations to third parties. The collaboration between Roche and us will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. In exchange for our contributions to the collaboration, Roche will be required to make additional milestone and royalty payments.

The term of the license and collaboration agreement generally ends upon the later of the expiration of the last-to-expire patent covering a licensed product and ten years from the first commercial sale of a licensed product. After the first anniversary of the effective date, Roche may terminate the license and collaboration agreement, on a licensed product-by-licensed product, licensed patent-by-licensed patent, and country-by-country basis, upon 180 days prior written notice to us, but is required to continue to make milestone and royalty payments to us if any royalties were payable on net sales of a terminated licensed product during the previous 12 months. The license and collaboration agreement may also be terminated by either party in the event the other party fails to cure a material breach under the license and collaboration agreement.

In connection with the execution of the license and collaboration agreement, we executed a common stock purchase agreement with Roche Finance Ltd, or Roche Finance, an affiliate of Roche. Under the terms of the common stock purchase agreement, in August 2007, Roche Finance purchased 1,975,000 shares of our common stock at $21.50 per share, for an aggregate purchase price of $42.5 million. Under the terms of the common stock purchase agreement, in the event we propose to sell or issue any of our equity securities, subject to specified exceptions, we agreed to grant to

Roche Finance the right to acquire additional securities, such that Roche Finance would be able to maintain its ownership percentage in us. Roche Finance agreed that until August 9, 2010, neither it nor any specified affiliates will acquire any of our securities or assets (other than an acquisition resulting in such entities beneficially owning less than 5% of our total outstanding voting securities), participate in any tender or exchange offer, merger or other business combination involving us or seek to control our management, board of

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directors or policies, subject to specified exceptions. Roche Finance also agreed that neither it nor any specified affiliates will sell or transfer any of our equity securities during the period prior to August 9, 2009 and will limit the volume of such sales or transfers in a single day during the following one-year period, in each case, for so long as Roche Finance and such affiliates beneficially own more than 2.5% of the total outstanding shares of our common stock.

In connection with the execution of the license and collaboration agreement and the common stock purchase agreement, we also executed a stock purchase agreement with Alnylam Europe and Roche Beteiligungs GmbH, or Roche Germany, an affiliate of Roche. Under the terms of the Alnylam Europe stock purchase agreement, we created a new, wholly-owned German limited liability company, Roche Kulmbach, into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from us all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million. The Alnylam Europe stock purchase agreement also includes transition services to be performed by Roche Kulmbach employees at various levels through August 2008. We will reimburse Roche for these services at an agreed-upon rate.

In connection with the license and collaboration agreement and the common stock purchase agreement, we incurred $27.5 million of license fees payable to our licensors, primarily Isis, in accordance with the applicable license agreements with those parties.

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.

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 5,267,865 shares of our common stock at a purchase price of $11.11 per share for an aggregate purchase price of $58.5 million, which, immediately after such issuance, represented 19.9% of our then outstanding common stock. Novartis owned approximately 13% of our common stock as of December 31, 2007.

Under the terms of the collaboration and license agreement governing the broad Novartis alliance, 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 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

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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. During 2007, we and Novartis agreed to focus on additional pre-clinical research prior to advancing this program into development.

Medtronic. In July 2007, we entered into an amended and restated collaboration agreement with Medtronic to pursue the development of therapeutic products for the treatment of neurodegenerative disorders. The amended and restated collaboration agreement supersedes the collaboration agreement entered into by the parties in February 2005, and continues the existing collaboration between the parties focusing on the delivery of RNAi therapeutics to specific areas of the brain using implantable infusion systems.

Under the terms of the amended and restated collaboration agreement, we and Medtronic will continue our existing development program focused on developing a combination drug-device product for the treatment of Huntington s disease. In addition, as provided for in our initial collaboration agreement with Medtronic, the parties may jointly agree to collaborate on additional product development programs for the treatment of other neurodegenerative diseases, which can be addressed by the delivery of siRNAs discovered and developed using our RNAi therapeutics platform to the human nervous system through implantable infusion devices developed by Medtronic. We will be responsible for supplying the siRNA component and Medtronic will be responsible for supplying the device component of any product resulting from the collaboration.

With respect to the initial product development program focused on Huntington s disease, the parties will each fund 50% of the development efforts for the United States while Medtronic is responsible for funding development efforts outside the United States. Medtronic will commercialize any resulting products and pay royalties to us based on net sales of any such products, which royalties in the United States are designed to approximate 50% of the profit associated with the sale of such product and which royalties in Europe are similar to more traditional pharmaceutical royalties, in that they are intended to reflect each party s contribution.

Each party has the right to opt out of its obligation to fund the program under the agreement at certain stages, and the agreement provides for revised economics based on the timing of any such opt out. Other than pursuant to the initial product development program, and subject to specified exceptions, neither party may research, develop, manufacture or commercialize products that use implanted infusion devices for the direct delivery of siRNAs to the human nervous system to treat Huntington s disease during the term of such program.

Unlike the initial collaboration agreement, the amended and restated collaboration agreement does not require Medtronic to make any equity investment in us.

The amended and restated collaboration agreement expires, on a product-by-product and country-by-country basis, upon expiration of the royalty term for the applicable product. The royalty term is the longer of a specified number of years from the first commercial sale of the applicable product and the expiration of the last-to-expire of specified patent rights. Royalties are paid at a lower level during any part of a royalty term in which specified patent coverage does not exist. Either party may terminate the amended and restated collaboration agreement on 60 days prior written notice if the other party materially breaches the agreement in specified ways and fails to cure the

breach within the 60-day notice period. Either party may also terminate the agreement in the event that specified pre-clinical testing does not yield results meeting specified success criteria.

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. Under the terms of the collaboration agreement with Biogen Idec, 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, if any, Biogen Idec would be required to pay us milestone and royalty payments. The pace and scope of future development of this program is the responsibility of Biogen Idec. We expect limited resources to be expended on this program in 2008.

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. The licenses that we have granted to Isis are non-exclusive licenses to our current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. We have also granted Isis the non-exclusive right to develop and commercialize siRNA products against a limited number of targets. In addition, we have 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 develops 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.

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 NIAID, a component of 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.

Department of Defense. In August 2007, we were awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus by DTRA, a DoD agency. This federal contract is

expected to provide us with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus. Viral hemorrhagic fevers are considered by federal agencies to be high priority agents that pose a potential risk to national security because they can be easily transmitted from person to person, result in high mortality rates and require special action for public health preparedness. This contract is

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with the DTRA 2007 Medical Science and Technology Chemical and Biological Defense Transformational Medical Technologies Initiative, whose mission is to provide state-of-the-art defense capabilities to United States military personnel by addressing traditional and non-traditional biological threats. Of the $38.6 million in funding, the government has committed to pay us up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract.

Delivery Technology. We are working to extend our capabilities in developing technology to achieve efficacious and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, we have entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, we are also providing funding to support the advancement of these delivery technologies. In connection with one such agreement with Tekmira, we issued 361,990 shares of common stock in a private placement in January 2007, valued at $7.9 million.

Merck. In September 2007, we and Merck & Co., Inc., or Merck, terminated our amended and restated research collaboration and license agreement. Pursuant to the termination agreement, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the amended and restated research collaboration and license agreement ceased as of the date of the termination agreement, subject to certain specified exceptions. The termination agreement further provides that, subject to certain conditions, we and Merck will each retain sole ownership and rights in our own intellectual property. We have no remaining deliverables under the amended and restated research collaboration and license agreement.

Licenses

To further enable the field and monetize 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 direct 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 certain circumstances. To date, we have granted InterfeRx licenses to a number of companies, including GeneCare, Nastech, Calando and Quark. In general, these licenses allow the licensees to discover, develop and commercialize RNAi therapeutics for a limited number of targets in return for upfront, milestone, license maintenance and/or royalty payments to us. In some cases, we also retained a right to negotiate the ability to co-promote and/or co-commercialize the licensed product, and in one case, we included the rights to discover, develop and commercialize RNAi therapeutics utilizing expressed RNAi (i.e., RNAi mediated by siRNAs generated from DNA constructs introduced into cells). In addition, Tekmira and Benitec have options to take InterfeRx licenses, subject to certain conditions. We have granted InterfeRx licenses to fewer than 15 gene targets in total, under both exclusive and non-exclusive licenses.

Research Reagents and Services. We have granted approximately 15 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 intellectual property position relevant to RNAi therapeutic products and delivery technologies. In this regard, we have amassed a portfolio of patents, patent applications and other intellectual property covering:

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

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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.

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 included are patents and patent applications covering targeted cleavage of mRNA directed by RNA-like oligonucleotides, double-stranded RNAs of particular lengths and particular structural features, such as blunt and/or overhanging ends. Our strategy has been to secure rights on an exclusive basis where possible or appropriate to the key patents and patent applications we believe cover the fundamental aspects of siRNAs. The following table lists patents and/or patent applications to which we have secured rights that we regard as being fundamental for the use of siRNAs as therapeutics.

Licensor/Patent Owner	Subject Matter	First Priority Date	Inventors	Status*	Alnylam Rights
Isis	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), EU (EP 0928290), additional applications pending in the U.S. and several foreign jurisdictions	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), additional applications pending in the U.S. and several foreign jurisdictions	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), Canada (CA 2359180), Australia (AU 778474), South Africa (2001/5909), Germany (DE 20023125 U1, DE 10066235 & DE 10080167),	Owned

				additional applications pending in the U.S. and several foreign jurisdictions	
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) and Australia (AU 774285), additional applications pending in the U.S. and several foreign jurisdictions	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 in the U.S. and many countries 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), EU (EP 1407044), South Africa (2003/3929), Singapore (96891), New Zealand (52588), Japan (Application No. 2002/546670), additional applications pending in the U.S. and many countries worldwide	Exclusive rights for therapeutic purposes

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Licensor/Patent Owner	Subject Matter	First Priority Date	Inventors	Status*	Alnylam Rights
Cold Spring Harbor Laboratory	RNAi uses in mammalian cells	3/16/2001	D. Beach, G. Hannon	Pending in the U.S. and many countries worldwide	Non-exclusive rights for therapeutic purposes
Stanford University	RNAi uses *in vivo*	7/23/2001	M.A. Kay, A.P. McCaffrey	Pending in the U.S. and many countries 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 co-owners. A separate entity, the University of Massachusetts, has licensed its purported interest separately to third parties.

We believe that we have a strong portfolio of broad rights to fundamental siRNA patents and patent applications that gives us broad freedom to operate. In addition, many of these rights are exclusive, which we believe prevents potential competitors from entering the field of RNAi without taking a license from us. 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 believe that the so-called Crooke patent, issued in several countries around the world, covers the use of all 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.

Through our acquisition of Ribopharma AG, now known as Alnylam Europe, we own the entire Kreutzer-Limmer patent portfolio, which includes pending applications in the United States and many countries worldwide. We believe that the Kreutzer-Limmer patent (EP 1144623), granted in Europe in 2002, was the first patent granted that specifically covers the use of small dsRNAs as therapeutics. The patent claims embrace therapeutic dsRNAs which are 15 to 21 nucleotide pairs in length. This patent survived an opposition challenge in amended form and the decision is now being appealed by, among others, Merck. The Kreutzer-Limmer series also includes a German Utility Model covering RNAi compositions. 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 Utility Model, which branched off the first European patent application, was registered by the German Patent and Trademark Office in 2003. In 2004, the Kreutzer-Limmer patent was granted in Australia (AU 778474). The second European Kreutzer-Limmer patent (EP 1214945) in the series was granted in Europe in 2005. This patent originated as a divisional application from the first Kreutzer-Limmer patent and extends the coverage of the first patent by covering critical aspects of dsRNA structure 15 to 49 nucleotide pairs

in length. We have received a decision to grant two patents stemming from the Kreutzer-Limmer EP 1144623 patent from the German Patent Office. The first, DE 10080167, which we received in October 2007, covers pharmaceutical compositions and uses of siRNAs with a length between 15 and 49 nucleotides that target certain broad categories of mammalian genes. The second, DE 10066235, which we received in November 2007, covers methods, uses and medicaments for siRNAs with a length of 15 to 49 nucleotide pairs expressed via vectors. Finally, the Canadian Intellectual Property Office has granted the Kreutzer-Limmer patent (CA 2359180) covering dsRNA structures of 15 to 49 nucleotide pairs in length.

The Glover patent series has resulted in several patent grants including in Europe (EP 1230375). This patent series stems from pioneering work of Zernicka-Goetz and co-workers who showed that dsRNAs can mediate RNAi

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in mammalian cells. Broad claims from this patent cover dsRNAs of any length or structure as mediators of RNAi in mammalian systems. We have an exclusive license to the Glover patent for therapeutic uses from Cancer Research Technology Limited.

The Tuschl patent applications filed by Max Planck Gesellschaft zur Förderung der Wissenschaften e.V, on the invention by Dr. Tuschl and his colleagues, which we call the Tuschl II patent series, cover what we believe are key structural features of siRNAs. Specifically, the Tuschl II patents and patent applications include claims directed to synthetic siRNAs, and the use of chemical modifications to stabilize siRNAs. In June 2006, the United States Patent and Trademark Office, or USPTO, issued U.S. Patent No. 7,056,704 and in July 2006 the USPTO issued U.S. Patent No. 7,078,196, each covering methods of making dsRNAs having a 3 overhang structure. In September 2007, the European Patent Office, or EPO, granted broad claims for the Tuschl II patent in Europe (EP 1407044). In February 2008, the Japanese Patent Office notified us of their intent to grant the Tuschl II patent in Japan (JP Application Number 2002/546670). 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 claims of the Fire and Mello patent do not cover the structural features of dsRNAs that are important for the biological activity of siRNAs in mammalian cells. We believe that these specific features are the subjects of the Crooke, Kreutzer-Limmer, Glover and Tuschl II patents and patent applications for which we have secured exclusive rights.

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.

Intellectual Property Related to Chemical Modifications

Our collaboration and license agreement with Isis provides us with rights to practice the inventions covered by over 180 issued patents worldwide, as well as rights based on future chemistry patent applications through March of 2009. These inventions cover chemical modifications we may wish to incorporate into our RNAi therapeutic products. Under the terms of our license agreement, Isis agreed not to grant licenses under these patents to any other organization for dsRNA 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 chemical modifications that may be incorporated into siRNAs to endow them with drug-like properties. We have filed a large number of patent applications relating to these novel and proprietary chemical modifications.

In conjunction with the internally developed and licensed technology from Isis, U.S. Patent No. 7,078,196, a patent in the Tuschl II patent series that 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. These 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 certain attractive gene targets as treatments for specific diseases. We recognize, however, that there may be a significant number of competing

applications filed by other organizations claiming siRNAs to treat the same gene target. Because we 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

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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. The Kreutzer-Limmer II patent series is pending in the United States and many foreign countries. Moreover, a patent in the Tuschl II patent series, U.S. Patent No. 7,078,196, claims methods of preparing siRNAs which mediate cleavage of an mRNA in mammalian cells and, therefore, covers methods of making 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 patent coverage will 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

We have expanded our internal research efforts to encompass several approaches regarding the delivery of siRNAs to mammalian cells, including exploring technology that may allow delivery of siRNAs to cells through the use of cationic lipids, cholesterol and carbohydrate conjugation, peptide and antibody-based targeting, and polymer conjugations. Our collaborative efforts include working with academic and corporate third parties to examine specific embodiments of these various approaches to delivery of siRNAs to appropriate cell tissue, and in-licensing of the most promising technology. For example, we have obtained an exclusive license from the University of British Columbia and Tekmira in the field of RNAi therapeutics to intellectual property covering cationic liposomes and their use to deliver nucleic acid to cells. The issued United States patents and foreign counterparts, 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 and to smaller biotechnology companies with fewer resources and expertise than we have. We believe that for most or all of our drug development programs, there will be one or more competing programs under development at 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 in those programs.

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

- other companies working to develop RNAi therapeutic products;
- 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 for therapeutics that treat the same disease for which we may also be developing treatments.

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

Companies working on chemically synthesized siRNAs include Merck, Roche, Opko Corporation, Nastech, Calando, Quark, Silence Therapeutics plc, or Silence Therapeutics, RXi Pharmaceuticals Corporation, a subsidiary of CytRx Corporation, Tekmira, Protiva Biotherapeutics, Inc., Intradigm, Inc. and Dicerna Pharmaceuticals, Inc. Many of these companies have licensed our intellectual property.

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

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Companies working on miRNA therapeutics include Rosetta Genomics, Santaris Pharma A/S, Miragen Therapeutics Inc. and Asuragen, Inc.

Antisense technology uses short, single-stranded, DNA-like molecules 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. In addition, a number of other companies have product candidates in various stages of pre-clinical and clinical development. Included in these companies are Genta Incorporated and AVI BioPharma, Inc. 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.

The competitive landscape continues to expand and we expect that additional companies will initiate programs focused on the development of RNAi therapeutic products using the approaches described above as well as potentially new approaches that may result in the more rapid development of RNAi therapeutics or more effective technologies for RNAi drug development or delivery.

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 complicated 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 $14.3 million in 2007. 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 and AstraZeneca PLC, which acquired MedImmune during 2007, worldwide Synagis sales were greater than $1.0 billion in 2007. MedImmune is also developing motavizumab (formerly known as Numax®), a humanized monoclonal antibody, which is being evaluated for its potential to prevent serious lower respiratory tract disease caused by RSV in pediatric patients at high risk of contracting RSV disease. Phase I and II studies have been reported showing that motavizumab appears to have a similar safety and pharmacokinetic profile to Synagis in infants. In addition, Novartis has a small molecule drug, RSV604, licensed from Arrow Therapeutics Ltd, which is in Phase II clinical trials. RSV604 is an oral drug that targets the viral N protein.

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, which includes Zetia, function by blocking cholesterol uptake from the diet and are utilized on their own or in combination with statins. Each of these competing drugs had sales of greater than $1.0 billion during 2007, according to published reports. With regard to future therapies, mipomersen, formerly ISIS 301012, is a lipid-lowering drug targeting apolipoprotein B-100 being developed by Isis

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in collaboration with Genzyme Corporation. Currently in Phase III development, mipomersen has been shown in Phase II trials to reduce cholesterol and other atherogenic lipids more than 40% beyond reductions achieved with current standard lipid-lowering drugs. A weekly injectable therapeutic, mipomersen is being developed primarily for patients at significant cardiovascular risk who are unable to achieve target cholesterol levels with statins alone or who are intolerant of statins.

Competing Drugs for Liver Cancer

There are a variety of surgical procedures, chemotherapeutics, radiation and other approaches that are used in the management of both primary and secondary liver cancer. However, for the majority of patients the prognosis remains poor with fatal outcomes within several months of diagnosis. In November 2007, the FDA approved Sorafenib, also called Nexavar®, for the treatment of un-ressectable liver cancer. Nexavar is the product of Onyx Pharmaceuticals, Inc. developed in collaboration with Bayer Pharmaceuticals Corporation.

There are also a large number of drugs in various stages of clinical development as cancer therapeutics, although the efficacy and safety of these newer drugs are difficult to ascertain at this point of development.

Competing Drugs for Huntington s Disease

While certain drugs are currently used to treat some of the symptoms of HD, no drug has been approved in the United States for the treatment of the underlying disease. Current pharmacological therapy for HD is limited to the management or alleviation of neurobehavioral or movement abnormalities associated with the disease. No disease modifying, disease slowing or neuroprotective agent is currently approved or used to treat HD, although there are several drugs in development.

Amarin Corporation plc s Miraxion, or AMR 101, is a semi-synthetic, ultra-pure derivative of eicosapentaenoic acid, or EPA, a fish oil, and is currently in Phase III development. The Avicena Group Inc. s HD-02, an ultra-pure creatine, is a candidate for prophylactic use for Huntington s disease. A Phase III trial of HD-02 is expected to start in the second half of 2008. Medivation Inc. s Dimebon™ is an orally-available small molecule that is believed to block the mitochondrial permeability transition pore, or MPTP, the glutamate N-methyl D-asparate, or NMDA, receptor and cholinesterase activity. The drug is currently being investigated as a treatment for HD in a Phase II trial and results are expected in the second quarter of 2008.

In addition, 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.

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. 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 to test or market 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, 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, submission to the FDA of a new drug application, or NDA, satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and FDA review and approval of the NDA. Satisfaction of FDA pre-market approval requirements typically takes several years, but may vary substantially depending upon the

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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, including the data derived from our clinical trials such as the GEMINI study, 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, analytical and stability data, a proposed clinical trial protocol and other information.

A 30-day waiting period after the filing of an IND application 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 approval process can result in substantial delay and expense. We, an institutional review board, or IRB, or the FDA may, at any time, suspend, terminate or 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, among other things, 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 application. The study protocol and informed consent information for patients in clinical trials must be submitted to IRBs for approval prior to initiation of the trial.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, which may overlap or be combined. 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, hypercholesterolemia, liver cancer, HD, or the various indications targeted in our preclinical discovery programs, will be regulated as a new drug by the FDA. FDA approval of an 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, and support dosing and administration for each pediatric subpopulation for which the drug is shown to be safe and effective. In some circumstances, the FDA may grant deferrals for the submission of some or all pediatric data, or full or partial waivers. The cost of preparing and submitting an NDA is substantial. Under federal law, NDAs are subject to

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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 that 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 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. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. Such conditions may include significant new studies which could delay any final approval. 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 IV 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 NDAs, 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, packaged or held meet standards, including cGMPs and any additional standards in the 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, submission of periodic reports, recordkeeping, product sampling and distribution. 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 FDA will not allow the product to be marketed as modified.

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If the FDA s evaluation of the NDA or BLA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or BLA 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 or BLA 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. To the extent that we rely on previously unapproved drug delivery systems, we may be subject to additional testing and approval requirements from the FDA above and beyond those described above.

Once an NDA or BLA 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, upon expiration of relevant patents, if any. 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 sponsor was required to provide support from new clinical trials to obtain such marketing approval. During such three-year exclusivity period, the FDA cannot grant approval of an ANDA 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

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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. For example, on September 27, 2007, the President signed the Food and Drug Administration Amendments Act of 2007, or FDAAA. The new legislation grants significant new powers to the FDA, many of which are aimed at improving the safety of drug products before and after approval. In particular, the new law authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information, and require risk evaluation and mitigation strategies, or REMS, for certain drugs, including certain currently approved drugs. In addition, it significantly expands the federal government s clinical trial registry and results databank and creates new restrictions on the advertising and promotion of drug products. Under the FDAAA, companies that violate these and other provisions of the new law are subject to substantial civil monetary penalties.

While we expect these provisions of the FDAAA, among others, to have a substantial effect on the pharmaceutical industry, the extent of that effect is not yet known. As the FDA issues regulations, guidance and interpretations relating to the new legislation, the impact on the industry, as well as our business, will become clearer. The new requirements and other changes that the FDAAA imposes may make it more difficult, and likely more costly, to obtain approval of new pharmaceutical products and to produce, market and distribute existing products.

In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and development of our product candidates and any products that we may commercialize. It is impossible to predict whether additional legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of any such changes 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.

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.

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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 pre-clinical 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.	Member/Whitehead Institute for Biomedical Research Professor/ Massachusetts Institute of Technology
Fritz Eckstein, Ph.D.	Professor/Max Planck Institute
Edward E. Harlow, Ph.D.	Chair/Harvard Medical School
Robert S. Langer, Ph.D.	Institute Professor/Massachusetts Institute of Technology
Judy Lieberman, M.D., Ph.D.	Senior Investigator/Immune Disease Institute Harvard Medical School Professor/Harvard Medical School
Stephen N. Oesterle, M.D.*	Senior Vice President for Medicine and Technology/Medtronic, Inc.
Paul R. Schimmel, Ph.D.	Ernest and Jean Hahn Professor/Skaggs Institute for Chemical Biology
Edward M. Scolnick, M.D.	Director of the Psychiatry Initiative/Broad Institute
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

* Dr. Oesterle participates as an observer on our scientific advisory board.

Employees

As of February 29, 2008, we had 129 employees, 102 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 Information, for financial information about geographic areas. The Notes to our consolidated financial statements are contained herein in Item 8.

Corporate Information

The Company comprises four entities, Alnylam Pharmaceuticals, Inc. and three wholly owned subsidiaries (Alnylam U.S., Inc., Alnylam Europe AG and Alnylam Securities Corporation). Alnylam Pharmaceuticals, Inc. is a Delaware corporation that was formed in May 2003. Alnylam U.S., Inc. is also a Delaware corporation that was formed in June 2002. Alnylam Securities Corporation is a Massachusetts corporation that was formed in December 2006. Alnylam Europe AG, which was incorporated in Germany in June 2000 under the name Ribopharma AG, was acquired by Alnylam Pharmaceuticals, Inc. 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 website 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.	45	Chief Executive Officer and Director
Barry E. Greene	44	President and Chief Operating Officer
Patricia L. Allen	46	Vice President of Finance and Treasurer

John M. Maraganore, Ph.D. has served as our Chief Executive Officer and as a member of our board of directors since December 2002. Dr. Maraganore also served as our President from December 2002 to December 2007. From April 2000 to December 2002, Dr. Maraganore served as Senior Vice President, Strategic Product Development at Millennium Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Maraganore serves as a member of the board of directors of the Biotechnology Industry Organization.

Barry E. Greene has served as our President and Chief Operating Officer since December 2007, as our Chief Operating Officer since he joined us in October 2003 and from February 2004 through December 2005 also served as our Treasurer. 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 explicitly disclaim any obligation to update any forward-looking statements to reflect events or circumstances that arise after the date hereof. 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 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 unproven technologies related to both RNAi and to the delivery of siRNAs to the relevant cell tissue;
- build and maintain a strong intellectual property portfolio;
- gain acceptance for the development of our product candidates and any products we commercialize;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

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

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

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

Relatively few drug candidates based on these discoveries have ever been tested in animals or humans. siRNAs may not naturally possess the inherent properties typically required of drugs, such as the ability to be stable in the body long enough to reach the tissues in which their effects are required, nor the ability to enter cells within these tissues in order to exert their effects. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these drug-like properties into siRNAs. We may spend large amounts of money trying to

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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, 2007, we had an accumulated deficit of $226.0 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 and will require substantial resources 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 alliances with pharmaceutical companies or funding from contracts with the government, but cannot be certain that we will be able to secure or maintain these alliances or contracts, meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments.

To become and remain consistently 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 consistently profitable, the market price of our common stock could decline. In addition, we may be unable to raise capital, expand our business, diversify our product offerings or continue our operations.

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

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

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

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

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

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

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

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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;

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.

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 us and our common stock purchase agreement with Roche contains a similar provision. While the exercise of these rights may provide us with additional funding under some circumstances, the exercise of these rights by Novartis or Roche 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 consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

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

The investment of our cash balance and our investments in marketable debt securities are subject to risks which may cause losses and affect the liquidity of these investments.

At December 31, 2007, we had $455.6 million in cash, cash equivalents and marketable securities. We have historically invested these amounts in corporate bonds, commercial paper, securities issued by the United States, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks, which may be affected by U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements. In addition, should

our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. These market risks associated with our investment portfolio may have a negative adverse effect on our results of operations, liquidity and financial condition.

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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 a defined but limited number of disease targets on an exclusive basis 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. The initial term of this collaboration expires in October 2008 but may be extended by Novartis for two additional one-year terms. Novartis may elect to terminate this collaboration in the event of a material uncured breach by us. We expect that a substantial amount of funding will come from this collaboration. If this collaboration is unsuccessful, or if it is terminated, our business could be adversely affected.

This agreement also provides Novartis with a non-exclusive option to a broad platform license 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 and far more experience than we do 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. Accordingly, the exercise by Novartis of this option could adversely affect our business.

Our agreement with Novartis allows us to continue to develop products on an exclusive basis 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, for a defined term, 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 around specific targets with other parties.

Our license and collaboration agreement with Roche is important to our business. If Roche does not successfully develop drugs pursuant to this agreement or it results in competition between us and Roche for the development of drugs targeting the same diseases, our business could be adversely affected.

In July 2007, we and, for limited purposes, Alnylam Europe, entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties as well as our collaboration agreements. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, which may be expanded to include other therapeutic areas under certain circumstances. As such, Roche could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases. Roche 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 Roche in the development of RNAi-based drugs targeting the same disease. Roche is required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees. If Roche fails to successfully develop products using this technology, we may not receive any such milestone or royalty payments.

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We may not be able to execute our business strategy if we are unable to enter into alliances with other companies that can provide business and scientific 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. In addition, we believe that other companies are expending substantial resources in developing safe and effective means of delivering siRNAs to relevant cell and tissue types. Accordingly, we have entered into alliances with other companies that we believe can provide such capabilities and intend to enter into additional alliances in the future. For example, we intend to enter into (1) non-exclusive platform alliances which will enable our collaborators to develop RNAi therapeutics and will bring in additional funding with which we can develop our RNAi therapeutics, and (2) alliances to jointly develop specific drug candidates and to jointly commercialize RNAi therapeutics, if they are approved and/or ex-U.S. market geographic partnerships on specific RNAi therapeutic programs. In such alliances, we may expect our collaborators to provide substantial capabilities in delivery of RNAi therapeutics to the relevant cell or tissue type, 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 on our drug targets. 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 Medtronic, NIAID and DTRA. 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 could be adversely affected if any collaborator terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future collaborations, if any, may not be scientifically or commercially successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. If a collaborator terminates its collaboration with us, for breach or otherwise, it would be difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. In addition, a collaborator, or in the event of a change in control of a collaborator, the successor entity, 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 developed without us.

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

We depend on government contracts 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, 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 for hemorrhagic fever virus, including the Ebola virus. 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 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 $23.0 million we expect to receive under this contract, we may not be able to develop therapeutics to treat Ebola.

In August 2007, DTRA awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus infection. This federal contract is expected to provide us with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus infection. This contract is with DTRA under its 2007 Medical Science and Technology Chemical and Biological Defense Transformational Medical Technologies Initiative, the mission of which is to provide state-of-the-art defense capabilities to United States military personnel by addressing traditional and non-traditional biological threats. Of the $38.6 million in funding, the government has committed to pay us up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract. If we do not receive the $38.6 million we expect to receive under this contract, we may not be able to develop therapeutics to treat hemorrhagic fever virus infection.

Regulus Therapeutics, our joint venture with Isis, is important to our business. If Regulus Therapeutics does not successfully develop drugs pursuant to this license and collaboration agreement or Regulus Therapeutics is sold to Isis or a third-party, our business could be adversely affected.

In September 2007, we and Isis created Regulus Therapeutics to discover, develop and commercialize microRNA therapeutics. Formed as a joint venture, Regulus Therapeutics intends to address therapeutic opportunities that arise from abnormal expression or mutations in miRNAs. Generally, we do not have rights to pursue miRNA therapeutics independently of Regulus Therapeutics. If Regulus Therapeutics is unable to discover, develop and commercialize microRNA therapeutics, our business could be adversely affected.

In addition, subject to certain conditions, we and Isis each have the right to initiate a buy-out of Regulus Therapeutics assets, including Regulus Therapeutics intellectual property and rights to licensed intellectual property. The limited liability company agreement provides that following such initiation of a buy-out, we and Isis will mutually determine whether to sell Regulus Therapeutics to us, Isis or a third party. We may not have sufficient funds to buy out Isis interest in Regulus Therapeutics and we may not be able to obtain the financing to do so. In addition, Isis may not be willing to sell their interest in Regulus Therapeutics. If Regulus Therapeutics is sold to Isis or a third party, we may lose our rights to participate in the development and commercialization of miRNA therapeutics. If we and Isis are unable to negotiate a sale of Regulus Therapeutics, Regulus Therapeutics will distribute and assign its rights, interests and assets to us and Isis in accordance with our percentage interests, except for Regulus Therapeutics intellectual property and license rights, to which each of us and Isis will receive co-exclusive rights, subject to certain specified exceptions. In this event, we could face competition from Isis in the development of miRNA therapeutics.

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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 utilize specialized formulations, such as liposomes, whose scale-up and manufacturing could be very difficult. We also have very limited experience in 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 siRNAs. We currently rely on several contract manufacturers for our supply of synthetic siRNAs. 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, which could result in unusable product and cause delays in our development process. In addition, to fulfill our siRNA requirements we may need to secure alternative suppliers of synthetic siRNAs. In addition to the manufacture of the synthetic siRNAs, we may have additional manufacturing requirements related to the technology required to deliver the siRNA to the relevant cell or tissue type. In some cases, the delivery technology we utilize is highly specialized or proprietary, and for technical and legal reasons, we may have access to only one or a limited number of potential manufacturers for such delivery technology.

The manufacturing process for any products that we may develop is subject to the FDA and foreign regulatory authority approval process and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority 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 supply. We may experience difficulty in obtaining adequate manufacturing capacity for our needs. If we are unable to obtain or maintain contract manufacturing for these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our products.

To the extent that we enter into manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner and consistent with regulatory requirements, 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 regulatory applications, or receiving regulatory approvals, for our products candidates;
- 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 some cases, the technical skills required to manufacture our product may be unique to the original manufacturer and we may have difficulty transferring such skills to a back-up nor alternate supplier, or we may be unable to transfer such skills 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

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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 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 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, many of which have substantially greater resources with which to reward qualified individuals than we do. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our business plan.

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

Since we commenced operations in 2002, we have grown substantially. Prior to our sale of our Kulmbach facility to Roche, we employed approximately 140 full time equivalent employees, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. As of December 31, 2007, we had approximately 120 employees in our facility in Cambridge, Massachusetts. We have access to our former employees in our Kulmbach facility who currently work for Roche for a transition period, after which we will no longer have access to the employees in that facility.

In addition, our rapid and substantial growth may place a strain on our administrative and operational infrastructure. 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. 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.

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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 RSV infection. In January 2008, we completed a Phase II trial designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV, and we intend to continue the clinical development of ALN-RSV01. However, 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 or early clinical trials of a drug candidate may not predict the results that will be obtained in subsequent human clinical trials. We, the FDA or other applicable regulatory authorities, or an IRB may suspend clinical trials of a drug candidate at any time for various reasons, including if we or they believe the subjects 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, the seasonality of infections 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, an IRB 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, among other things, 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 trials;

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;

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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 candidates; or

unfavorable FDA or other regulatory agency inspection and review of a clinical trial site or records of any clinical or pre-clinical investigation.

Even if we successfully complete clinical trials of our drug candidates, any given drug candidate may not prove to be an effective treatment for the diseases for which it was being tested.

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. For example, we believe that product candidates we develop for Parkinson s disease, 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 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 United States 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 marketed. 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 limited 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. For example, the recently enacted Food and Drug Administration Amendments Act of 2007, or FDAAA, may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, market and distribute products after approval. The FDAAA grants a variety

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of new powers to the FDA, many of which are aimed at improving the safety of drug products before and after approval. In particular, it authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information, and require risk evaluation and mitigation strategies, or REMS, for certain drugs, including certain currently approved drugs. In addition, it significantly expands the federal government s clinical trial registry and results databank and creates new restrictions on the advertising and promotion of drug products. Under the FDAAA, companies that violate the new law are subject to substantial civil monetary penalties.

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 the product candidates that we are currently developing are 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. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the number of approvals to market new drugs has declined.

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, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not assure approval by regulatory authorities outside the United States and vice versa.

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 or continue 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 anticipate or participants may drop out of our clinical trials at a higher rate than we 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;

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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;

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; and

effects of our drug candidates may not be clear, or we may disagree with regulatory authorities, including the FDA, about how to interpret the data generated in our clinical trials.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing United States 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, 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 potentially new routes of administration;

the success of our physician education programs;

the availability of government and third-party payor reimbursement;

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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, benefits and costs of the treatments.

Even if we develop RNAi therapeutic products for the prevention or treatment of infection by hemorrhagic fever viruses such as Ebola and/or pandemic flu virus, 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 hemorrhagic fever viruses such as Ebola or the pandemic flu. 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 Ebola program is to develop RNAi therapeutic targeting gene sequences that are highly conserved across known Ebola viruses, if the sequence of any Ebola 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 Ebola could be stockpiled by governments as part of their biodefense preparations, they may not elect to purchase such product, or if they purchase our products, they may not do so at prices and volume levels that are profitable for us.

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

If we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products 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;

exclusion from participation in government-funded healthcare programs;

exclusion from eligibility for the award of government contracts for our products;

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties 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

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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 or the likely 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 seeking to reduce the prices charged for pharmaceutical 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 United States law, drugs that are not usually self-administered may be eligible for coverage by the Medicare program if:

they are incident to a physician s services;

they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standard of medical practice;

they are not excluded as immunizations; and

they have been approved by the FDA.

There may be significant delays in obtaining coverage for newly-approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA. Moreover, eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for new drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed in recent years. These proposals have included prescription drug benefit legislation that was enacted and took effect in January 2006 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. Recent proposed legislation has been introduced in Congress that, if enacted, would permit more widespread re-importation of drugs from foreign countries into the United States. This could include re-

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importation from foreign countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decrease in the price we receive for any approved products, which, in turn, could impair our ability to generate revenue. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales.

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.

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, until recently, in 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 employed in our German facility complied 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 Patents, Licenses and Trade Secrets

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

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

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applications are confidential until the patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date which will not be filed in foreign countries, third parties may have filed patent applications for 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. While issued patents are presumed valid, this does not guarantee that the patent will survive a validity challenge or be held enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, adjudged unenforceable or circumvented. 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. Adding to the uncertainty of our current intellectual property portfolio and our ability to secure and enforce future patent rights are the outcome of a legal dispute surrounding the implementation of certain continuation and claims rules promulgated by the USPTO, which were scheduled to take effect November 1, 2007, but which are now enjoined), and the outcome of Congressional efforts to reform the Patent Act of 1952. 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, among others, Isis, MIT, the Whitehead Institute for Biomedical Research, Max Planck Innovation, Stanford University, and Tekmira. We also intend to enter into additional licenses to third party intellectual property in the future.

Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents issue in respect of

these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

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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. We have obtained important grants and issuances of RNAi patents and have licensed many of these patents on an exclusive basis. Our patents and patent applications claim many different methods, compositions and processes relating to the discovery, development and commercialization of RNAi therapeutics. As the field is maturing, patent applications are being fully processed by national patent offices around the world. There is 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, reexamination 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 1144623, 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 September 2006, the EPO opposition division upheld the patent with amended claims. This decision has been appealed by two of the opponents, including Merck and Silence Therapeutics. 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 a second 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. Furthermore, one party has filed a notice of opposition regarding the European Patent EP 1352061, the European regional phase of a patent family commonly referred to as Kreutzer-Limmer II. The proceedings in the EPO and Australian Patent Office may take several years before an outcome becomes final.

In addition, five parties have filed Notices of Opposition in the EPO against the Glover patent. A hearing for this opposition will be held in July 2008, after which the Opposition Division will render a decision, which may include upholding the patent claims as granted or in amended form or cancelling the claims altogether. Either party may appeal the decision by the Opposition Division.

There are also 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

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other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management s efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties patent rights. In addition to any damages we might have to pay, a court could require us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially acceptable terms, if at all. In addition, such licenses are likely to be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Moreover, we expect that a number of our collaborations will provide that royalties payable to us for licenses to our intellectual property may be offset by amounts paid by our collaborators to third parties who have competing or superior intellectual property positions in the relevant fields, which could result in significant reductions in our revenues from products developed through collaborations.

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

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

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

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Risks Related to 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

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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, hypercholesterolemia, liver cancer and HD, and have a number of additional discovery programs targeting other diseases. Virazole and Synagis are currently marketed for the treatment of certain RSV patients, and numerous drugs are currently marketed or used for the treatment of hypercholesterolemia, liver cancer and HD as well. 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, including delivery 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 companies that are working in the field of RNAi. In addition, we granted licenses or options for

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licenses to Isis, GeneCare, Benitec, Nastech, Calando, Tekmira, Quark and 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 was one of our collaborators and a licensee under our intellectual property for specified disease targets until September 2007, at which time we and Merck agreed to terminate our collaboration. As a result of its acquisition of Sirna in December 2006, and in light of the mutual termination of our collaboration, Merck, which has substantially more resources and experience in developing drugs than we do, may become a direct competitor.

In addition, as a result of agreements that we have entered into, Roche has obtained, and Novartis has the right to obtain, broad, non-exclusive licenses to certain aspects of our technology that give them the right to compete with us in certain circumstances.

We also compete with companies working to develop antisense-based drugs. Like RNAi product candidates, antisense drugs target messenger RNAs, or 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. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for drugs that target mRNAs to silence specific genes.

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

Risks Related to Our Common Stock

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

The market price of our common stock 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 or cause a decline in our common stock should Novartis decide to sell all or a portion of its shares.

Novartis held approximately 13% of our outstanding common stock as of December 31, 2007. 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

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

In addition, if Novartis decides to sell all or a portion of its shares in a rapid or disorderly manner, our stock price could be negatively impacted.

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 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. As of February 29, 2008, we lease approximately 84,000 square feet of office and laboratory space in Cambridge, Massachusetts. The two leases for this property expire in September 2011. 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 the fiscal year ended December 31, 2007.

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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 periods indicated:

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

Year Ended December 31, 2007:	High	Low
First Quarter	$ 22.94	$ 16.66
Second Quarter	$ 20.68	$ 15.06
Third Quarter	$ 34.85	$ 14.87
Fourth Quarter	$ 37.35	$ 26.84

Holders of record

As of February 29, 2008, there were approximately 62 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 2008 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 SEC, 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 2007, 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	12/30/2005	12/29/2006	12/31/2007
Alnylam Pharmaceuticals, Inc.	$ 100.00	$ 124.29	$ 222.30	$ 356.07	$ 483.86
Nasdaq Stock Market (U.S.) Index	$ 100.00	$ 109.70	$ 112.03	$ 123.08	$ 133.48
Nasdaq Pharmaceutical Index	$ 100.00	$ 103.32	$ 113.77	$ 111.36	$ 117.11

* $100 invested on May 28, 2004, the date on which our common stock was first publicly traded, in our 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 for each of the five years in the period ended December 31, 2007 are derived from our audited consolidated financial statements. 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. Historical results are not necessarily indicative of future results.

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

	Year Ended December 31,				
	2007	2006	2005	2004	2003
Statement of Operations Data:					
Net revenues	$ 50,897	$ 26,930	$ 5,716	$ 4,278	$ 176
Operating expenses(1)	144,074	66,431	49,188	36,542	25,233
Loss from operations	(93,177)	(39,501)	(43,472)	(32,264)	(25,057)
Net loss	(85,466)	(34,608)	(42,914)	(32,654)	(25,033)
Net loss attributable to common stockholders	$ (85,466)	$ (34,608)	$ (42,914)	$ (35,367)	$ (27,939)
Net loss per common share basic and diluted	$ (2.21)	$ (1.09)	$ (1.96)	$ (2.98)	$ (29.64)
Weighted average common shares outstanding basic and diluted	38,657	31,890	21,949	11,886	943
(1) Non-cash stock-based compensation included in operating expenses	$ 14,472	$ 8,304	$ 4,597	$ 4,106	$ 3,455

	December 31,				
	2007	2006	2005	2004	2003
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 455,602	$ 217,260	$ 80,002	$ 46,046	$ 23,193
Working capital	381,468	199,859	63,930	41,606	20,345
Total assets	493,791	240,006	98,348	66,107	35,183
Notes payable	6,758	9,136	7,395	7,201	1,859
Redeemable convertible preferred stock					55,189
Total stockholders equity (deficit)	199,168	201,174	61,779	46,142	(26,707)

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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 the expression of 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 broad new 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 applying our technological expertise to build a pipeline of RNAi therapeutics to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Our lead RNAi therapeutic program, ALN-RSV01, is in Phase II clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which is reported to be the leading cause of hospitalization in infants in the United States and also occurs in the elderly and in immune compromised adults. In February 2008, we reported positive results from our Phase II experimental infection clinical trials, referred to as the GEMINI study. The GEMINI study was designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01. In this study, ALN-RSV01 was safe and well tolerated and demonstrated statistically significant anti-viral activity, including an approximately 40% reduction in viral infection and a 95% increase in infection-free patients ($p<0.01$). We intend to initiate a second Phase II human clinical trial of ALN-RSV01 in naturally infected adult patients during the first half of 2008. We submitted an investigational new drug, or IND, application for ALN-RSV01 to the United States Food and Drug Administration, or FDA, in November 2005, and have completed a number of Phase I clinical trials on this experimental drug carried out in both the United States and Europe. The results from these Phase I trials and the initial Phase II trial have been presented at medical conferences. ALN-RSV01 was found to be safe and well tolerated when administered intranasally or by nebulizer.

In pre-clinical development programs, which are programs for which we have established targeted timing for human clinical trials, we are working on a number of programs including ALN-PCS, an RNAi therapeutic targeting a gene called proprotein convertase subtilisn/kexin type 9, or PCSK9, for the treatment of hypercholesterolemia, ALN-VSP, an RNAi therapeutic being developed for the treatment of liver cancer and potentially other cancers that is designed to target both vascular endothelial growth factor, or VEGF, and kinesin spindle protein, or KSP, and ALN-HTT, an RNAi therapeutic that is designed to target Huntington s disease, which we are developing in collaboration with Medtronic, Inc., or Medtronic.

We have pre-clinical discovery programs, which are programs for which we have yet to establish targeted timing for human clinical trials, for RNAi therapeutics for the treatment of a broad range of diseases, including viral hemorrhagic fever, including the Ebola virus, progressive multifocal leukoencephalopathy, or PML, a CNS disease caused by viral infection in immune compromised patients, pandemic flu, Parkinson s disease and cystic fibrosis, the inherited respiratory disease, or CF, as well as other undisclosed programs.

We also are working internally and with third-party collaborators to develop the capabilities to deliver our RNAi therapeutics directly to specific sites of disease, such as the delivery of ALN-RSV01 to the lungs, which we refer to as Direct RNAi[tm]. In addition, we are working to extend our capabilities to advance the development of RNAi therapeutics that are administered by intravenous, subcutaneous or intramuscular approaches, which we refer to as Systemic RNAi[tm]. During 2007, we obtained an exclusive worldwide license to the liposomal delivery formulation

technology of Tekmira Pharmaceuticals Corporation, or Tekmira, formerly know as Inex Pharmaceuticals Corporation, for the discovery, development and commercialization of lipid-based nanoparticle formulations for the delivery of RNAi therapeutics. We also signed an agreement with the Massachusetts Institute of Technology, or MIT, Center for Cancer Research to sponsor an exclusive five-year research program focused on the delivery of RNAi therapeutics. We have other RNAi therapeutic delivery collaborations and intend to continue to collaborate with academic and corporate third parties, to evaluate different delivery options, including with respect to Direct RNAi and Systemic RNAi.

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We rely on the strength of our intellectual property portfolio relating to the development and commercialization of small interfering RNAs, or 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. We believe that no other company possesses a portfolio of such broad and exclusive rights to the fundamental RNAi patents and patent applications required for the development and commercialization of RNAi therapeutics.

In addition, our expertise in RNAi therapeutics and broad intellectual property estate have allowed us to form alliances with leading companies, including F. Hoffmann-La Roche Ltd, or Roche, Novartis Pharma AG, or Novartis, Medtronic 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 Institutes of Health, or NIH, and the Defense Threat Reduction Agency, or DTRA, an agency of the United States Department of Defense, or DoD. We have established collaborations and, in some instances, received funding from a number of major medical and disease associations, including The University of Texas Southwestern Medical Center, or UTSW, the Mayo Clinic, The Michael J. Fox Foundation and the Cystic Fibrosis Foundation Therapeutics, or CFTT. Finally, to further enable the field and monetize our intellectual property rights, we have also entered into approximately 20 license agreements with other biotechnology companies interested in developing RNAi therapeutic products and research companies that commercialize RNAi reagents or services.

In September 2007, we and Isis Pharmaceuticals, Inc., or Isis, established Regulus Therapeutics LLC, or Regulus Therapeutics, a joint venture focused on the discovery, development and commercialization of microRNA, or miRNA, therapeutics. Because miRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, miRNA therapeutics represent a new approach to target the pathways of human disease. Regulus Therapeutics combines our and Isis technologies, know-how and intellectual property relating to miRNA therapeutics.

We commenced operations in June 2002. We have focused our efforts since inception primarily on business planning, research and development, acquiring, filing and expanding intellectual property rights, recruiting management and technical staff, and raising capital. Since our inception, we have generated significant losses. As of December 31, 2007, we had an accumulated deficit of $226.0 million. Through December 31, 2007, we have funded our operations primarily through the net proceeds from the sale of equity securities and payments under strategic alliances. Through December 31, 2007, a substantial portion of our total net revenues have been collaboration revenues derived from our strategic alliances with Roche, Novartis and Merck & Co., Inc., or Merck, and from the United States government in connection with our development of treatments for hemorrgagic fever viruses, including Ebola. We expect our revenues to continue to be derived primarily from new and existing strategic alliances, 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 never achieved profitability on an annual basis and we expect to incur additional losses over the next several years. We expect our net losses to continue primarily due to research and development activities relating to our drug development programs, collaborations 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 be derived primarily from payments under new and existing strategic alliances, which may include license and other fees, funded research and development payments and milestone payments, government and foundation funding and proceeds from the sale of equity.

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. Our most advanced program is focused on

the treatment of RSV infection. Our other development programs are focused on the treatment of hypercholesterolemia, liver cancer and potentially other cancers, and Huntington s disease. We also have discovery programs to develop RNAi therapeutics for the treatment of a broad range of diseases, including viral hemorrhagic fever, including the Ebola virus, PML, pandemic flu, Parkinson s disease, CF, several other diseases that are the subject of our collaboration with Novartis, and other undisclosed programs. In addition, we are working internally

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and with external collaborators to develop the capabilities to deliver our RNAi therapeutics both directly to the specific sites of disease and systemically and we intend to continue to collaborate with academic and corporate third parties to evaluate different delivery options.

There is a risk that any drug discovery and development program may not produce revenue for a variety of reasons, including the possibility that we will not be able to adequately demonstrate the safety and efficacy of the product candidate. 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, particularly those related to developing safe and effective ways of delivering siRNAs into cells and tissues;

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

the cost, timing and success of regulatory filings and 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 plan 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, Tekmira, MIT and Isis, as well as a number of other entities, to obtain rights to important intellectual property in the field of RNAi. In addition, our collaboration strategy is to form (1) non-exclusive platform alliances where our collaborators obtain access to our capabilities and intellectual property to develop their own RNAi therapeutic products and (2) 50/50 co-development and/or ex-U.S. market geographic partnerships on specific RNAi therapeutic programs. We have entered into a broad, non-exclusive platform license agreement with Roche, under which we and Roche also will collaborate on RNAi drug

discovery for one or more disease targets. We also have discovery and development alliances with Novartis and Medtronic. Two of the programs we are pursuing under our alliances with Novartis and Medtronic are 50/50 co-development programs.

We have also entered into contracts with government agencies, including NIAID and DTRA. We have established collaborations and in some instances, received funding from, a number of major medical and disease associations including UTSW, the Mayo Clinic, The Michael J. Fox Foundation and the CFTT. To further enable the field and monetize our intellectual property rights, we also grant licenses to biotechnology companies under our InterfeRx^{tm} program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. As of February 29, 2008, we had granted such licenses, on both an

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exclusive and nonexclusive basis, to approximately 20 companies, and options to take such licenses to two additional companies.

Roche. In July 2007, we and, for limited purposes, Alnylam Europe AG, or Alnylam Europe, entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement, which became effective in August 2007, we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include other therapeutic areas upon payment of an additional specified amount.

In consideration for the rights granted to Roche under the license and collaboration agreement, Roche paid us $273.5 million in upfront cash payments. Roche is also required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees.

Under the license and collaboration agreement, we and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets, subject to our contractual obligations to third parties. The collaboration between Roche and us will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. In exchange for our contributions to the collaboration, Roche will be required to make additional milestone and royalty payments.

In connection with the execution of the license and collaboration agreement, in August 2007, we executed a common stock purchase agreement with Roche Finance, pursuant to which Roche Finance purchased 1,975,000 shares of our common stock at $21.50 per share, for an aggregate purchase price of $42.5 million.

In connection with the execution of the license and collaboration agreement and the common stock purchase agreement, we also executed a stock purchase agreement with Alnylam Europe and Roche Germany. Under the terms of the Alnylam Europe stock purchase agreement, we created a new, wholly-owned German limited liability company, Roche Kulmbach, into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from us all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million.

In connection with the license and collaboration agreement and the common stock purchase agreement, we incurred $27.5 million of license fees payable to our licensors, primarily Isis, in accordance with the applicable license agreements with those parties.

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. In October 2005, Novartis purchased 5,267,865 shares of our common stock at a purchase price of $11.11 per share for an aggregate purchase price of $58.5 million, which, immediately after such issuance, represented 19.9% of our then outstanding common stock. Novartis owned approximately 13% of our common stock as of December 31, 2007.

Under the terms of the collaboration and license agreement governing the broad Novartis alliance, 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.

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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. Under the terms of the Novartis flu agreement, we and Novartis have joint responsibility for development of RNAi therapeutics for pandemic flu. 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. During 2007, we and Novartis agreed to focus on additional pre-clinical research prior to advancing this program into development.

Medtronic. In July 2007, we entered into an amended and restated collaboration agreement with Medtronic to pursue the development of therapeutic products for the treatment of neurodegenerative disorders. The amended and restated collaboration agreement supersedes the collaboration agreement entered into by the parties in February 2005, and continues the existing collaboration between the parties focusing on the delivery of RNAi therapeutics to specific areas of the brain using implantable infusion systems.

Under the terms of the amended and restated collaboration agreement, we and Medtronic will continue our existing development program focused on developing a combination drug-device product for the treatment of Huntington s disease. In addition, as provided for in our initial collaboration agreement with Medtronic, the parties may jointly agree to collaborate on additional product development programs for the treatment of other neurodegenerative diseases, which can be addressed by the delivery of small interfering RNAs, or siRNAs, discovered and developed using our RNAi therapeutics platform, to the human nervous system through implantable infusion devices developed by Medtronic. We will be responsible for supplying the siRNA component and Medtronic will be responsible for supplying the device component of any product resulting from the collaboration.

With respect to the initial product development program focused on Huntington s disease, the parties will each fund 50% of the development efforts for the United States while Medtronic is responsible for funding development efforts outside the United States. Medtronic will commercialize any resulting products and pay royalties to us based on net sales of any such products, which royalties in the United States are designed to approximate 50% of the profit associated with the sale of such product and which royalties in Europe are similar to more traditional pharmaceutical royalties, in that they are intended to reflect each party s contribution.

Each party has the right to opt out of its obligation to fund the program under the agreement at certain stages, and the agreement provides for revised economics based on the timing of any such opt out. Other than pursuant to the initial product development program, and subject to specified exceptions, neither party may research, develop, manufacture or commercialize products that use implanted infusion devices for the direct delivery of siRNAs to the human nervous system to treat Huntington s disease during the term of such program.

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. Under the terms of the collaboration agreement with Biogen Idec, 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, if any, Biogen Idec would be required to pay us milestone and royalty payments. The pace and scope of future development of this program is the responsibility of Biogen Idec. We expect limited resources to be expended on this program in 2008.

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. 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 develops 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. 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. In August 2007, as a result of certain payments

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received by us in connection with the Roche alliance, we made payments totaling $26.5 million to Isis. In October 2005, as a result of certain payments received by us in connection with the Novartis agreements, we made payments totaling $3.7 million to Isis. These license fees were charged to research and development expenses in their respective periods.

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.

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 NIAID. 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. 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.

Department of Defense. In August 2007, we were awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus by DTRA. This federal contract is expected to provide us with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus. Viral hemorrhagic fevers are considered by federal agencies to be high priority agents that pose a potential risk to national security because they can be easily transmitted from person to person, result in high mortality rates and require special action for public health preparedness. This contract is with the DTRA 2007 Medical Science and Technology Chemical and Biological Defense Transformational Medical Technologies Initiative, whose mission is to provide state-of-the-art defense capabilities to United States military personnel by addressing traditional and non-traditional biological threats. Of the $38.6 million in funding, the government has committed to pay us up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract.

Delivery Technology. We are working to extend our capabilities in developing technology to achieve efficacious and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, we have entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, we are also providing funding to support the advancement of these delivery technologies.

Merck. In September 2007, we terminated our amended and restated research collaboration and license agreement with Merck. Pursuant to the termination agreement, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the amended and restated research collaboration and license agreement ceased as of the date of the termination agreement, subject to certain specified exceptions. The termination agreement further provides that, subject to certain conditions, we and Merck will each retain sole ownership and rights in our own intellectual property. We have no remaining deliverables under the amended and restated research collaboration and license agreement.

Joint Venture (Regulus Therapeutics LLC)

In September 2007, we and Isis established Regulus Therapeutics, a joint venture focused on the discovery, development and commercialization of miRNA therapeutics. Because miRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, miRNA therapeutics represent a new approach to target the pathways of human disease. Regulus Therapeutics combines the strengths and assets of our and Isis technologies, know-how and intellectual property relating to miRNA therapeutics. In addition, we believe Regulus Therapeutics has assembled a strong leadership team, as well as leading authorities in the field of miRNA research to

lead this new venture.

Regulus Therapeutics most advanced program is an miRNA therapeutic that targets miR-122 for the treatment of hepatitis C virus, or HCV, infection, a significant disease worldwide for which emerging therapies target viral genes and, therefore, are prone to viral resistance. Regulus Therapeutics is targeting miR-122, an endogenous host gene required for viral infection by HCV. In addition to the miR-122 program, Regulus Therapeutics is also actively

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exploring additional areas for development of miRNA therapeutics, including cancer, other viral diseases, metabolic disorders and inflammatory diseases.

We and Isis own 49% and 51%, respectively, of Regulus Therapeutics. Regulus Therapeutics is operated as an independent company with a separate board of directors, scientific advisory board and management team. In connection with the execution of the limited liability company agreement, we, Isis and Regulus Therapeutics entered into a license and collaboration agreement to pursue the discovery, development and commercialization of therapeutic products directed to miRNAs. Under the terms of the license and collaboration agreement, we and Isis assigned to Regulus Therapeutics specified patents and contracts covering miRNA-specific technology. In addition, each of us granted to Regulus Therapeutics an exclusive, worldwide license under our rights to other miRNA-related patents and know-how to develop and commercialize therapeutic products containing compounds that are designed to interfere with or inhibit a particular miRNA, subject to our and Isis existing contractual obligations to third parties. Regulus Therapeutics also has the right to request a license from us and Isis to develop and commercialize therapeutic products directed to other miRNA compounds, which license is subject to our and Isis approval and to each such party s existing contractual obligations to third parties. Regulus Therapeutics also grants to us and Isis an exclusive license to technology developed or acquired by Regulus Therapeutics for use solely within our respective fields (as defined in the license and collaboration agreement), but specifically excluding the right to develop, manufacture or commercialize the therapeutic products for which we and Isis granted rights to Regulus Therapeutics. In addition, we made an initial cash contribution to Regulus Therapeutics of $10.0 million, resulting in us and Isis making initial capital contributions to Regulus Therapeutics of approximately equal aggregate value.

After a sufficient portfolio of data is obtained with respect to each miRNA compound drug candidate developed by Regulus Therapeutics, Regulus Therapeutics may elect to continue to pursue the development and commercialization of products directed to such miRNA compound and related miRNA compounds, in which event Regulus Therapeutics would be obligated to pay us and Isis a royalty on net sales of any such resulting products. If Regulus Therapeutics decides not to continue to pursue the development and commercialization of products directed to particular miRNA compounds, either we or Isis may pursue development and commercialization of such Regulus Therapeutics products. Development and commercialization of such products by either party would be subject to the payment to Regulus Therapeutics of a specified upfront fee, royalties on net sales, milestone payments upon achievement of specified regulatory events and a portion of income received from sublicensing rights.

In connection with the execution of the limited liability company agreement and the license and collaboration agreement, we also executed a services agreement with Isis and Regulus Therapeutics. Under the terms of the services agreement, we and Isis agreed to provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services, as set forth in an operating plan mutually agreed upon by us and Isis. Pursuant to this agreement, we and Isis generally will be paid by Regulus Therapeutics for these services.

Critical Accounting Policies and 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 and disclosure of contingent liabilities in our consolidated financial statements. Actual results may differ from these estimates under different assumptions or conditions and could have a material impact on our reported results. While our significant accounting policies are more fully described in the Notes to our consolidated financial statements included elsewhere 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:

Revenue Recognition

Our business strategy includes entering into collaborative license and development agreements with biotechnology and pharmaceutical companies for the development and commercialization of our product candidates.

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The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical and pre-clinical development milestones and royalties on product sales. We follow the provisions of the Securities and Exchange Commission s Staff Accounting Bulletin No. 104, Revenue Recognition, Emerging Issues Task Force Issue No. 00-21, Accounting for Revenue Arrangements with Multiple Deliverables, or EITF 00-21, Emerging Issues Task Force Issue No. 99-19, Reporting Revenue Gross as a Principal Versus Net as an Agent, and Emerging Issues Task Force 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.

Non-refundable license fees are recognized as revenue when we have a contractual right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and we have no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations such as research and steering committee services, can be separated or whether they must be accounted for as a single unit of accounting in accordance with EITF 00-21. We recognize up-front license payments as revenue upon delivery of the license only if the license has stand-alone value and the fair value of the undelivered performance obligations, typically including research and/or steering committee services, can be determined. If the fair value of the undelivered performance obligations can be determined, such obligations would then be accounted for separately as performed. If the license is considered to either not have stand-alone value or have standalone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement would then be accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue will be recognized. Revenue will be recognized using either a proportional performance or straight-line method. We recognize revenue using the proportional performance method when we can reasonably estimate the level of effort required to complete our performance obligations under an arrangement and such performance obligations are provided on a best-efforts basis. Direct labor hours or full-time equivalents are typically used as the measure of performance. Revenue recognized under the proportional performance method would be determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of substantive milestones, by the ratio of level of effort incurred to date to estimated total level of effort required to complete our performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance method, as of each reporting period.

If we cannot reasonably estimate the level of effort required to complete our performance obligations under an arrangement, then revenue under the arrangement would be recognized as revenue on a straight-line basis over the period we expect to complete our performance obligations. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line basis, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which we expect to complete our aggregate performance obligations.

For revenue generating arrangements where we, as a vendor, provide consideration to a licensor or collaborator, as a customer, we apply the provisions of EITF 01-9. EITF 01-9 addresses the accounting for revenue arrangements where

both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the selling price unless we receive an identifiable benefit for the payment and we can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of selling price are recorded first as a reduction of revenue, to the extent of

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both cumulative revenue recorded to date and of probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer and then as an expense. Payments that are not deemed to be a reduction of selling price would be recorded as an expense.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within the next twelve months are classified as long-term deferred revenue. As of December 31, 2007, we have short-term and long-term deferred revenue of $59.2 million and $204.1 million, respectively, related to our collaborations.

Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with our existing collaboration agreements, we have recorded on our balance sheet short-term and long-term deferred revenue based on our best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next twelve months. Amounts that we expect will not be recognized prior to the next twelve months are classified as long-term deferred revenue. However, this estimate is based on our current operating plan and, if our operating plan should change in the future, we may recognize a different amount of deferred revenue over the next twelve-month period.

The estimate of deferred revenue also reflects management s estimate of the periods of our involvement in certain of our collaborations. Our performance obligations under these collaborations consist of participation on steering committees and the performance of other research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in revenue recognition amounts. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that we recognize and record in future periods.

Roche. We recorded $278.2 million as deferred revenue in connection with the Roche alliance. This amount represents the aggregate proceeds received from Roche, $331.0 million, net of the amount allocated for financial statement purposes to the common stock issuance of $51.3 million, and the net book value of Alnylam Europe of $1.5 million. Roche is also required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees. In addition, we have agreed with Roche to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets, referred to as the Discovery Collaboration, subject to our existing contractual obligations to third parties. The collaboration between Roche and us will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. Our performance obligations under the license and collaboration agreement, including participation in the steering committee and research conducted as part of the Discovery Collaboration, are expected to cease five years from the effective date of the license and collaboration agreement.

The proceeds allocated to the common stock issuance of $51.3 million were based on the fair value on the date the shares were issued. We have concluded that the license issued to Roche, the steering committee services and the services we will be required to perform under the Discovery Collaboration should be treated as a single unit of accounting. Accordingly, the remaining consideration received has been recorded as deferred revenue and will be amortized into revenue over the five-year period during which we are required to provide services under the license and collaboration agreement. We are initially recording revenue on a straight-line basis over five years because we are unable to reasonably estimate the total level of effort required under the license and collaboration agreement. When, and if, we are able to make reasonable estimates of our remaining efforts under the collaboration, we will modify the method of recognition and utilize the proportional performance method. As future milestones are achieved, and to the extent they are within the five year term, the amounts will be recognized as revenue prospectively over the remaining period of performance.

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

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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. We only include milestone payments that we believe are probable of being received. 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.

Government Contracts. Revenue under government cost reimbursement contracts is recognized as we perform the underlying research and development activities.

Accounting for Income Taxes

Effective January 1, 2007, we adopted the provisions of Financial Accounting Standards Board, or FASB, Interpretation No. 48, Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement 109, or FIN 48, which clarifies the accounting for income tax positions by prescribing a minimum recognition threshold that a tax position is required to meet before being recognized in the financial statements. FIN 48 also provides guidance on the derecognition of previously recognized deferred tax items, measurement, classification, interest and penalties, accounting in interim periods, disclosure and transition. Under FIN 48, we recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained upon examination by the taxing authorities, based on the technical merits of the tax position. The tax benefits recognized in our financial statements from such a position are measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate resolution.

We operate in the United States and Germany where our income tax returns are subject to audit and adjustment by local tax authorities. The nature of the uncertain tax positions is often very complex and subject to change and the amounts at issue can be substantial. We develop our cumulative probability assessment of the measurement of uncertain tax positions using internal experience, judgment and assistance from professional advisors. Estimates are refined as additional information becomes known. Any outcome upon settlement that differs from our current estimate may result in additional tax expense in future periods.

We recognize income taxes when transactions are recorded in our consolidated statements of operations, with deferred taxes provided for items that are recognized in different periods for financial statement and tax reporting purposes. We record a valuation allowance to reduce the deferred tax assets to the amount that is more likely than not to be realized. In addition, we estimate our exposures relating to uncertain tax positions and establish reserves for such exposures when they become probable and reasonably estimable.

At December 31, 2007, we had federal and state net operating loss, or NOL, carryforwards of $132.7 million and $145.5 million, respectively, available to reduce future taxable income, that will expire at various dates beginning in 2008 through 2027. At December 31, 2007, federal and state research and development and other credit carryforwards were $2.3 million and $1.9 million, respectively, available to reduce future tax liabilities, that will expire at various

dates beginning in 2018 through 2027. At December 31, 2007, foreign tax credits were $3.1 million, available to reduce future tax liabilities, that expire in 2017. We have concluded that it is more likely than not that our deferred tax assets, including those associated with these carryforwards, will not be realized and, accordingly, have recorded a full valuation allowance. This assessment was based on our estimates of future taxable income which involve significant judgment.

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Accounting for Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of 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 accordance with SFAS 123, as amended, and EITF Issue No. 96-18, Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, 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, 2007, we used a weighted-average expected stock-price volatility assumption of 64%. Due to our short history of being a public company, after adopting SFAS 123R, we estimated the expected life of option grants made through September 30, 2007 using the simplified method prescribed under Staff Accounting Bulletin No. 107 since the grants qualify as plain-vanilla options. This method averages the contractual term of the stock options (10 years) with the vesting term (2.2 years). During the three months ended December 31, 2007, we changed our expected life assumption to be based on the equal weighting of the historical data of (i) our stock price and (ii) the stock prices of our pharmaceutical and biotechnology peers. Our weighted average expected term was 6.0 years for the year ended December 31, 2007. We utilize a dividend yield of zero 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, 2007, the estimated fair value of unvested employee awards was $36.8 million, net of estimated forfeitures. This amount will be recognized over the weighted average remaining vesting period of approximately 1.6 years for these awards. Stock-based employee compensation expense was $11.9 million for the year ended December 31, 2007. However, the total amount of stock-based 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 80% of our options will actually vest, and therefore have applied an annual forfeiture rate of 5.4% to all unvested options as of December 31, 2007. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest.

Accounting for Joint Venture

We account for our interest in Regulus Therapeutics using the equity method of accounting. We have concluded that Regulus Therapeutics qualifies as a variable interest entity under FASB Interpretation No. 46R,

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Consolidation of Variable Interest Entities an interpretation of Accounting Research Bulletin No. 51, or FIN 46R. The limited liability company agreement contains transfer restrictions on each of Isis and our interests and, as a result, we and Isis are considered related parties under paragraph 16(d)(1) of FIN 46R. Because we and Isis are related parties and collectively own 100% of Regulus Therapeutics, the determination of which entity would be considered the primary beneficiary is based on which entity is most closely associated with Regulus Therapeutics. Following the guidance in paragraph 17 of FIN 46R, we have concluded that Isis is the primary beneficiary and, accordingly, we have not consolidated Regulus Therapeutics and account for our investment under the equity method of accounting.

Results of Operations

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

	Year Ended December 31,		
	2007	**2006**	**2005**
Net revenues	$ 50,897	$ 26,930	$ 5,716
Operating expenses	144,074	66,431	49,188
Loss from operations	(93,177)	(39,501)	(43,472)
Net loss	$ (85,466)	$ (34,608)	$ (42,914)

Discussion of Results of Operations for 2007 and 2006

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

	Year Ended December 31,	
	2007	**2006**
Roche	$ 17,571	$
Novartis	14,670	21,775
Government contract	8,989	786
Other research collaborator	8,261	2,508
InterfeRx program, research reagent licenses and other	1,406	1,861
Total net revenues from research collaborators	$ 50,897	$ 26,930

Revenues increased significantly for the year ended December 31, 2007 as compared to the year ended December 31, 2006, primarily as a result of our August 2007 alliance with Roche. We received upfront payments totaling $331.0 million under the Roche alliance, of which $51.3 million was allocated to the purchase of 1,975,000 shares of our common stock and $278.2 million is being recognized as revenue on a straight-line basis over five years under the Roche alliance. The Alnylam Europe stock purchase agreement also includes transition services to be performed by Roche Kulmbach employees at various levels through August 2008. We reimburse Roche for these services at an agreed-upon rate. We recorded $4.2 million of these services as contra revenue (a reduction of revenues) during 2007.

The decrease in Novartis revenues during the year ended December 31, 2007 compared to the year ended December 31, 2006 was due to a decrease in the number of resources allocated to the broad Novartis alliance. The decrease in Novartis revenues was also due to a decrease in the number of resources allocated to, as well as lower external expense reimbursement under, our Novartis flu alliance, as a result of the shift in focus during 2007 on additional pre-clinical research prior to advancing the pandemic flu program into development.

For the year ended December 31, 2007, government contract revenues increased as a result of our collaboration with NIAID, which began in the fourth quarter of 2006, and our collaboration with DTRA, which began in the third quarter of 2007.

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Other research collaborator revenues consisted primarily of research funding and amortization of upfront payments or license fees from Biogen Idec and Merck. The increase in other research collaborator revenues in 2007 is primarily the result of our collaboration with Biogen Idec, which began in the fourth quarter of 2006 and the termination of our Merck collaboration agreement in September 2007. We were recognizing the remaining deferred revenue under the Merck agreement on a straight-line basis over the remaining period of expected performance of four years. As a result of the termination, we recognized an aggregate of $3.5 million during the third quarter of 2007, which represented all of the remaining deferred revenue under the Merck agreement.

The decrease in InterfeRx program, research reagent licenses and other revenues for the year ended December 31, 2007 compared to the prior year was due to upfront payments pursuant to license agreements entered into under our InterfeRx program in the prior year.

Total deferred revenues of $263.3 million at December 31, 2007 consists of payments received from collaborators, primarily Roche, that we have yet to recognize pursuant to our revenue recognition policies.

For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances, collaborations, government contracts and licensing activities and to continue to increase significantly as a result of our August 2007 alliance with Roche.

Operating Expenses

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

	2007	% of Total Operating Expenses	2006	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 120,686	84%	$ 49,260	74%	$ 71,426	145%
General and administrative	23,388	16%	17,171	26%	6,217	36%
Total operating expenses	$ 144,074	100%	$ 66,431	100%	$ 77,643	117%

Certain reclassifications have been made to prior years financial statements to conform to the 2007 presentation.

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:

	2007	% of Expense Category	2006	% of Expense Category	Increase $	Increase %
Research and development						
License fees	$ 42,207	35%	$ 4,040	8%	$ 38,167	945%

Clinical trial and manufacturing	20,662	17%	10,019	20%	10,643	106%
External services	18,292	15%	6,001	12%	12,291	205%
Compensation and related	13,201	11%	10,666	22%	2,535	24%
Non-cash stock-based compensation	9,363	8%	5,006	10%	4,357	87%
Facilities-related	8,511	7%	6,315	13%	2,196	35%
Lab supplies and materials	6,154	5%	5,462	11%	692	13%
Other	2,296	2%	1,751	4%	545	31%
Total research and development expenses	$ 120,686	100%	$ 49,260	100%	$ 71,426	145%

During the year ended December 31, 2007, our research and development expenses increased compared to the year ended December 31, 2006 primarily as a result of an increase in license fees consisting of $27.5 million in

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payments due to certain entities, primarily Isis, in connection with the Roche alliance and $14.7 million in charges for licenses for certain delivery technologies. The increase was also due to an increase in clinical trial and manufacturing expenses in support of our clinical program for RSV, for which we began Phase II trials in June 2007, as well as higher manufacturing expenses related to our pre-clinical development programs. The increase in external services was due to higher expenses related to our pre-clinical programs for the treatment of hypercholesterolemia, liver cancer and Ebola, as well as higher expenses associated with our delivery-related collaborations. The increase in compensation-related expenses and facilities-related expenses was due to additional research and development headcount over the past year to support our alliances and expanding product pipeline. The increase in non-cash stock-based compensation was due primarily to one-time charges of $2.9 million from restricted stock grants and stock option modifications in August 2007 relating to the transfer of our former German employees to Roche Kulmbach as part of our alliance with Roche.

We expect to continue to devote a substantial portion of our resources to research and development expenses and, excluding the impact of the license fees we paid as a result of the Roche alliance in 2007, we expect that research and development expenses will increase in 2008 as we continue development of our and our collaborators product candidates and focus on delivery-related 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. In addition, a significant portion of our research and development costs is not tracked by project as it benefits multiple projects or our technology platform. 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. In addition, we are reimbursed under our government contracts for certain allowable costs including direct internal and external costs. 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 and government contracts.

General and administrative. The following table summarizes 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:

	2007	% of Expense Category	2006	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 8,248	35%	$ 5,162	30%	$ 3,086	60%
Non-cash stock-based compensation	5,109	22%	3,298	19%	1,811	55%
Compensation and related	4,647	20%	3,546	21%	1,101	31%
Facilities-related	2,486	10%	2,736	16%	(250)	(9)%
Insurance	654	3%	652	4%	2	0%
Other	2,244	10%	1,777	10%	467	26%
Total general and administrative expenses	$ 23,388	100%	$ 17,171	100%	$ 6,217	36%

The increase in general and administrative expenses in 2007 compared to the prior year was due primarily to professional service fees, which were the result of increased business development activities, including work related to our alliance with Roche and our Regulus Therapeutics joint venture with Isis. The increase in compensation and related expenses was due primarily to an increase in headcount to support the overall corporate growth of the company. The increase in non-cash stock-based compensation was due primarily to one-time charges of $0.9 million from restricted stock grants and stock option modifications in August 2007 relating to the transfer of our former German employees to Roche Kulmbach as part of our alliance with Roche.

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Interest income was $15.4 million in 2007 compared to $6.2 million in 2006. The increase was due to our higher average cash, cash equivalent and marketable securities balances, primarily from the $331.0 million in proceeds we received in August 2007 from our alliance with Roche.

Interest expense was $1.1 million in 2007 and $1.0 million in 2006. Interest expense in each year related to borrowings under our lines of credit used to finance capital equipment purchases.

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 collaborator	3,294	4,423
InterfeRx program and research reagent licenses	1,439	422
Other	422	125
Total net revenues	$ 26,930	$ 5,716

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 collaborator revenues consist of revenues from Biogen Idec, Merck, NIAID and other government and foundation revenues. The decrease in revenues from other research collaborators was related to a $2.7 million decrease in revenues related primarily 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 NIAID 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.

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.

Operating Expenses

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

	2006	% of Total Operating Expenses	2005	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 49,260	74%	$ 34,977	71%	$ 14,283	41%
General and administrative	17,171	26%	14,211	29%	2,960	21%
Total operating expenses	$ 66,431	100%	$ 49,188	100%	$ 17,243	35%

Certain reclassifications have been made to prior years financial statements to conform to the 2007 presentation.

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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	22%	$ 6,895	20%	$ 3,771	55%
Clinical trial and manufacturing	10,019	20%	537	2%	9,482	1766%
Facilities-related	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 and other fees	4,040	8%	6,904	20%	(2,864)	(41)%
Other	1,751	4%	946	3%	805	85%
Total research and development expenses	$ 49,260	100%	$ 34,977	100%	$ 14,283	41%

During the year ended December 31, 2006, our research and development expenses increased due primarily 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 during the year ended December 31, 2006 as compared to the year ended December 31, 2005 was due primarily to clinical trial and manufacturing expenses in support of our RSV clinical program, which began in December 2005. The increase in compensation and related expenses, and lab supplies and materials expenses was due to additional research and development headcount during 2006 to support our alliances and expanding product pipeline. The increase in stock-based compensation for the year ended December 31, 2006 was due primarily to our adoption of SFAS 123R on January 1, 2006.

General and administrative. The following table summarizes 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:

	2006	% of Expense Category	2005	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 5,162	30%	$ 4,122	29%	$ 1,040	25%
Compensation and related	3,546	21%	3,339	23%	207	6%
Non-cash stock-based compensation	3,298	19%	2,166	15%	1,132	52%
Facilities-related	2,736	16%	1,893	14%	843	45%

Insurance	652	4%	616	4%	36	6%
Other	1,777	10%	2,075	15%	(298)	(14)%
Total general and administrative expenses	$ 17,171	100%	$ 14,211	100%	$ 2,960	21%

As indicated in the table above, the increase in general and administrative expenses in 2006 was due primarily to higher stock-based compensation expenses related to our adoption of SFAS 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.

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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.

Liquidity and Capital Resources

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

	Year Ended December 31,		
	2007	2006	2005
Net loss	$ (85,466)	$ (34,608)	$ (42,914)
Adjustments to reconcile net loss to net cash used in operating activities	29,834	12,633	9,672
Changes in operating assets and liabilities	252,151	(2,655)	16,757
Net cash provided by (used in) operating activities	196,519	(24,630)	(16,485)
Net cash used in investing activities	(277,425)	(30,046)	(40,418)
Net cash provided by financing activities	58,635	166,631	52,617
Effect of exchange rate on cash	(527)	243	(229)
Net (decrease) increase in cash and cash equivalents	(22,798)	112,198	(4,515)
Cash and cash equivalents, beginning of period	127,955	15,757	20,272
Cash and cash equivalents, end of period	$ 105,157	$ 127,955	$ 15,757

Since we commenced operations in 2002, we have generated significant losses. As of December 31, 2007, we had an accumulated deficit of $226.0 million. As of December 31, 2007, we had cash, cash equivalents and marketable securities of $455.6 million, compared to cash, cash equivalents and marketable securities of $217.3 million as of December 31, 2006. The increase in our cash, cash equivalents and marketable securities at December 31, 2007 was due primarily to our receipt of $331.0 million of up-front cash payments under our Roche alliance. 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. The increase in net cash provided by operating activities for the year ended December 31, 2007 compared to the year ended December 31, 2006 was due primarily to the proceeds received from our August 2007 alliance with Roche. Offsetting the proceeds from the Roche alliance, the main components of our use of cash in operating activities for the year ended December 31, 2007 consisted of the net loss and changes in our working capital. 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 consist primarily of non-cash license fees, stock-based compensation and depreciation and amortization. We had an increase in deferred revenue of $245.0 million for the year ended December 31, 2007 due to the proceeds received from our Roche alliance. Additionally, accrued expenses and collaboration receivables increased $7.2 million and $1.2 million, respectively, for the year ended December 31, 2007. We expect that we will require significant amounts of cash to fund our operating activities for the foreseeable future 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, 2007, net cash used in investing activities of $277.4 million resulted primarily from purchases of marketable securities of $544.4 million due primarily to the investments made with the proceeds from the Roche alliance, partially offset by sales and maturities of marketable securities of $283.3 million. Also included in our investing activities for the year ended December 31, 2007 was a $10.0 million cash contribution made to Regulus Therapeutics in connection with its formation, as well as purchases of property and equipment of $7.8 million related to the expansion of our Cambridge facility. For the year ended December 31, 2006, net cash used in investing activities of $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.

Financing activities

For the year ended December 31, 2007, net cash provided by financing activities was $58.6 million compared to $166.6 million for the year ended December 31, 2006. The main components of net cash provided by financing activities for the year ended December 31, 2007 consisted primarily of proceeds of $42.5 million from our sale of 1,975,000 shares of common stock to Roche in connection with the establishment of the Roche alliance. For the year ended December 31, 2006, net cash provided by financing activities was primarily a result of the aggregate net proceeds of $163.3 million from our follow-on public offerings in January and December 2006.

In March 2006, we entered into an agreement with Oxford Finance Corporation, or Oxford, 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. In May 2007, we borrowed an aggregate of $1.0 million from Oxford pursuant to the agreement. These amounts are being repaid in 36 to 48 monthly installments. As of December 31, 2007, we are no longer able to draw down funds under the Oxford line of credit.

In March 2004, we entered into an equipment line of credit with Lighthouse Capital Partners V, L.P., or Lighthouse, to finance leasehold improvements and equipment purchases of up to $10.0 million. All draw-downs began to be repaid over 48 months beginning September 30, 2005. On the maturity of each equipment advance under the line of credit, we are required to pay, in addition to the principal and interest due, 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, 2007, we had an aggregate outstanding principal balance of $6.8 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 current alliances, including our Roche alliance, will be sufficient to fund our planned operations for at least the next several years, during which time we expect to further the development of our product candidates, extend the capabilities of our technology platform, 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, commence clinical trials for and commercialize any product candidates.

In the longer term, we may seek additional funding through additional 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;
- the timing, receipt and amount of funding under current and future government contracts, if any;
- our ability to maintain and establish 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;
- progress in the research and development programs of Regulus Therapeutics; and
- the timing, receipt and amount of sales and royalties, if any, from our potential products.

Off-Balance Sheet Arrangements

In connection with a certain license agreement, we are required to indemnify the licensor for certain damages arising in connection with the intellectual property rights licensed 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 No. 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

In the table below, we set forth our enforceable and legally binding obligations and future commitments, as well as obligations related to contracts that we are likely to continue, regardless of the fact that they were cancelable as of December 31, 2007. Some of the figures that we include in this table are based on management s estimate and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties, and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table.

	Payments Due by Period				
Contractual Obligations	**2008**	**2009 and 2010**	**2011 and 2012**	**After 2012**	**Total**
Operating lease obligations(1)	$ 3,296	$ 6,592	$ 2,472	$	$ 12,360
Short and long-term debt(2)	4,268	3,993	79		8,340
Purchase commitments(3)	3,045				3,045
Technology-related commitments(4)	6,193	6,192	4,056	4,687	21,128
Loan commitment(5)	5,000				5,000
Total contractual cash obligations	$ 21,802	$ 16,777	$ 6,607	$ 4,687	$ 49,873

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(1) Relates to our Cambridge, Massachusetts non-cancelable operating lease agreements.

(2) Relates to our lines of credit with Oxford and Lighthouse. Includes a balloon interest payment of $0.9 million that we are required to pay in 2009 under the Lighthouse line of credit.

(3) Includes commitments related to non-cancelable purchase orders, clinical and pre-clinical agreements and other significant purchase commitments for good or services.

(4) Relates to our fixed payment obligations under license agreements, as well as other payments related to technology research and development.

(5) Relates to a loan commitment to Tekmira for capital equipment expenditures.

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. Because we cannot reasonable predict the likelihood, timing or amount of such payments, we have excluded them from the table above.

Recent Accounting Pronouncements

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements, or SFAS 157. SFAS 157 clarifies the principle that fair value should be based on the assumptions market participants would use when pricing an asset or liability and establishes a fair value hierarchy that prioritizes the information used to develop those assumptions. Under the standard, fair value measurements would be separately disclosed by level within the fair value hierarchy. In November 2007, the FASB deferred the effective date of SFAS 157 for certain nonfinancial and nonrecurring assets and liabilities. Other than the partial deferral, SFAS 157 is effective for us beginning in 2008. We do not expect SFAS 157 to have a material impact on our consolidated financial statements. We are evaluating the impact of SFAS 157 on our nonfinancial assets and liabilities within the scope of SFAS 157.

In February 2007, the FASB issued SFAS No. 159, The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of FAS 115, or SFAS 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. SFAS 159 is effective for fiscal years beginning after November 15, 2007. We do not anticipate the adoption of SFAS 159 will have a material impact on our consolidated financial statements.

In June 2007, the FASB reached a consensus on Emerging Issues Task Force Issue No. 07-03, Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities, or EITF 07-03. EITF 07-03 requires companies to defer and capitalize, until the goods have been delivered or the related services have been rendered, non-refundable advance payments for goods that will be used or services that will be performed in future research and development activities. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. We do not expect EITF 07-03 will have a material impact on our consolidated financial statements.

In December 2007, the FASB reached a consensus on Emerging Issues Task Force Issue 07-1, Accounting for Collaborative Arrangements, or EITF 07-1. EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators

based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. Further, EITF 07-1 clarifies that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to EITF 01-9. EITF 07-1 will be effective beginning on January 1, 2009. We are evaluating the potential impact of EITF 07-1 on our consolidated financial statements.

In December 2007, the FASB issued SFAS No. 141R, Business Combinations, or SFAS 141R. SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquiree and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial

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effects of the business combination. SFAS 141R is effective for fiscal years beginning after December 15, 2008. We are evaluating the potential impact of SFAS 141R on our consolidated financial statements.

In December 2007, the FASB issued SFAS No. 160, Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51, or SFAS 160. SFAS 160 changes the accounting for and reporting of noncontrolling or minority interests (now called noncontrolling interest) in consolidated financial statements. We do not anticipate the adoption of SFAS 160 will have a material impact on our consolidated financial statements.

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 in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. 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, 2007 would impact the net fair value of such interest-sensitive financial instruments by $1.4 million. A downgrade in the credit rating of an issuer of a debt security or further deterioration of the credit markets could result in a decline in the fair value of the debt instrument. We have not recorded any significant impairment charges to our marketable securities as of December 31, 2007.

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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, 2007. 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, 2007, the Company s internal control over financial reporting is effective based on those criteria.

The effectiveness of the Company s internal control over financial reporting as of December 31, 2007 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report. This report appears on page 77.

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Report of Independent Registered Public Accounting Firm

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

In our opinion, the consolidated financial statements listed in the accompanying index present fairly, in all material respects, the financial position of Alnylam Pharmaceuticals, Inc. and its subsidiaries at December 31, 2007 and 2006, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2007 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company s management is responsible for these financial statements and for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management s Annual Report on Internal Control over Financial Reporting. Our responsibility is to express opinions on these financial statements and on the Company s internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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.

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 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.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 7, 2008

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ALNYLAM PHARMACEUTICALS, INC.

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

	December 31, 2007	2006
ASSETS		
Current assets:		
Cash and cash equivalents	$ 105,157	$ 127,955
Marketable securities	350,445	89,305
Collaboration receivables	5,031	3,829
Prepaid expenses and other current assets	2,926	1,695
Total current assets	463,559	222,784
Property and equipment, net	13,810	12,173
Intangible assets, net	968	1,933
Restricted cash	6,152	2,313
Other assets	173	803
Investment in joint venture (Regulus Therapeutics LLC)	9,129	
Total assets	$ 493,791	$ 240,006
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 3,826	$ 4,085
Accrued expenses	11,724	4,479
Income taxes payable	3,497	
Current portion of notes payable	3,795	3,217
Deferred revenue	59,249	11,144
Total current liabilities	82,091	22,925
Deferred revenue, net of current portion	204,067	6,786
Deferred rent	5,200	3,202
Notes payable, net of current portion	2,963	5,919
Other long-term liabilities	302	
Total liabilities	294,623	38,832
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, 2007 and 2006		
Common stock, $0.01 par value, 125,000,000 shares authorized; 40,772,967 shares issued and outstanding at December 31, 2007; 37,050,631 shares issued and outstanding at December 31, 2006	408	371

Additional paid-in capital	424,453	340,779
Deferred stock-based compensation		(89)
Accumulated other comprehensive income	300	640
Accumulated deficit	(225,993)	(140,527)
Total stockholders equity	199,168	201,174
Total liabilities and stockholders equity	$ 493,791	$ 240,006

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,		
	2007	**2006**	**2005**
Net revenues from research collaborators	$ 50,897	$ 26,930	$ 5,716
Operating expenses:			
Research and development(1)	120,686	49,260	34,977
General and administrative(1)	23,388	17,171	14,211
Total operating expenses	144,074	66,431	49,188
Loss from operations	(93,177)	(39,501)	(43,472)
Other income (expense):			
Equity in loss of joint venture (Regulus Therapeutics LLC)	(1,075)		
Interest income	15,393	6,177	1,549
Interest expense	(1,083)	(1,029)	(969)
Other expense	(279)	(255)	(22)
Total other income (expense)	12,956	4,893	558
Loss before income taxes	(80,221)	(34,608)	(42,914)
Provision for income taxes	(5,245)		
Net loss	$ (85,466)	$ (34,608)	$ (42,914)
Comprehensive loss:			
Net loss	$ (85,466)	$ (34,608)	$ (42,914)
Foreign currency translation	(598)	665	(534)
Unrealized gain (loss) on marketable securities	258	117	(28)
Comprehensive loss	$ (85,806)	$ (33,826)	$ (43,476)
Net loss per common share basic and diluted	$ (2.21)	$ (1.09)	$ (1.96)
Weighted average common shares used to compute basic and diluted net loss per common share	38,657	31,890	21,949

(1) Non-cash stock-based compensation expenses included in operating expenses are as follows:

Research and development	$ 9,363	$ 5,006	$ 2,431
General and administrative	5,109	3,298	2,166

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

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY
(In thousands, except share amounts)

	Common Stock		Additional Paid-in	Deferred Stock-based	Accumulated Other Comprehensive Income	Accumulated	Total Stockholders
	Shares	Amount	Capital	Compensation	(Loss)	Deficit	Equity
Balance at December 31, 2004	20,848,848	$ 208	$ 112,216	$ (3,697)	$ 420	$ (63,005)	$ 46,142
Exercise of common and restricted stock options and warrants	199,750	2	184				186
Issuance of common stock	5,589,657	57	54,273				54,330
Deferred compensation related to stock options and restricted stock			2,661	(2,661)			
Amortization of deferred compensation expense related to stock options and restricted stock			699	3,898			4,597
Foreign currency translation					(534)		(534)
Unrealized loss on marketable securities					(28)		(28)
Net loss						(42,914)	(42,914)
Balance at December 31, 2005	26,638,255	267	170,033	(2,460)	(142)	(105,919)	61,779
Exercise of common stock options and warrants	539,425	5	998				1,003
Issuance of common stock	56,990	1	591				592

Deferred compensation related to stock options and restricted stock			1,614	(467)			1,147
Amortization of deferred compensation expense related to stock options and restricted stock			4,318	2,838			7,156
Issuance of common stock upon public offerings, net of offering costs of $6,586	9,815,961	98	163,225				163,323
Foreign currency translation					665		665
Unrealized gain on marketable securities					117		117
Net loss						(34,608)	(34,608)
Balance at December 31, 2006	37,050,631	371	340,779	(89)	640	(140,527)	201,174
Exercise of common stock options	1,247,808	12	9,232				9,244
Issuance of common stock	2,474,528	25	59,874				59,899
Stock based compensation expense			14,364	89			14,453
Foreign currency translation					(598)		(598)
Joint venture stock compensation (Regulus Therapeutics LLC)			204				204
Unrealized gain on marketable securities					258		258
Net loss						(85,466)	(85,466)
Balance at December 31, 2007	40,772,967	$ 408	$ 424,453	$	$ 300	$ (225,993)	$ 199,168

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,		
	2007	2006	2005
Cash flows from operating activities:			
Net loss	$ (85,466)	$ (34,608)	$ (42,914)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	4,082	4,070	2,982
Deferred income tax provision	1,889		
Non-cash stock-based compensation	14,472	8,304	4,597
Non-cash license expense	7,909	130	2,093
Charge for 401(k) company stock match	407	129	
Equity in loss of joint venture (Regulus Therapeutics LLC)	1,075		
Changes in operating assets and liabilities:			
Proceeds from landlord tenant improvements	2,621	1,106	
Collaboration receivables	(1,194)	(3,220)	243
Prepaid expenses and other assets	(4,348)	(336)	(256)
Accounts payable	(264)	2,088	1,025
Income taxes payable	3,497		
Accrued expenses and other	6,843	611	(12)
Deferred revenue	244,996	(2,904)	15,757
Net cash provided by (used in) operating activities	196,519	(24,630)	(16,485)
Cash flows from investing activities:			
Purchases of property and equipment	(7,788)	(4,986)	(1,947)
Disposals of property and equipment	2,342		
Increase in restricted cash	(839)		
Investment in Regulus Therapeutics LLC	(10,000)		
Purchases of marketable securities	(544,394)	(172,303)	(70,882)
Sales and maturities of marketable securities	283,254	147,243	32,411
Net cash used in investing activities	(277,425)	(30,046)	(40,418)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of issuance costs	61,011	164,890	52,423
Proceeds from notes payable	957	4,000	1,037
Repayments of notes payable	(3,333)	(2,259)	(843)
Net cash provided by financing activities	58,635	166,631	52,617
Effect of exchange rate on cash	(527)	243	(229)
Net (decrease) increase in cash and cash equivalents	(22,798)	112,198	(4,515)

Cash and cash equivalents, beginning of period	127,955	15,757	20,272
Cash and cash equivalents, end of period	$ 105,157	$ 127,955	$ 15,757
Supplemental disclosure of cash flows			
Cash paid for interest	$ 890	$ 726	$ 633
Supplemental disclosure of non-cash financing activities			
Common stock issued in connection with license agreements	$ 7,909	$ 130	$ 2,093

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 novel therapeutics based on RNA interference (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, generating revenues through licensing agreements and ultimately developing and commercializing RNAi therapeutics for its own account. The Company has devoted substantially all of its efforts to business planning, research and development, acquiring, filing and expanding 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 wholly-owned subsidiaries (Alnylam U.S., Inc., Alnylam Europe AG (Alnylam Europe) and Alnylam Securities Corporation). Alnylam Pharmaceuticals, Inc. is a Delaware corporation that was formed on May 8, 2003. Alnylam U.S., Inc. 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. All significant intercompany accounts and transactions have been eliminated. The Company uses the equity method of accounting to account for its investment in Regulus Therapeutics LLC (Regulus Therapeutics).

Reclassifications

Certain reclassifications have been made to prior years financial statements to conform to the 2007 presentation.

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 consolidated 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, 2007 and 2006, 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 revenues from collaborations have been generated from primarily Novartis Pharma AG and one of its affiliates (collectively, Novartis), F. Hoffmann-La Roche Ltd and certain of its affiliates (collectively, Roche), and Merck & Co., Inc. (Merck). Novartis owned approximately 13% of the Company s outstanding common stock as of December 31, 2007. In 2007, the Company had revenue from Roche, Novartis and the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), which accounted for 35%, 29% and 15%, respectively, of the Company s total revenue. In 2006 the Company had revenue from Novartis and Merck, which accounted for 81% and 3%, respectively, of the Company s

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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. Receivables from Novartis, NIAID and the Defense Threat Reduction Agency (DTRA), an agency of the United States Department of Defense (DoD), represented approximately 43%, 36% and 15%, respectively of the Company s collaboration receivables balance at December 31, 2007. Receivables from Novartis represented approximately 70% of the Company s collaboration receivables balance at December 31, 2006.

Fair Value of Financial Instruments

The carrying amounts of the Company s financial instruments, which include cash equivalents, collaboration receivables, accounts payable, accrued expenses and notes payable, approximate their fair values at December 31, 2007 and 2006.

Investments in Marketable Securities

The Company invests its excess cash balances in short-term and long-term marketable debt securities. The Company accounts for its investments in debt securities under Statement of Financial Accounting Standards (SFAS) No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* The Company classifies its investments in marketable debt securities as either held-to-maturity or available-for-sale based on facts and circumstances present at the time it purchased the securities. As of each balance sheet date presented, the Company classified all of its investments in debt securities as available-for-sale. The Company reports available-for-sale investments at fair value as of each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value) in stockholders equity. Realized gains and losses are determined on the specific identification method and are included in investment income. If any adjustment to fair value reflects a decline in the value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is other than temporary and, if so, marks the investment to market through a charge to its consolidated statement of operations. The Company did not record any significant impairment charges related to its marketable securities during the years ended December 31, 2007, 2006 or 2005. The Company s marketable securities are classified as cash equivalents if the original maturity, from the date of purchase, is ninety days or less, and as marketable securities if the original maturity, from the date of purchase, is in excess of ninety days.

The following table summarizes the Company s marketable securities at December 31, 2007 and 2006, in thousands:

	December 31, 2007			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper (Due within 1 year)	$ 210,213	$ 177	$ (1)	$ 210,389
Municipal notes (Due within 1 year)	61,605			61,605
Municipal notes (Due after 1 year through 2 years)	7,340	12		7,352
Corporate notes (Due within 1 year)	6,452		(12)	6,440

Corporate notes (Due after 1 year through 2 years)	37,345	108	(41)	37,412
U.S. Government obligations (Due after 1 year through 2 years)	27,193	54		27,247
Total	$ 350,148	$ 351	$ (54)	$ 350,445

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

	December 31, 2006			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper (Due within 1 year)	$ 69,787	$ 33	$	$ 69,820
Corporate notes (Due within 1 year)	19,483	2		19,485
Total	$ 89,270	$ 35	$	$ 89,305

Revenue Recognition

The Company has entered into collaboration agreements with biotechnology and pharmaceutical companies, including Roche, Novartis, Merck and Biogen Idec, Inc. (Biogen Idec). The terms of the Company s collaboration agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical and pre-clinical development milestones and royalties on product sales. The Company follows the provisions of the Securities and Exchange Commission s (SEC) Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition in Financial Statements,* Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21), EITF No. 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent,* and EITF No. 01-9, *Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products)* (EITF 01-9).

Non-refundable license fees are recognized as revenue when the Company has a contractual right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and the Company has no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations such as research and steering committee services, can be separated or whether they must be accounted for as a single unit of accounting in accordance with EITF 00-21. The Company recognizes up-front license payments as revenue upon delivery of the license only if the license has stand-alone value and the fair value of the undelivered performance obligations, typically including research and/or steering committee services, can be determined. If the fair value of the undelivered performance obligations can be determined, such obligations are accounted for separately as such obligations are fulfilled. If the license is considered to either not have stand-alone value or have standalone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement would then be accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company determines the period over which the performance obligations will be performed and revenue will be recognized. Revenue will be recognized using either a proportional performance or straight-line method. The Company recognizes revenue using the proportional performance method when the level of effort required to

complete its performance obligations under an arrangement can be reasonably estimated and such performance obligations are provided on a best-efforts basis. Direct labor hours or full-time equivalents are typically used as the measure of performance. Revenue recognized under the proportional performance method would be determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of substantive milestones, by the ratio of level of effort incurred to date to estimated total level of effort required to complete its performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance method, as of each reporting period.

If the level of effort to complete its performance obligations under an arrangement cannot be reasonably estimated, then revenue under the arrangement would be recognized as revenue on a straight-line basis over the

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

period the Company is expected to complete its performance obligations. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line basis, as of the period ending date.

Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

For revenue generating arrangements where the Company, as a vendor, provides consideration to a licensor or collaborator, as a customer, the Company applies the provisions of EITF 01-9. EITF 01-9 addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the selling price unless the Company receives an identifiable benefit for the payment and it can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of selling price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and of probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer and then as an expense. Payments that are not deemed to be a reduction of selling price would be recorded as an expense.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within the next twelve months are classified as long-term deferred revenue. As of December 31, 2007, the Company has short-term and long-term deferred revenue of $59.2 million and $204.1 million, respectively, related to its collaborations.

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, facilities, supplies, external services, clinical trial and manufacturing costs and overhead directly related to the Company s research and development department as well as costs to acquire technology licenses.

In 2007, the Company reclassified $0.5 million and $0.3 million of patent costs that were recorded as research and development costs to general and administrative expenses for the years ended December 31, 2006 and 2005, respectively.

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, 2007, 2006 and 2005, the Company charged to research and development expense $42.2 million, $4.0 million and $6.1 million, respectively, of costs associated with license fees. The increase in license fees for 2007 was primarily the result of $27.5 million in payments due to certain entities, primarily Isis Pharmaceuticals, Inc. (Isis), in connection with the Roche alliance and $14.7 million in charges for licenses for certain delivery technologies.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Accounting for Stock-Based Compensation

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS No. 123R, *Share-Based Payment, an amendment of FASB Statements Nos. 123 and 95* (SFAS 123R), 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 all awards granted to employees under 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. 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 EITF Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* under which compensation expense is generally recognized over the vesting period of the award, which is generally the period during which services are rendered by such non-employees. 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. Stock options granted by the Company to non-employees, other than members of the Company s 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 Financial Accounting Standards Board (FASB) Interpretation No. 28, *Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans.*

Foreign Currency

The Company s foreign subsidiary, Alnylam Europe (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. Net realized gains and losses from foreign currency transactions are included in the consolidated statements of operations. The Company recognized a gain of $0.1 million during 2007, a loss of $0.3 million during 2006 and a gain of $0.1 million during 2005 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 as the functional currency is not the United States dollar. The Company also includes unrealized gains and losses on certain marketable securities in other comprehensive loss.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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), and unvested restricted stock awards. Because the inclusion of potential common shares would be anti-dilutive for all periods presented, diluted net loss per common share is the same as basic net loss per common share.

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

	December 31,		
	2007	**2006**	**2005**
Options to purchase common stock	5,304	4,650	3,907
Warrants to purchase common stock			53
Unvested restricted common stock	57		55
Options that were exercised before vesting	11	40	73
	5,372	4,690	4,088

Segment Information

The Company operates in a single reporting segment, the discovery, development and commercialization of RNAi therapeutics. 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, 2007 and 2006, in thousands:

	December 31,	
	2007	**2006**
Long-lived tangible assets:		
United States	$ 13,810	$ 10,077
Germany		2,096
Total long-lived tangible assets	$ 13,810	$ 12,173

Recent Accounting Pronouncements

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements* (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 to improve disclosures about those measures. This standard formalizes the measurement principles to be utilized in determining fair value for purposes such as derivative valuation and impairment analysis. In November 2007, the FASB deferred the effective date of SFAS 157 for certain nonfinancial and nonrecurring assets and liabilities. Other than the partial deferral, SFAS 157 is effective for the Company beginning in 2008. The Company does not expect SFAS 157 to have a material impact on its consolidated financial statements. The Company is evaluating the impact of SFAS 157 on its nonfinancial assets and liabilities within the scope of SFAS 157.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of SFAS 115* (SFAS 159). The new statement allows entities to choose, at specified election dates, to measure at fair value eligible financial assets and liabilities 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. SFAS 159 is effective for fiscal years beginning after November 15, 2007. The Company does not anticipate the adoption of SFAS 159 will have a material impact on its consolidated financial statements.

In June 2007, the FASB reached a consensus on EITF Issue No. 07-03, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* (EITF 07-03). EITF 07-03 requires companies to defer and capitalize, until the goods have been delivered or the related services have been rendered, non-refundable advance payments for goods that will be used or services that will be performed in future research and development activities. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. The Company does not expect EITF 07-03 will have a material impact on its consolidated financial statements.

In December 2007, the FASB reached a consensus on EITF Issue 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. Further, EITF 07-1 clarifies that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to EITF 01-9. EITF 07-1 will be effective for the Company beginning on January 1, 2009. The Company is evaluating the potential impact of EITF 07-1 on its consolidated financial statements.

In December 2007, the FASB issued SFAS No. 141R, *Business Combinations* (SFAS 141R). SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquiree and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. SFAS 141R is effective for fiscal years beginning after December 15, 2008. The Company is evaluating the potential impact of SFAS 141R on its consolidated financial statements.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51* (SFAS 160). SFAS 160 changes the accounting for and reporting of noncontrolling or minority interests (now called noncontrolling interest) in consolidated financial statements. The Company does not anticipate the adoption of SFAS 160 will have a material impact on its consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

3. INTANGIBLE ASSETS

Intangible assets at December 31, 2007 and 2006 are as follows, in thousands:

	December 31, 2007	2006
Core Technology	$ 2,410	$ 3,054
Workforce	437	437
	2,847	3,491
Less accumulated amortization:		
Core Technology	(1,442)	(1,185)
Workforce	(437)	(373)
Total accumulated amortization	(1,879)	(1,558)
	$ 968	$ 1,933

During the years ended December 31, 2007, 2006 and 2005, the Company recorded $0.3 million, $0.4 million and $0.5 million, respectively, of amortization expense related to its core technology and workforce intangibles, of which the entire amount is included in research and development expenses. Workforce intangibles were fully amortized during 2007. Core technology is being amortized over its estimated useful life of ten years through 2013. During 2007, the Company reduced its intangible assets by $0.6 million as a result of the realization of pre-acquisition deferred tax assets associated with net operating loss carryforwards.

In connection with the establishment of the Roche alliance described in Note 11, the Company also executed a Share Purchase Agreement (the Alnylam Europe Purchase Agreement) with Alnylam Europe and Roche Beteiligungs GmbH, an affiliate of Roche Basel and Roche Finance (Roche Germany). Under the terms of the Alnylam Europe Purchase Agreement, which became effective in August 2007, the Company created a new, wholly-owned German limited liability company (Roche Kulmbach), into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from the Company all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million.

4. PROPERTY AND EQUIPMENT

Property and equipment consist of the following at December 31, 2007 and 2006, in thousands:

	Useful Life	December 31, 2007	2006

Laboratory equipment	5 years	$ 7,963	$ 9,903
Computer equipment and software	3 years	2,080	2,065
Furniture and fixtures	5 years	1,271	914
Leasehold improvements	*	9,172	7,056
Construction in progress		3,702	1,127
		24,188	21,065
Less: accumulated depreciation and amortization		(10,378)	(8,892)
		$ 13,810	$ 12,173

* shorter of asset life or lease term

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Depreciation expense was $3.8 million, $3.4 million and $2.6 million for the years ended December 31, 2007, 2006 and 2005, respectively.

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. The agreement allowed the Company to draw down amounts under the line of credit through December 31, 2007 upon adherence to certain conditions. 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 and 2007, the Company borrowed an aggregate of $5.2 million from Oxford pursuant to the agreement at fixed rates ranging from 10.0% to 10.4%. As of December 31, 2007, there was $3.3 million outstanding under this line of credit with Oxford.

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 fixed rates of 9.25% to 10.25%, and matures 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 principal and interest due, 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, 2007, there was $3.5 million outstanding under this line of credit with Lighthouse.

At December 31, 2007, future cash payments under the notes payable to Lighthouse and Oxford, including interest, are as follows, in thousands:

Year Ending December 31,	
2008	$ 4,268
2009	3,513
2010	480
2011	79
Total through 2011	8,340
Less: portion representing interest	1,582
Principal	6,758
Less: current portion	3,795

Long-term notes payable	$ 2,963

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, 2007 and 2006.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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, 2007 and 2006.

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 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, 2007, the Company was committed to make the following fixed license payments under existing license agreements, in thousands:

Year Ending December 31,	
2008	$ 516
2009	316
2010	351
2011	356
2012	406
Thereafter	4,687
Total	$ 6,632

In January 2007, Tekmira Pharmaceuticals Corporation (Tekmira), formerly Inex Pharmaceuticals, Inc., granted the Company an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics. In connection with Tekmira s license grant, the Company agreed to make available to Tekmira a $5.0 million loan for capital equipment expenditures related to manufacturing services performed by Tekmira beginning in 2008.

Operating Leases

The Company leases office and laboratory space in Cambridge, Massachusetts under non-cancelable operating lease agreements. The Company also had a lease in Kulmbach, Germany through August 2007. Total rent expense, including operating expenses, under these operating leases was $4.7 million, $2.6 million and $1.9 million, for the years ended December 31, 2007, 2006 and 2005, respectively.

In 2003, the Company entered into an operating lease to rent laboratory and office space in Cambridge, Massachusetts through September 2011. In March 2006, the Company amended its lease agreement to rent additional space in this same facility. The Company has the option to extend the lease for two successive five-year extensions.

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.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In October 2007, the Company subleased from Archemix Corp. (Archemix) 22,456 rentable square feet of office and laboratory space in the same location as the Company s corporate headquarters (the Sublease). The initial term of the Sublease will expire in September 2011, and the Company holds an option to extend the lease for an additional 48-month period, subject to certain termination rights granted to each of the Company and Archemix. In addition and in connection with the execution of the Sublease, the Company issued a letter of credit in favor of Archemix in the amount of $0.8 million. The underlying cash securing this letter of credit has been classified as long-term restricted cash in the accompanying consolidated balance sheets.

In connection with the Roche alliance, Roche purchased the assets of Alnylam Europe, which included the lease for the facility in Kulmbach, Germany.

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

Year Ending December 31,	
2008	$ 3,296
2009	3,296
2010	3,296
2011	2,472
Total	$ 12,360

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, 2007.

7. STOCKHOLDERS EQUITY

Preferred Stock

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 Company s Board of Directors upon its issuance. At December 31, 2007, there were no shares of preferred stock outstanding.

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

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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.

Public Offerings of Common Stock

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 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 the SEC 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 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 a registration statement filed with the SEC in November 2006.

8. STOCK INCENTIVE PLANS

Stock Plans

As of December 31, 2007, the Company s 2004 Stock Incentive Plan (the 2004 Plan) provides for the granting of restricted stock awards and stock options to purchase up to 8,257,146 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 originally included 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. In September 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 Directors, or such other amount as the Board of Directors deems appropriate, 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

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

purchase 15,000 shares of common stock. 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. Stock options granted by the Company to non-employee directors (i) upon their appointment to the Board of Directors 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.

At December 31, 2007, an aggregate of 5,898,878 shares of common stock were reserved for issuance under the Company s stock plans, including outstanding options to purchase 5,304,021 shares of common stock and 594,857 shares were available for future grant under the 2004 Plan. Each option shall expire within 10 years of issuance. Stock options granted by the Company generally vest as to 25% 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.

Stock-Based Compensation

In December 2004, the FASB issued 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 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.

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS 123R using the modified-prospective-transition method. 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 comprised 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. Under the provisions of SFAS 123R, the Company recorded $11.9 million and $6.1 million of stock-based compensation for the years ended December 31, 2007 and 2006, respectively, related to employee stock options and the 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 (FIN 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 $2.6 million, $2.2 million and $2.1 million of non-employee stock-based compensation expense for the years ended December 31, 2007, 2006 and 2005, respectively.

The Company granted the members of the Regulus Therapeutics scientific advisory board and board of directors options to purchase 46,000 and 22,500 shares of common stock, respectively, during 2007. In addition, the Company granted options to purchase 60,000 shares of common stock to the chief executive officer of Regulus Therapeutics during 2007. In addition to the total stock-based compensation expense stated above, the Company recorded $0.2 million of stock-based compensation expense related to these option grants in equity in loss of joint venture in its consolidated statements of operations using the method prescribed by FIN 28.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In connection with the closing of the sale of Alnylam Europe to Roche, the Company granted 95,109 shares of restricted stock of the Company to certain employees of Roche Kulmbach. In connection with the closing, the Company also accelerated 177,233 of unvested outstanding stock options of certain Alnylam Europe employees. The Company recorded $3.8 million of stock-based compensation expense during 2007 related to the restricted share grants and the stock option modifications.

Total compensation cost for all stock-based payment arrangements for the years ended December 31, 2007, 2006 and 2005 was $14.7 million, $8.3 million and $4.6 million, respectively. No amounts relating to the stock-based compensation have been capitalized.

The following table illustrates the effect on net loss and net loss per common 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 year ended December 31, 2005, in thousands, except per share amounts. For purposes of this pro-forma 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
Net loss, as reported	$ (42,914)
Add: Total stock-based compensation expense determined under the intrinsic value method for all employee awards	2,484
Deduct: Total stock-based compensation expense determined under the fair value method for all employee awards	(6,285)
Pro forma net loss	$ (46,715)
Basic and diluted net loss per common share, as reported	$ (1.96)
Basic and diluted net loss per common share, pro forma	$ (2.13)

Valuation Assumptions for Stock Plans and Employee Stock Purchase Plan

The fair value of stock options at date of grant, based on the following assumptions, was estimated using the Black-Scholes option-pricing model. During the nine months ended September 30, 2007, the Company s expected stock-price volatility assumption was 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 the Company s publicly traded stock. During the three months ended December 31, 2007, the Company s expected stock-price volatility assumption is based on a combination of implied volatilities of its publicly traded stock option prices as well as the historical volatility of the Company s publicly traded stock. During the nine months ended September 30, 2007, 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). During the three months ended December 31, 2007, in anticipation of the sunset of the simplified method provided for in SAB 107, the expected life assumption is based on the equal weighting of the Company s historical data and the historical data of the Company s pharmaceutical and biotechnology peers. 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. 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.

	2007	2006	2005
Risk-free interest rate	4.4-4.7%	4.70%	3.97%
Expected dividend yield			
Expected option life	6.0-6.1 years	6.1 years	5 years
Expected volatility	64-67%	67%	68%

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

At December 31, 2007, there remained $36.8 million of unearned compensation expense related to unvested employee stock options to be recognized as expense over a weighted-average period of approximately 1.6 years.

Stock Option Activity

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

	Number of Options	Weighted Average Exercise Price
Outstanding, December 31, 2006	4,649,959	$ 10.03
Granted	2,071,819	$ 27.08
Exercised	(1,247,808)	$ 7.39
Cancelled	(169,949)	$ 14.05
Outstanding, December 31, 2007	5,304,021	$ 17.18
Exercisable at December 31, 2005	1,550,510	$ 2.54
Exercisable at December 31, 2006	1,953,502	$ 4.44
Exercisable at December 31, 2007	1,913,468	$ 7.49

The weighted average remaining contractual life for options outstanding and exercisable at December 31, 2007 was 8.4 years and 7.0 years, respectively.

The aggregate intrinsic value of outstanding options at December 31, 2007 was $66.2 million, of which $41.3 million related to exercisable options. The intrinsic value of options exercised was $24.6 million, $7.6 million and $1.6 million for the years ended December 31, 2007, 2006 and 2005, respectively. The weighted average fair value of stock options granted as part of the 2004 Plan was $16.58, $12.95 and $7.21 for the years ended December 31, 2007, 2006 and 2005, respectively.

Restricted Stock Awards

The following table summarizes the activity of the Company s restricted stock awards:

	Number of Options	Weighted Average Grant Date Fair Value
Unvested at December 31, 2006		$

Granted	95,109	$	25.98
Vested	(38,060)	$	25.98
Forfeited		$	
Unvested at December 31, 2007	57,049	$	25.98

The total fair value of restricted stock awards that vested during the year ended December 31, 2007 was $1.0 million.

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 as adopted, the Company made one offering each year, at the end of which employees could purchase shares of common stock through payroll deductions made over the term of the offering. Initially, the annual offering period began on the 1st day of November each year and

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

ended on the 31st day of October the following year. In June 2007, the Compensation Committee of the Board of Directors amended the offering period of the 2004 Purchase Plan to provide that each offering period will be for a period of six months, beginning with the offering period commencing on November 1, 2007. 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 Company issued 29,723, 40,530 and 51,792 shares during 2007, 2006 and 2005, respectively, and as of December 31, 2007, 193,744 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 was $10.61, $8.16 and $4.18 for the years ended December 31, 2007, 2006 and 2005, respectively. 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, 2007 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 (liability) asset as of December 31, 2007, 2006 and 2005 are as follows, in thousands:

	2007	2006	2005
Deferred tax assets:			
Net operating loss carryforwards	$ 49,910	$ 21,656	$ 10,248
Research and development credits	3,582	3,456	2,153
Foreign tax credits	3,072		
Capitalized research and development and start-up costs	12,750	13,674	15,931
Deferred revenue	2,745	7,211	8,390
Deferred compensation	3,237	1,731	
Intangible assets	1,540	3,100	1,529
Other	3,674	1,706	843
Total deferred tax assets	80,510	52,534	39,094
Deferred tax liabilities:			
Intangible assets	(365)	(1,004)	(1,104)
Deferred tax asset valuation allowance	(80,510)	(50,863)	(37,690)
Net deferred tax (liability) asset	$ (365)	$ 667	$ 300

Income tax expense for the years ended December 31, 2007 and 2006 was as follows, in thousands:

	2007	2006
Foreign:		
Current	$ 3,356	$
Deferred	1,889	
Provision for income taxes	$ 5,245	$

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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, 2007, 2006 and 2005:

	2007	2006	2005
At U.S. federal statutory rate	34.0%	34.0%	34.0%
State taxes, net of federal effect	5.8	5.3	5.6
Foreign tax credit	3.8		
Foreign dividends	(6.6)		
Other permanent items	(0.8)	(5.4)	(3.4)
Deemed gain on Roche Germany transaction	(6.3)		
Research credits	0.4	4.2	2.5
Valuation allowance	(36.7)	(38.0)	(38.4)
Effective income tax rate	(6.4)%	0.1%	0.3%

As required by SFAS No. 109, *Accounting for Income Taxes,* 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. Accordingly, the deferred tax assets have been fully reserved at December 31, 2007. Management reevaluates the positive and negative evidence on a quarterly basis. The valuation allowance increased by $29.6 million, $13.2 million and $16.6 million for the years ended December 31, 2007, 2006 and 2005, respectively, primarily due to net operating loss carryforwards which the Company has recorded a full valuation allowance against.

At December 31, 2007, the Company had federal and state net operating loss carryforwards of $132.7 million and $145.5 million available, respectively, to reduce future taxable income, that will expire at various dates beginning in 2008 through 2027. At December 31, 2007, federal and state research and development and other credit carryforwards were $2.3 million and $1.9 million, respectively, available to reduce future tax liabilities, that expire at various dates beginning in 2018 through 2027. At December 31, 2007, foreign tax credits were $3.1 million, available to reduce future tax liabilities, that expire in 2017. 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.

The net operating loss carryforward includes approximately $10.7 million of deductions related to the exercise of stock options subsequent to the adoption of SFAS 123(R). This amount represents an excess tax benefit as defined under SFAS 123(R) and has not been included in the gross deferred tax asset reflected for net operating losses.

In June 2006, the FASB issued Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement No. 109* (FIN 48). This statement clarifies the criteria that an individual tax position must satisfy for some or all of the benefits of that position to be recognized in a company s financial statements. The Company

adopted FIN 48 on January 1, 2007. The implementation of FIN 48 did not have a material impact on the Company s consolidated financial statements, results of operations or cash flows. At the adoption date of January 1, 2007, and also at December 31, 2007, the Company had no unrecognized tax benefits.

The tax years 2002 through 2006 remain open to examination by major taxing jurisdictions to which the Company is subject, which are primarily in the United States, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service or state tax authorities if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

other jurisdictions for any tax years. The Company recognizes both accrued interest and penalties related to unrecognized benefits in income tax expense. The Company has not recorded any interest and penalties on any unrecognized tax benefits since its inception.

10. 401(K) SAVINGS PLAN

The Company sponsors a savings plan for its employees in the United States, 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). Participants may contribute up to 60% of their annual base salary to the 401(k) 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 12,706 and 7,866 shares of common stock during the years ended December 31, 2007 and 2006, respectively, in connection with matching contributions under the 401(k) Plan.

11. SIGNIFICANT AGREEMENTS

Roche Alliance

In July 2007, the Company and, for limited purposes, Alnylam Europe, entered into a License and Collaboration Agreement (the LCA) with Roche. Under the LCA, which became effective in August 2007, the Company granted Roche a non-exclusive license to the Company s intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to the Company s existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include other therapeutic areas upon payment of an additional specified amount.

In consideration for the rights granted to Roche under the LCA, Roche paid the Company $273.5 million in upfront cash payments. Roche is also required to make payments to the Company upon achievement of specified development and sales milestones set forth in the LCA and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees.

Under the LCA, the Company and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets (Discovery Collaboration), subject to the Company s existing contractual obligations to third parties. The collaboration between Roche and the Company will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. In exchange for the Company s contributions to the collaboration, Roche will be required to make additional milestone and royalty payments.

The term of the LCA generally ends upon the later of the expiration of the last-to-expire patent covering a licensed product and ten years from first the commercial sale of a licensed product. After the first anniversary of the effective date, Roche may terminate the LCA, on a licensed product-by-licensed product, licensed patent-by-licensed patent, and country-by-country basis, upon 180 days prior written notice to the Company, but is required to continue to make

milestone and royalty payments to the Company if any royalties were payable on net sales of a terminated licensed product during the previous twelve months. The LCA may also be terminated by either party in the event the other party fails to cure a material breach under the LCA.

In July 2007, the Company executed a Common Stock Purchase Agreement (the Common Stock Purchase Agreement) with Roche Finance Ltd, an affiliate of Roche (Roche Finance). Under the terms of the Common Stock Purchase Agreement, on August 9, 2007, Roche Finance purchased 1,975,000 shares of the Company s common stock at $21.50 per share, for an aggregate purchase price of $42.5 million. The Company recorded this issuance using the closing price of the Company s common stock on August 9, 2007, the date the shares were issued

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

to Roche. Based on the closing price of $25.98, the fair value of the shares issued was $51.3 million, which was $8.8 million in excess of the proceeds received from Roche for the issuance of the Company s common stock. As a result, the Company allocated $8.8 million of the up-front payment from the LCA to the common stock issuance.

Under the terms of the common stock purchase agreement, in the event the Company proposed to sell or issue any of its equity securities, subject to specified exceptions, it agreed to grant to Roche Finance the right to acquire, at fair value, additional securities, such that Roche Finance would be able to maintain its ownership percentage in the Company.

In connection with the execution of the LCA and the Common Stock Purchase Agreement, the Company also executed the Alnylam Europe Purchase Agreement with Alnylam Europe and Roche Germany. Under the terms of the Alnylam Europe Purchase Agreement, which became effective in August 2007, the Company created Roche Kulmbach, into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from the Company all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million. The Alnylam Europe Purchase Agreement also includes transition services to be performed by Roche Kulmbach employees at various levels through August 2008.

The Company reimburses Roche for these services at an agreed-upon rate. The Company recorded $4.2 million for these services as contra revenue (a reduction of revenues) in the period incurred. In addition, in connection with the closing of the Alnylam Europe Purchase Agreement, the Company granted restricted stock of the Company to certain employees of Roche Kulmbach. In connection with the closing, the Company also accelerated the unvested portion of the outstanding stock options of certain Alnylam Europe employees. The Company recorded $3.8 million of stock-based compensation expense during 2007 related to the restricted share grants and the stock option modifications.

In summary, the Company received upfront payments totaling $331.0 million under the Roche alliance, which include an upfront payment under the LCA of $273.5 million, $42.5 million under the Common Stock Purchase Agreement and $15.0 million for the Roche Kulmbach shares under the Alnylam Europe Purchase Agreement.

The Company recorded $278.2 million as deferred revenue in connection with the Roche alliance. This amount represents the aggregate proceeds received from Roche of $331.0 million, net of the amount allocated to the common stock issuance of $51.3 million, and the net book value of Alnylam Europe of $1.5 million.

The Company has determined that the deliverables under the Roche alliance include the license, the Alnylam Europe assets and employees, the steering committees (Joint Steering Committee and Future Technology Committee) and the services that Alnylam will be obligated to perform under the Discovery Collaboration. The Company has concluded that, pursuant to paragraph 9 of EITF 00-21, the license and assets of Alnylam Europe are not separable from the undelivered services, i.e., the steering committees and Discovery Collaboration services, and, accordingly the license and the services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Roche alliance, the steering committee services and the Discovery Collaboration services are the final deliverables and all such services will end, contractually, five years from the effective date of the LCA. The Company is recognizing the Roche-related revenue on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to complete its service obligations under the LCA. The Company will continue to reassess

whether it can reasonably estimate the level of effort required to fulfill its obligations under the Roche alliance. In particular, when the Discovery Collaboration commences, the Company may be able to make such an estimate. When, and if, the Company can make a reasonable estimate of its remaining efforts under the collaboration, the Company would modify its method of recognition and utilize a proportional performance method. As future milestones are achieved, and to the extent they are within the five year term, the amounts will be recognized as revenue prospectively over the remaining period of performance.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In connection with the LCA and the Common Stock Purchase Agreement, the Company incurred $27.5 million of license fees payable to the Company s licensors, primarily Isis, during 2007, in accordance with the applicable license agreements with those parties. These fees were charged to research and development expense.

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).

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 $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 13% of the Company s outstanding common stock at December 31, 2007.

The Company 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.

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 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 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.

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

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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.

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 significant funding from Novartis for its efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits. During 2007, the Company and Novartis agreed to focus on additional pre-clinical research prior to advancing this program into development.

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 is focused on the discovery and development of therapeutics based on RNAi for the potential treatment of progressive multifocal leukoencephalopathy (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, upon the successful development and utilization of a product resulting from the collaboration, if any, Biogen Idec will be required to pay the Company milestone and royalty payments. The Company is recognizing revenue under the Biogen Idec collaboration on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to fulfill its obligations under this collaboration. The pace and scope of future development of this program is the responsibility of Biogen Idec.

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. The Company obtained the remaining 50% exclusive rights upon the acquisition of Ribopharma AG in

July 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

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

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.

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 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. 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 August 2007, as a result of certain payments received by the Company in connection with the Roche alliance, the Company made payments totaling $26.5 million 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 $3.7 million to Isis. These license fees were charged to research and development expenses in their respective periods.

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.

NIH Contract

In September 2006, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever viruses, including the Ebola virus, with NIAID. The federal contract could 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. 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. Revenue

under government cost reimbursement contracts is recognized as the Company performs the underlying research and development activities.

Department of Defense Contract

In August 2007, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus with DTRA. The federal contract could provide the Company

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus infection. Of the $38.6 million in funding, the government has committed to pay the Company up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract. Revenue under government cost reimbursement contracts is recognized as the Company performs the underlying research and development activities.

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 amended and restated the Research Collaboration and License Agreement, dated September 8, 2003, between the Company and Merck, as amended. In September 2007, the Company and Merck terminated the Amended License Agreement (the Termination Agreement). Pursuant to the Termination Agreement, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the Amended License Agreement ceased as of the date of the Termination Agreement, subject to certain specified exceptions. The Termination Agreement further provides that, subject to certain conditions, the Company and Merck will each retain sole ownership and rights in their own intellectual property. The Company has no remaining deliverables under the Amended License Agreement. The Company was recognizing the remaining deferred revenue of $3.5 million under the Amended License Agreement, related to upfront cash payments and additional license fee payments received from Merck, on a straight-line basis over the remaining period of expected performance of four years. As a result of the Termination Agreement, the Company recognized this remaining deferred revenue of $3.5 million.

Delivery Technology

The Company is working to extend its capabilities in developing technology to achieve efficacious and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, the Company has entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, the Company is also providing funding to support the advancement of these delivery technologies. The Company incurred $14.7 million in upfront license fees related to these agreements during the year ended December 31, 2007. In connection with one such agreement with Tekmira, the Company issued to Tekmira 361,990 shares of common stock in January 2007. These shares had a value of $7.9 million, which amount was expensed during the year ended December 31, 2007.

12. INVESTMENT IN JOINT VENTURE (REGULUS THERAPEUTICS LLC)

In September 2007, the Company entered into a joint venture with Isis to create a new Delaware limited liability company, Regulus Therapeutics LLC (Regulus Therapeutics), to focus on the discovery, development and commercialization of microRNA (miRNA) therapeutics, a potential new class of drugs to treat the pathways of human disease. The Company and Isis own 49% and 51%, respectively, of Regulus Therapeutics.

Under the terms of the Limited Liability Company Agreement among the Company, Isis and Regulus Therapeutics (the LLC Agreement), Regulus Therapeutics will be operated as an independent company and governed by a managing board comprised of an equal number of directors appointed by each of the Company and Isis. In consideration for the Company s and Isis initial interests in Regulus Therapeutics, each party agreed to grant Regulus

Therapeutics exclusive licenses to its intellectual property for certain miRNA therapeutic applications as well as certain patents in the miRNA field. In addition, the Company agreed to make an initial cash contribution to Regulus Therapeutics of $10.0 million, resulting in the Company and Isis making approximately equal aggregate initial capital contributions to Regulus Therapeutics.

In connection with the execution of the LLC Agreement, the Company, Isis and Regulus Therapeutics entered into a license and collaboration agreement (the Regulus Therapeutics Collaboration Agreement) to pursue the

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

discovery, development and commercialization of therapeutic products directed to miRNAs. Under the terms of the Regulus Therapeutics Collaboration Agreement, the Company and Isis each assigned to Regulus Therapeutics specified patents and contracts covering miRNA therapeutic-specific technology. In addition, each of the Company and Isis granted to Regulus Therapeutics an exclusive, worldwide license under its rights to other miRNA therapeutic-related patents and know-how to develop and commercialize therapeutic products containing compounds that are designed to interfere with or inhibit a particular miRNA, subject to the Company s and Isis existing contractual obligations to third parties. Regulus Therapeutics was also granted the right to request a license from the Company and Isis to develop and commercialize therapeutic products directed to other miRNA compounds, which license is subject to the Company s and Isis approval and to each such party s existing contractual obligations to third parties. Regulus Therapeutics also granted to the Company and Isis an exclusive license to technology developed or acquired by Regulus Therapeutics for use solely within the Company s and Isis respective fields (as defined in the Regulus Therapeutics Collaboration Agreement), but specifically excluding the right to develop, manufacture or commercialize the therapeutic products for which the Company and Isis granted rights to Regulus Therapeutics.

The Regulus Therapeutics Collaboration Agreement ends if, prior to first commercial sale of any product, all development activities cease under the collaboration. The Regulus Therapeutics Collaboration Agreement otherwise expires, on a product-by-product and country-by-country basis, upon the later of expiration of marketing exclusivity for such product or a specified number of years from first commercial sale. If Regulus Therapeutics, the Company or Isis commits an uncured material breach of the Regulus Therapeutics Collaboration Agreement, the Regulus Therapeutics Collaboration Agreement may be terminated with respect to the breaching party or a buy-out may be initiated under the LLC Agreement, depending on the nature of the breach.

In connection with the execution of the LLC Agreement and Regulus Therapeutics Collaboration Agreement, the Company also executed a Services Agreement (the Services Agreement) with Isis and Regulus Therapeutics. Under the terms of the Services Agreement, the Company and Isis agreed to provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services, as set forth in an operating plan mutually agreed upon by the Company and Isis. The Services Agreement provides that the Company and Isis generally will be paid by Regulus Therapeutics for services. Subject to certain exceptions, the Services Agreement will terminate upon the termination or expiration of the LLC Agreement or the Regulus Therapeutics Collaboration Agreement.

The Company has concluded that Regulus Therapeutics qualifies as a variable interest entity under FASB Interpretation No. 46R, *Consolidation of Variable Interest Entities an interpretation of Accounting Research Bulletin No. 51* (FIN 46R). The LLC Agreement contains transfer restrictions on each of Isis and the Company s LLC interests and, as a result, Isis and the Company are considered related parties under paragraph 16(d)(1) of FIN 46R. The Company has assessed which entity would be considered the primary beneficiary under FIN 46R and has concluded that Isis is the primary beneficiary and, accordingly, the Company has not consolidated Regulus Therapeutics. The Company accounts for its investment in Regulus Therapeutics using the equity method of accounting. The Company will recognize the first $10.0 million of losses of Regulus Therapeutics as equity in loss of joint venture in its consolidated statement of operations because the Company is responsible for funding those losses through its initial $10.0 million cash contribution. Thereafter, the Company will recognize 49% of the losses of Regulus Therapeutics.

The Company accounted for its interest in Regulus Therapeutics using the equity method of accounting. Under this method, the reimbursement of expenses to the Company is recorded as a reduction to research and development expenses. At December 31, 2007, the Company s investment in the joint venture was $9.1 million, which is recorded as an investment in joint venture (Regulus Therapeutics LLC) in the consolidated balance sheets under the equity method.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

13. 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, 2007	June 30, 2007	September 30, 2007	December 31, 2007
	(In thousands, except per share data)			
Revenues	$ 7,217	$ 9,133	$ 16,315	$ 18,232
Operating expenses	31,211	24,086	67,653	21,124
Net (loss) income	(21,645)	(12,691)	(52,792)	1,662
Net (loss) income per common share basic and diluted	$ (0.58)	$ (0.34)	$ (1.35)	$ 0.04
Weighted average common shares basic	37,376	37,534	39,025	40,710
Weighted average common shares diluted	37,376	37,534	39,025	42,763

	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 common shares basic and diluted	30,028	32,010	32,122	33,048

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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, 2007. 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, 2007, 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 report on the effectiveness of our internal control over financial reporting 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, 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9A(T). CONTROLS AND PROCEDURES

Not applicable.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We will file with the SEC 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, 2007. The information required by this item is incorporated herein by reference to the information contained under the sections captioned Proposal One Election of Class I 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

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Committee Interlocks and Insider Participation , Employment Arrangements and Compensation Committee Report of the Proxy Statement.

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 ACCOUNTING 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

All 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 7, 2008.

ALNYLAM PHARMACEUTICALS, INC.

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

John M. Maraganore, Ph.D.
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 7, 2008.

Name	Title
/s/ John M. Maraganore, Ph.D. John M. Maraganore, Ph.D.	Director 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/ John K. Clarke John K. Clarke	Director
/s/ Victor J. Dzau, M.D. Victor J. Dzau, M.D.	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
Edward M. Scolnick, M.D.	Director
/s/ Phillip A. Sharp, Ph.D.	Director

Phillip A. Sharp, Ph.D.	
/s/ Kevin P. Starr	Director
Kevin P. Starr	
/s/ James L. Vincent	Director
James L. Vincent	

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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 filed on August 11, 2005 (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 (filed 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
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 filed on August 11, 2005 (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, as amended
10.9	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)
10.10	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)
10.11	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)

10.12* 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)

10.13* 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)

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Exhibit No.	Exhibit
10.14	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)
10.15	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 filed on August 11, 2005 (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference)
10.16	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)
10.17	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)
10.18	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)
10.19	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)
10.20	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)
10.21	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)
10.22	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)
10.23	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 filed on August 11, 2005 (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference)
10.24	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)
10.25	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)

10.26	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)

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Exhibit No.	Exhibit
10.27	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)
10.28	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 17, 2006 (File No. 000-50743) and incorporated herein by reference)
10.29	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 Current Report on Form 8-K filed on April 6, 2006 (File No. 000-50743) and incorporated herein by reference)
10.30	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 filed on March 16, 2006 (File No. 000-50743) for the annual period ended December 31, 2005 and incorporated herein by reference)
10.31	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 10.3 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)
10.32	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)
10.33	License and Collaboration Agreement, entered into as of July 8, 2007, by and among F. Hoffmann-La Roche, Ltd, Hoffman-La Roche Inc., the Registrant and, for limited purposes, Alnylam Europe AG (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.34	Common Stock Purchase Agreement dated as of July 8, 2007 between the Registrant and Roche Finance Ltd (filed as Exhibit 10.2 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.35	Share Purchase Agreement, dated as of July 8, 2007, among Alnylam Europe AG, the Registrant and Roche Pharmaceuticals GmbH (filed as Exhibit 10.3 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.36	Amended and Restated Collaboration Agreement, entered into as of July 27, 2007, by and between the Registrant and Medtronic, Inc. (filed as Exhibit 10.4 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.37	License and Collaboration Agreement, entered into as of September 6, 2007, by and among the Registrant, Isis Pharmaceuticals, Inc. and Regulus Therapeutics LLC (filed as Exhibit 10.5 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.38	

	Limited Liability Company Agreement of Regulus Therapeutics LLC, dated as of September 6, 2007 (filed as Exhibit 10.6 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.39	Termination Agreement, dated as of September 18, 2007, by and between Merck & Co., Inc. and the Registrant (filed as Exhibit 10.7 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)

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Exhibit No.	Exhibit
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.