ALNYLAM PHARMACEUTICALS, INC.
Form 10-K
February 18, 2011

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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, 2010

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

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was

required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). 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. (Check one):

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o	Smaller reporting company o
		(Do not check if a smaller reporting company)	

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

The aggregate market value of the registrant s common stock, $0.01 par value per share (Common Stock), held by non-affiliates of the registrant, based on the last sale price of the Common Stock at the close of business on June 30, 2010, was $446,579,243. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and holder of ten percent or more of the outstanding Common Stock have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

At January 31, 2011, the registrant had 42,343,623 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 2011 annual meeting of stockholders, which the registrant intends to file 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, 2010, are incorporated by reference into Part II, Item 5 and Part III of this Form 10-K.

ALNYLAM PHARMACEUTICALS, INC.
ANNUAL REPORT ON FORM 10-K
For the Year Ended December 31, 2010

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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, may, could, intend plan, target, goal and 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 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.

Our core product strategy, which we refer to as Alnylam 5x15, is focused on the development and commercialization of innovative RNAi therapeutics for the treatment of genetically defined diseases. Under our core product strategy, we expect to progress five RNAi therapeutic programs into advanced stages of clinical development by the end of 2015. As part of this strategy, our goal is to develop product candidates with the following shared characteristics: a genetically defined target and disease; the potential to have a significant impact in high unmet need patient populations; the ability to leverage our existing RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of a new drug application, or NDA, with a focused patient database and possible accelerated paths for commercialization. We intend to commercialize products arising from this core product strategy on our own in the United States and potentially certain other countries, and we intend to enter into alliances to develop and commercialize any such products in other global territories. We are currently advancing three core programs in clinical or pre-clinical development: ALN-TTR for the treatment of transthyretin-mediated amyloidosis, or ATTR; ALN-PCS for the treatment of severe hypercholesterolemia; and ALN-HPN for the treatment of refractory anemia. As part of our core product strategy, we also expect to designate and start pre-clinical development of two additional RNAi therapeutic candidates targeting genetically defined diseases by the end of 2011.

While focusing our efforts on our core product strategy, we also intend to continue to advance additional development programs through existing or future alliances. We have three partner-based programs in clinical or pre-clinical development, including ALN-RSV01 for the treatment of respiratory syncytial virus, or RSV, infection, ALN-VSP for the treatment of liver cancers and ALN-HTT for the treatment of Huntington s disease, or HD.

Our most advanced core product development program, ALN-TTR, targets the transthyretin, or TTR, gene, for the treatment of ATTR, a hereditary, systemic disease associated with severe morbidity and mortality caused by a mutation in the TTR gene that leads to the extracellular deposition of amyloid fibrils. In July 2010, we initiated a Phase I clinical trial for ALN-TTR01, a systemically delivered RNAi therapeutic. ALN-TTR01 employs a first-

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generation lipid nanoparticle, or LNP, formulation. The Phase I clinical trial for ALN-TTR01 is being conducted in Portugal, Sweden, the United Kingdom and France, and is a randomized, blinded, placebo-controlled dose escalation study designed to enroll approximately 28 ATTR patients. The primary objective is to evaluate the safety and tolerability of a single dose of intravenous ALN-TTR01. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-TTR01 and assessment of pharmacodynamic activity based on measurements of circulating TTR serum levels. In January 2011, The Committee for Orphan Medicinal Products, or COMP, of the European Medicines Agency, or EMA, adopted a positive opinion for ALN-TTR01 designation as an orphan medicinal product for the treatment of familial amyloidotic polyneuropathy, or FAP, one of the predominant forms of ATTR. A positive opinion by the COMP precedes official designation of ALN-TTR01 as an orphan drug by the European Commission, or EC. In parallel with the development of ALN-TTR01, we are also advancing ALN-TTR02 utilizing a second-generation LNP formulation.

Our second core product development program is ALN-PCS. We are developing ALN-PCS, a systemically delivered RNAi therapeutic, for the treatment of severe hypercholesterolemia. ALN-PCS targets a gene called proprotein convertase subtilisin/kexin type 9, or PCSK9, which is involved in the regulation of LDL receptor, or LDLR, levels on hepatocytes and the metabolism of LDL cholesterol, or LDL-c, which is also commonly referred to as bad cholesterol. Pre-clinical studies with ALN-PCS demonstrated a greater than 50% reduction in levels of LDL-c, which result is rapidly achieved and durable after a single dose. ALN-PCS employs a second-generation LNP formulation.

We recently designated ALN-HPN as our third core product development program. ALN-HPN is a systemically delivered RNAi therapeutic targeting hepcidin, a genetically validated gene in iron homeostasis, for the treatment of refractory anemia. Anemia of chronic disease, or ACD, occurs in patients with end-stage renal disease, cancer and chronic inflammatory disease. ACD patients who are refractory to erythropoiesis-stimulating agents and intravenous iron define a condition of refractory anemia for which there is substantial unmet need. Pre-clinical studies with a small interfering RNA, or siRNA, targeting hepcidin demonstrated the ability to silence the gene and increase serum iron levels. ALN-HPN also employs a second-generation LNP formulation.

As noted above, while focusing our efforts on our core product strategy, we also intend to continue to advance additional partner-based development programs, including ALN-RSV, ALN-VSP and ALN-HTT, through existing or future alliances.

In February 2010, we initiated a multi-center, global, randomized, double-blind, placebo-controlled Phase IIb clinical trial to evaluate the clinical efficacy as well as safety of aerosolized ALN-RSV01 in adult lung transplant patients naturally infected with RSV. This trial is ongoing and is expected to enroll up to 76 adult lung transplant patients who will be randomized in a one-to-one drug to placebo ratio. The primary endpoint is a reduction in the incidence of new or progressive bronchiolitis obliterans syndrome, or BOS, a potentially life-threatening complication in lung transplant patients. We have formed collaborations with Cubist Pharmaceuticals, Inc., or Cubist, and Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko Kirin, for the development and commercialization of RNAi products for the treatment of RSV. Under our agreement with Cubist, we are developing ALN-RSV01 for adult transplant patients at our sole discretion and expense and Cubist has the right to opt into collaborating with us on ALN-RSV01 in the future. In December 2010, we and Cubist jointly made a portfolio decision to put the development of ALN-RSV02, a second-generation compound for the pediatric population, on hold.

In March 2009, we initiated a Phase I clinical trial for ALN-VSP, which was our first systemically delivered RNAi therapeutic to enter clinical development. ALN-VSP is comprised of two siRNAs, one targeting vascular endothelial growth factor, or VEGF, and the other targeting kinesin spindle protein, or KSP, and employs a first-generation LNP formulation. We are developing ALN-VSP for the treatment of liver cancers, including both primary and secondary liver cancers. This Phase I clinical trial is a multi-center, open label, dose escalation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous ALN-VSP in up to approximately 55 patients

with advanced solid tumors with liver involvement. During 2010 and early 2011, we reported preliminary results from this Phase I clinical trial demonstrating that ALN-VSP was generally well tolerated. Results from pharmacodynamic measurements provide preliminary evidence of biological activity, and biopsy data demonstrate both tissue levels of ALN-VSP and also human proof-of-concept for an RNAi mechanism of action. We intend to partner our ALN-VSP program prior to initiating a Phase II clinical trial.

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A third partner-based development program is ALN-HTT, an RNAi therapeutic candidate targeting the huntingtin gene, for the treatment of HD, which we are developing in collaboration with Medtronic, Inc., or Medtronic. In November 2010, we and Medtronic entered into an agreement with CHDI Foundation, Inc., or CHDI, under which CHDI has agreed to initially fund approximately 50% of the costs of this program up to the point at which an investigational new drug application, or IND, can be filed with the United States Food and Drug Administration, or FDA, or a comparable foreign regulatory filing can be made.

We also continue to work internally and with third-party collaborators to develop new technologies to deliver our RNAi therapeutics both directly to specific sites of disease, and systemically by intravenous or subcutaneous administration. We have numerous RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options.

We believe that the strength of our intellectual property portfolio relating to the development and commercialization of siRNAs as therapeutics provides us a leading position with respect to this therapeutic modality. This includes ownership of, or exclusive rights to, issued patents and pending patent applications claiming fundamental features of siRNAs and RNAi therapeutics as well as those claiming crucial chemical modifications and promising delivery technologies. We believe that no other company possesses a portfolio of such broad and exclusive rights to the patents and patent applications required for the commercialization of RNAi therapeutics. Given the importance of our intellectual property portfolio to our business operations, we intend to vigorously enforce our rights and defend against challenges that have arisen or may arise in this area.

In addition, our expertise in RNAi therapeutics and broad intellectual property estate have allowed us to form alliances with leading companies, including Isis Pharmaceuticals, Inc., or Isis, Medtronic, Novartis Pharma AG, or Novartis, Biogen Idec Inc., or Biogen Idec, F. Hoffmann-La Roche Ltd, or Roche, Takeda Pharmaceutical Company Limited, or Takeda, Kyowa Hakko Kirin and Cubist. 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. We have established collaborations with and, in some instances, received funding from major medical and disease associations, including CHDI. Finally, to further enable the field and monetize our intellectual property rights, we also grant licenses to biotechnology companies for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest under our InterfeRx™ program, and to research companies that commercialize RNAi reagents or services under our research product licenses.

We also seek to form or advance new ventures and opportunities in areas outside our primary focus on RNAi therapeutics. For example, during 2009 and 2010, we presented data regarding the application of RNAi technology to improve the manufacturing processes for biologics, including recombinant proteins and monoclonal antibodies. We are advancing these applications of RNAi technology in an internal effort referred to as Alnylam Biotherapeutics. We have formed, and intend to form additional, collaborations through this effort with third-party biopharmaceutical companies. Additionally, in 2007, we and Isis established Regulus Therapeutics Inc., or Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. Because microRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, microRNA therapeutics represent a possible new approach to target the pathways of human disease. Regulus has formed collaborations with GlaxoSmithKline, or GSK, and sanofi-aventis to advance its efforts. Given the broad applications for RNAi technology, in addition to our efforts on Alnylam Biotherapeutics and Regulus, we believe new ventures and opportunities will be available to us.

In September 2010, as a result of the planned completion of the fifth and final year of the research program under our collaboration and license agreement with Novartis and our reduced need for service-based collaboration resources, we undertook a corporate restructuring to focus our resources on our most promising programs and significantly reduce our cost structure. The corporate restructuring included a reduction of our overall workforce by approximately 25%.

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RNA Interference

RNAi is a natural biological pathway that occurs 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.

Opportunity for Therapeutics Based on RNAi

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 an siRNA. They showed that laboratory-synthesized siRNAs could be introduced into the cell and suppress production of specific target proteins by cleaving and degrading the messenger RNA, or mRNA, of the specific gene that encodes that specific protein. Because it is possible to design and synthesize siRNAs specific to any gene of interest, the entire human genome is accessible to RNAi, and we therefore believe that RNAi therapeutics have the potential to become a broad new class of drugs.

In May 2001, one of our scientific founders, Dr. Thomas Tuschl, published the first scientific paper demonstrating that siRNAs can be synthesized in the laboratory using chemical or biochemical methods and when introduced or delivered into mammalian cells, can silence the activity of a specific gene. Since the Tuschl publication and the seminal Tuschl II patent, which is licensed exclusively to us for therapeutic applications, the use of siRNAs has been broadly adopted by academic and industrial researchers for the fundamental study of the function of genes. This has resulted in a significant number of publications focused on the use of RNAi and has made the Tuschl publication one of the most cited papers in basic biologic research. Reflecting this, siRNAs are a growing segment of the market for research reagents and related products and services.

Beyond its use as a basic research tool, we believe that RNAi can form the basis of a broad new class of drugs for the treatment of disease. Drugs based on the RNAi mechanism could offer numerous opportunities and benefits, which may include:

Ability to target proteins that cannot be targeted effectively by existing drug classes. Over the last decade, the understanding of human disease has advanced enormously, and many proteins that play fundamental roles in human disease have been identified. Paradoxically, greater than 80% of these key proteins cannot be targeted effectively with existing drug approaches like small molecules or proteins such as monoclonal antibodies. These so called undruggable targets are potentially accessible to siRNAs as they are made by mRNAs that can be targeted with RNAi.

Ability to treat a broad range of diseases. The ability to make siRNAs that target virtually any gene to suppress the production of virtually any protein whose presence or activity causes disease suggests a broad potential for application in a wide range of diseases.

Inherently potent mechanism of action. We expect the inherent catalytic nature of the RNAi mechanism to allow for a high degree of potency and durability of effect for RNAi-based therapeutics, which we believe distinguishes RNAi from other approaches.

Simplified discovery of product candidates. In contrast to the often arduous and slow drug discovery process for proteins and small molecules, the identification of siRNA product candidates has been, and we expect will continue to be, much simpler, quicker and less costly because it involves relatively standard processes that are directed by the known gene target sequences and can be applied in a similar fashion to many successive product candidates.

We have reported on our advances in developing siRNAs as potential drugs in a large number of peer-reviewed publications and meetings, including publications by Alnylam scientists in the journals *Nature, Nature Medicine, Nature Biotechnology, Cell* and *Proceedings of the National Academy of Sciences,* or *PNAS.*

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Our Product Platform

Our product platform provides a capability for a systematic approach to identifying RNAi therapeutic product candidates through sequence selection, potency selection, stabilization by chemical modification, improvement of biodistribution and cellular uptake by various chemical conjugates and formulations. Key to the therapeutic application of siRNAs is the ability to successfully deliver siRNAs to target tissues and achieve cellular uptake of the siRNA into the inside of the cell where the RNAi machinery, called RNA-induced silencing complex, or RISC, is active. In some tissues, including the respiratory tract and central nervous system, the direct RNAi delivery approach, which employs the direct or local application of siRNAs, achieves cellular uptake and gene knockdown. For other tissues, such as the liver, systemic RNAi delivery has been employed, where tissue access comes via intravenous or subcutaneous injection of the siRNA into the bloodstream and where cellular uptake can be achieved by formulation with other biomaterials, such as LNPs, or the conjugation of the siRNA with other molecules, such as small chemical groups. siRNA delivery is a key focus for our internal research team and is also the focus of numerous current academic and corporate collaborations. We have demonstrated RNAi therapeutic activity towards multiple genes, in multiple organs and in multiple species, including humans, as recently demonstrated by biopsy results from our Phase I clinical trial for ALN-VSP, as well as in the GEMINI trial for ALN-RSV01.

We believe that we have continued to make considerable progress in developing our product platform. As part of these efforts and as documented in several key 2010 publications, during 2010, we continued to make further advances relating to the delivery of RNAi therapeutics, both internally and together with our collaborators. With the progress we have made to date and expect to make in the future, we believe we are well positioned to pursue multiple therapeutic opportunities.

Our progress has enabled us to advance a number of development programs for RNAi therapeutics that are administered directly to diseased tissues, including ALN-RSV01 and ALN-HTT. Our progress in achieving delivery of RNAi therapeutics through systemic RNAi has been demonstrated by Phase I data on our first systemically delivered RNAi therapeutic, ALN-VSP, for the treatment of liver cancers, and the initiation in 2010 of a Phase I clinical trial for ALN-TTR01, our second systemically delivered RNAi therapeutic, for the treatment of ATTR. ALN-VSP and ALN-TTR01 both utilize a first-generation delivery technology developed by Tekmira Pharmaceuticals Corporation, or Tekmira. In parallel with ALN-TTR01, we are advancing ALN-TTR02 utilizing a second-generation LNP formulation, as well as ALN-PCS, for the treatment of severe hypercholesterolemia, and ALN-HPN, for the treatment of refractory anemia. We recognize, however, that challenges remain with respect to the development of RNAi-based therapeutics, including achieving effective delivery of siRNAs to target cells and tissues, and we therefore regard further development of our product platform as an ongoing priority.

Our Product Pipeline

Our core product strategy is focused on the development and commercialization of innovative RNAi therapeutics for the treatment of genetically defined diseases. Under our core product strategy, we expect to progress five RNAi therapeutic programs into advanced stages of clinical development by the end of 2015. As part of this strategy, our goal is to develop product candidates with the following shared characteristics: a genetically defined target and disease; the potential to have a significant impact in high unmet need patient populations; the ability to leverage our existing RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of an NDA, with a focused patient database and possible accelerated paths for commercialization. We intend to commercialize products arising from this core product strategy on our own in the United States and potentially certain other countries, and we intend to enter into alliances to develop and commercialize any such products in other global territories. We are currently advancing three core programs in clinical or pre-clinical development: ALN-TTR for the treatment of ATTR; ALN-PCS for the treatment of severe hypercholesterolemia; and ALN-HPN for the treatment of refractory anemia. As part of our core

product strategy, we also expect to designate and start pre-clinical development of two additional RNAi therapeutic candidates targeting genetically defined diseases by the end of 2011.

While focusing our efforts on our core product strategy, we also intend to continue to advance additional development programs through existing or future alliances. We have three partner-based programs in clinical or pre-

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clinical development, including ALN-RSV01 for the treatment of RSV, ALN-VSP for the treatment of liver cancers and ALN-HTT for the treatment of HD.

The following is a summary of our product development programs as of January 31, 2011:

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 $106.4 million in 2010, $108.7 million in 2009 and $96.9 million in 2008.

Core Product Development Programs

Our core product development programs are described in more detail below.

TTR-Mediated Amyloidosis (ATTR)

Market Opportunity. ATTR is a hereditary, systemic disease caused by a mutation in a protein predominantly made in the liver, known as TTR. Mutations in this protein result in the accumulation of toxic deposits of the wild-type and mutant protein in several tissues, including the peripheral nervous system, heart and/or gastrointestinal tract, which leads to FAP and/or familial amyloidotic cardiomyopathy, or FAC. FAP is associated with severe pain and loss of autonomic nervous system function, whereas FAC is associated with heart failure. Typical onset for ATTR occurs between the fourth and sixth decades of life, and the disease is often fatal within five to 15 years of onset. In its severest form, ATTR represents a significant unmet medical need with high rates of morbidity and mortality. ATTR is an orphan, or rare, disease, affecting approximately 50,000 people worldwide.

Current Treatments. There are no existing disease-modifying treatments for ATTR. Currently, liver transplantation is the only available treatment for FAP. However, less than 3,000 FAP patients qualify for this costly and invasive procedure and, even following liver transplantation, the disease continues to progress for many of these patients, presumably due to normal TTR being deposited into preexisting fibrils. Moreover, there is a shortage of donors to provide healthy livers for transplantation. The only currently available treatments for FAC are aimed at relief of symptoms, such as diuretics, or water pills, to treat the swelling of the ankles, one of the symptoms of FAC. In 2010, FoldRx Pharmaceuticals, Inc., or FoldRx, a wholly owned subsidiary of Pfizer Inc., or Pfizer, filed a marketing authorization application, or MAA, for tafamidis, an oral small molecule stabilizer of TTR, with the EMA. Tafamidis has orphan drug status in the European Union, or EU, for the treatment of FAP associated with ATTR.

Alnylam Program. ALN-TTR is an RNAi therapeutic candidate targeting the TTR gene for the treatment of ATTR. TTR is a carrier for thyroid hormone and retinol binding protein and is produced almost exclusively in the liver. We believe TTR is a suitable target for an RNAi therapeutic formulated to maximize delivery to liver cells.

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ALN-TTR targets wild-type and all known mutant forms of TTR, including the predominant V30M mutation, which is the major mutation of ATTR, particularly in FAP, and therefore is a potential therapeutic for the treatment of all forms of ATTR, including FAP and FAC.

In July 2010, we initiated a Phase I clinical trial for ALN-TTR01, a systemically delivered RNAi therapeutic, that employs a first-generation LNP formulation. The Phase I clinical trial for ALN-TTR01 is being conducted in Portugal, Sweden, the United Kingdom and France, and is a randomized, blinded, placebo-controlled dose escalation study designed to enroll approximately 28 ATTR patients, with patients being enrolled into sequential cohorts of increasing doses currently ranging from 0.01 to 0.4 mg/kg. The primary objective is to evaluate the safety and tolerability of a single dose of intravenous ALN-TTR01. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-TTR01 and assessment of pharmacodynamic activity based on measurements of circulating TTR serum levels. In January 2011, the COMP adopted a positive opinion for ALN-TTR01 designation as an orphan medicinal product for the treatment of FAP. A positive opinion by the COMP precedes official designation of ALN-TTR01 as an orphan drug by the EC. Orphan Drug Designation by the EC provides regulatory and financial incentives for companies developing orphan drugs to develop and market therapies that treat a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the EU. In addition to a ten-year period of marketing exclusivity in the EU after product approval, Orphan Drug Designation provides companies with protocol assistance from the EMA during the product development phase, direct access to centralized marketing authorization and reduced regulatory fees.

In parallel with the development of ALN-TTR01, we are also advancing ALN-TTR02 utilizing a second-generation LNP formulation.

In pre-clinical studies with hTTR V30M transgenic mice, ALN-TTR treatment led to potent and robust reduction of mutant V30M TTR mRNA levels in the liver and mutant protein levels in the circulation. In non-human primates, administration of ALN-TTR resulted in potent reduction of wild-type TTR. Moreover, durability studies in transgenic mice and non-human primates demonstrated reduction of TTR serum protein and liver mRNA levels for at least three weeks post-administration of ALN-TTR. When administered to hTTR V30M transgenic mice, ALN-TTR blocked the deposition of mutant V30M TTR protein in a number of tissues known to be affected by the disease, including sciatic nerve, sensory ganglion, intestine, esophagus and stomach.

Our findings demonstrate the potential benefit of an RNAi therapeutic targeting TTR for the treatment of ATTR. Moreover, siRNA treatment may provide benefits not observed with liver transplantation based on the ability to simultaneously reduce the expression of mutant and wild-type TTR. ATTR is also one example of a number of orphan indications where there is a significant unmet need and the potential for early biomarker data in clinical studies, enabling rapid proof-of-concept and a clear opportunity for a large therapeutic impact in patients.

Severe 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-c, or bad cholesterol, in the blood, is one of the major risk factors for CAD. This condition occurs when excess LDL-c in the bloodstream is deposited in the walls of blood vessels. The abnormal buildup of LDL-c forms clumps, or plaque, that narrow and harden artery walls. As the clumps grow, they can clog the arteries and restrict the flow of blood to the heart. The buildup of plaque in coronary arteries increases a person s risk of having a heart attack. Although current therapies are effective in many patients, studies have shown that as many as 45% of high-risk patients with elevated LDL-c do not achieve adequate control of their high cholesterol level with existing treatments, which include drugs known as statins. Currently, in the United States, there are more than 500,000 patients with high cholesterol levels not controlled by the use of existing lipid lowering therapies. These patients are viewed as having severe

hypercholesterolemia and constitute a potential target population for ALN-PCS.

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) and Vytorin® (ezetimibe/simvastatin), which reduces dietary cholesterol uptake from the gut, may also be used either on its own or in combination with a statin. Despite these

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therapies, there are many patients who have severe hypercholesterolemia and require more intensive treatment. In addition, some patients do not tolerate current treatments, with an estimate, based on extensive clinical study results, of at least five percent of those treated with a statin having to stop such treatment because of side-effects. In patients with very high uncontrolled cholesterol levels, a procedure called lipid apheresis is used, which 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. ALN-PCS is a systemically delivered RNAi therapeutic targeting PCSK9 for the treatment of severe hypercholesterolemia. We are advancing ALN-PCS using a second-generation LNP formulation for systemic delivery. ALN-PCS targets PCSK9, which is involved in the regulation of LDLR levels on hepatocytes and the metabolism of LDL-c. PCSK9 is a widely acknowledged target for the treatment of hypercholesterolemia. PCSK9 is a protein that is produced by the liver and 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. Published studies indicate that, if PCSK9 activity could be reduced, the liver s uptake of LDL-c should increase and blood cholesterol levels should decrease. In fact, published case reports have shown individuals with a genetic mutation in PCSK9 that lowers its activity and results in increased liver LDL-c uptake and decreased 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, studies have 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.

We began our ALN-PCS program in collaboration with The University of Texas Southwestern Medical Center, or UTSW. As part of the UTSW collaboration, we and UTSW are testing RNAi therapeutic candidates targeting PCSK9 in certain UTSW animal models. Non-human primate data for our ALN-PCS program demonstrated a greater than 50% reduction in levels of LDL-c, which result is rapidly achieved and durable after a single dose.

Refractory Anemia

Market Opportunity. Anemia is the clinical manifestation of a decrease in circulating red blood cell mass and is usually detected by low blood hemoglobin concentrations. Symptoms include fatigue and dizziness, and generally have a significant impact on the patient s quality of life. Anemia of chronic disease, or ACD, occurs in patients with end-stage renal disease, or ESRD, cancer and chronic inflammatory disorders. There are also additional genetic causes, such as iron-refractory iron deficiency anemia. ACD patients who are refractory to erythropoiesis-stimulating agents, or ESAs, which stimulate red blood cell production, and intravenous iron, define a condition of refractory anemia for which there is a substantial unmet need. Currently in the United States, there are approximately 500,000 patients with ESRD and approximately 50,000 ESRD patients with refractory anemia.

Current Treatments. There are several treatment options available for anemia, depending on its cause and severity, which may include oral or intravenous iron supplements, blood transfusions and ESAs. However, there are currently no approved therapies for the treatment of refractory anemia. Treatment for this condition is largely supportive, including blood transfusion in patients with symptomatic anemia.

Alnylam Program. We recently designated ALN-HPN as our third core development program. ALN-HPN is a systemically delivered RNAi therapeutic targeting hepcidin, a genetically validated gene in iron homeostasis, for the treatment of refractory anemia. Pre-clinical studies with an siRNA targeting hepcidin demonstrated the ability to silence the gene and increase serum iron levels. We are advancing ALN-HPN using a second-generation LNP formulation for systemic delivery.

Partner-Based Product Development Programs

While focusing our core efforts on advancing the product development programs described above, we also intend to continue to advance additional product development programs through existing or future alliances, including those described below.

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Respiratory Syncytial Virus (RSV) 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, including lung transplant recipients. RSV infection typically results in cold-like symptoms, but can lead to more serious respiratory illnesses in these populations such as croup, pneumonia and bronchiolitis, and in extreme cases, severe illness and death. A study published in 2005 in the *New England Journal of Medicine* estimates that over 170,000 elderly adults are hospitalized with RSV each year. In addition, experts estimate that the overall prevalence of lung transplants in the United States is between 8,000 to 10,000. The annual incidence of RSV infection in lung transplant patients can be up to ten percent.

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. However, this product is approved only for treatment of hospitalized infants and young children with severe lower respiratory tract infections due to RSV. Administration of this product is complicated and requires elaborate environmental reclamation devices because of potential harmful effects on healthcare personnel exposed to the drug. In addition, Ribavirin is used by some centers in the treatment of RSV in lung transplant patients.

Two other products, a monoclonal antibody known as Synagis® (palivizumab) and an immune globulin known as 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 February 2008, we reported positive results from 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 one-to-one to receive either ALN-RSV01 or placebo treatment prior to and after experimental infection with a wild-type clinical strain of RSV. ALN-RSV01 was found to be safe and well tolerated and demonstrated statistically significant reduction (40%) in viral infection rate and a 95% increase in infection-free patients ($p<0.01$), as compared to placebo.

In July 2009, we and Cubist reported results from a Phase IIa clinical trial assessing the safety and tolerability of aerosolized ALN-RSV01 versus placebo in a randomized, double-blind trial of 24 adult lung transplant patients naturally infected with RSV. This clinical trial achieved its primary objective of demonstrating the safety and tolerability of ALN-RSV01. In particular, there were no drug-related serious adverse events or discontinuations. Baseline imbalances in day 0 viral load and the time to symptom onset between the treatment groups made it difficult to interpret the trends favoring ALN-RSV01 observed in certain antiviral measures. The patient-reported symptom scores showed a trend towards reduced scores favoring ALN-RSV01. At the 90-day endpoint, all patients survived and the incidence of intubation, new respiratory infection or acute rejection was comparable across ALN-RSV01 and placebo groups. The trial was not powered to demonstrate clinical outcomes due to the small sample size and, accordingly, such data were considered exploratory. Prospectively defined clinical secondary endpoints at 90 days included recovery of lung function (forced expiratory volume in the first second, or FEV_1) as measured by spirometry and clinical determination of new or progressive BOS, a potentially life-threatening complication in lung transplant patients. Based on the data from this small trial, ALN-RSV01 treatment was associated with a statistically significant decrease in the total incidence of new or progressive BOS at 90 days compared to placebo ($p=0.02$), with 50% of placebo patients showing new or progressive BOS as compared with only 7.1% of ALN-RSV01-treated patients. Despite the small patient numbers, we believe that these data may be important since the incidence of BOS following RSV infection in lung transplant patients can be a predictor of graft failure and overall survival. The incidence of BOS in lung transplant patients infected with RSV results in approximately 50% mortality within three to five years of onset.

In February 2010, we initiated a multi-center, global, randomized, double-blind, placebo-controlled Phase IIb clinical trial to evaluate the clinical efficacy as well as safety of aerosolized ALN-RSV01 in adult lung transplant patients naturally infected with RSV. The objective of this Phase IIb clinical trial is to repeat and extend the clinical results observed in the Phase IIa clinical trial described above. This trial is ongoing and is expected to enroll up to 76

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adult lung transplant patients who will be randomized in a one-to-one drug to placebo ratio. The primary endpoint is reduction in the incidence of new or progressive BOS at day 180.

We have formed collaborations with Cubist and Kyowa Hakko Kirin for the development and commercialization of RNAi products for the treatment of RSV. We have an agreement to jointly develop and commercialize certain RNAi products for the treatment of RSV with Cubist in North America. Cubist has responsibility for developing and commercializing any such products in the rest of the world outside of Asia, and Kyowa Hakko Kirin has the responsibility for developing and commercializing any RNAi products for the treatment of RSV in Asia. Under our agreement with Cubist, we are developing ALN-RSV01 for adult transplant patients at our sole discretion and expense. Cubist has the right to opt into collaborating with us on ALN-RSV01 in the future, which right may be exercised for a specified period of time following the completion of our Phase IIb trial, subject to the payment by Cubist of an opt-in fee representing reimbursement of an agreed upon percentage of certain of our development expenses for ALN-RSV01. In December 2010, we and Cubist jointly made a portfolio decision to put the development of ALN-RSV02, a second-generation compound for the pediatric population, on hold.

Liver Cancer

Market Opportunity. Cancer affecting the liver, known as either primary or secondary liver cancer, is associated with one of the poorest survival rates in oncology and represents a major unmet medical need affecting a large number of patients worldwide. Primary liver cancer, also known as hepatocellular carcinoma, or HCC, is one of the most common cancers worldwide, with more than 700,000 people diagnosed each year. Secondary liver cancer, also known as metastatic liver cancer, is cancer that spreads to the liver from another part of the body like the colon, stomach, pancreas, breast, lung or skin. Worldwide, more than 500,000 people are diagnosed with secondary liver cancer each year.

Current Treatments. The treatment options for liver cancer 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. In November 2007, the FDA approved Sorafenib, also called Nexavar®, for the treatment of un-resectable liver cancer. 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. 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 at the time of diagnosis 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 three percent 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. ALN-VSP is a systemically delivered RNAi therapeutic for the treatment of advanced solid tumors with liver involvement. ALN-VSP contains two siRNAs formulated using a first-generation LNP formulation. ALN-VSP is designed to target two genes critical in the growth and development of cancer, KSP and VEGF. KSP is a key component of the cellular machinery that mediates chromosome separation during cell division, which is critical for tumor proliferation. As such, it represents an important target for blocking tumor growth. 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.

In March 2009, we initiated a Phase I clinical trial for ALN-VSP. This Phase I clinical trial is a multi-center, open label, dose escalation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous ALN-VSP in approximately 55 patients with advanced solid tumors with liver involvement. We intend to

partner our ALN-VSP program prior to initiating a Phase II clinical trial.

In November 2010, we reported interim safety data from this Phase I clinical trial showing that 127 doses of ALN-VSP at dose levels of 0.1 to 1.25 mg/kg had been administered to 28 patients, with two to 13 doses administered per patient, and was generally well tolerated. The majority of the patients treated had colorectal cancer, a primary tumor that often metastasizes to the liver. No dose-dependent trends were observed in clinical or

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laboratory adverse events, including liver function tests. A patient with advanced pancreatic neuroendocrine cancer with extensive involvement of the liver developed hepatic failure five days following the second dose at 0.7 mg/kg, and subsequently died; this was deemed possibly related to the study drug. At 1.25 mg/kg, a patient experienced grade three thrombocytopenia after the first dose; this was deemed related to the study drug and was resolved within five days. There have been three acute infusion reactions at 0.4, 0.7 and 1.25 mg/kg; all three patients tolerated further treatment with prolongation of infusion duration.

In addition to the safety data reported in November, in June 2010, we reported DCE-MRI results from patients treated at the 0.1 to 0.7 mg/kg dose levels that suggested an anti-VEGF effect in the majority of treated patients. In 62% of evaluable liver tumors, there was a greater than 40% decline in Ktrans (measure of blood flow), an effect that is comparable to what has been observed with other anti-VEGF drugs in solid tumors.

This Phase I clinical trial is also designed to obtain tumor biopsies for histological and molecular analyses from patients on a voluntary basis. In January 2011, we reported preliminary results from the molecular analyses of post-treatment tumor biopsies from eight patients receiving doses of ALN-VSP ranging from 0.4 to 1.25 mg/kg. Five of these biopsy samples were obtained from tumor in the liver and three were taken from tumor located outside the liver. The two siRNAs targeting VEGF and KSP that comprise ALN-VSP were detected in almost all of these biopsy samples at concentrations ranging from 0.3 to 142 ng/g tissue. These levels of siRNA are pharmacologically relevant since in pre-clinical studies with systemically delivered siRNAs, a tissue level of 1 ng/g has been shown to be associated with 50% target gene silencing.

RNAi is an endogenous cellular enzymatic process whereby siRNAs mediate sequence-dependent cleavage of target mRNAs; cleavage of the target mRNA is highly precise, occurring exactly ten nucleotide positions from the 5 -end of the siRNA antisense strand. 5 RACE is a non-quantitative method that has been established to identify the specific cleavage product that would be indicative of the RNAi mechanism. As reported in a January 2011 presentation, three patients in the Phase I clinical trial have had biopsies that were of sufficient quality to permit blinded 5 RACE analysis for the VEGF target mRNA. All three biopsy samples were from the 0.4 mg/kg dose group, and post-treatment biopsy samples were comprised of 80% to 100% normal liver. In two patients whose post-treatment biopsies were performed two days after dosing, the 5 RACE assay combined with deep sequencing showed that approximately 27% and 29% of all VEGF-derived mRNA fragments corresponded exactly to the predicted RNAi-mediated cleavage product. By contrast, a pre-dose biopsy available for one of those patients contained only approximately one percent predicted VEGF cleavage product, and analysis of banked normal liver and tumor samples from untreated patients showed a background level of only 0.1% to 0.7%. Compared to these low background levels, the amount of predicted VEGF cleavage product in the two post-treatment biopsies was highly statistically significant ($p<0.0001$). In the third patient at 0.4 mg/kg whose post-treatment biopsy was obtained seven days post-dose, there was no detectable increase in the predicted VEGF cleavage product compared to the pre-dose biopsy. We believe the 5 RACE data from these two human biopsies provide clear evidence of RNAi in humans following systemic administration of LNP-formulated siRNA.

Pre-clinical data in mouse tumor model studies have demonstrated efficacy of ALN-VSP, including suppression of the targeted genes, demonstration of an RNAi mechanism of action, formation of monoasters, a characteristic feature of KSP inhibition, anti-angiogenic effects resulting from VEGF inhibition, tumor reduction, and extension of survival. Moreover, the pharmacodynamic effect of KSP targeting has been demonstrated in both hepatic and extrahepatic tumors in murine models of hepatocellular carcinoma and colorectal cancer.

Huntington s Disease (HD)

Market Opportunity. HD is an 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 ten to 20 years after initial diagnosis. The disease is associated with the production of an altered form of a protein known as huntingtin, the presence of which 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 have an approximate 50% risk of developing the disease in their lifetimes.

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Current Treatments. The current treatment of this severe disease is supportive care and therapy for symptomatic relief, with no drugs or therapies available that have been shown to slow the underlying disease progression and the inexorable erosion of the patient s nerve cell functionality.

Alnylam Program. In collaboration with Medtronic, we are developing a novel drug-device product incorporating an RNAi therapeutic candidate targeting the huntingtin gene, delivered using an implantable infusion device, that will protect these cells by suppressing huntingtin mRNA and the disease causing protein. Alnylam scientists and collaborators have presented the data from our ALN-HTT program comprised of *in vitro*, rodent and non-human primate data supporting the continued development of ALN-HTT for the treatment of HD, including: demonstration that an siRNA targeting the huntingtin gene achieves sufficient distribution for coverage of brain regions affected in HD; data evidencing that direct delivery of the siRNA to the CNS results in robust silencing of the huntingtin gene mRNA, which silencing was achieved at substantial distances from the infusion site, an important step towards translating this delivery approach from pre-clinical models to the larger human brain; and, results showing that ALN-HTT was well tolerated following continuous direct CNS administration over a period of approximately one month.

The ALN-HTT program 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. In November 2010, we and Medtronic entered into an agreement with CHDI, under which CHDI has agreed to initially fund approximately 50% of the costs of this program up to the point at which an IND or comparable foreign regulatory application can be filed.

Discovery Programs

In addition to our core development efforts on ATTR, severe hypercholesterolemia and refractory anemia, and our additional partner-based programs in RSV, liver cancer and HD, we are conducting additional research activities to discover novel RNAi therapeutic product candidates with a focus on genetically defined diseases.

In addition to these programs, as part of our collaboration with Takeda, we have research activities to discover RNAi therapeutics directed to one or more undisclosed targets.

Our Collaboration and Licensing Strategy

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

Our collaboration strategy is to form (1) non-exclusive platform and/or multi-target discovery alliances where our collaborators obtain access to our capabilities and intellectual property to develop their own RNAi therapeutic products; and (2) worldwide or specific geographic partnerships on select RNAi therapeutic programs. For example, we have entered into a broad, non-exclusive platform license agreement with Takeda, under which we are also collaborating with Takeda on RNAi drug discovery for one or more disease targets. We have also established product alliances with Cubist and Medtronic for the development and commercialization of ALN-RSV and ALN-HTT, respectively. In addition, we have entered into a product alliance with Kyowa Hakko Kirin for the development and commercialization of ALN-RSV in territories not covered by the Cubist agreement, which include Japan and other markets in Asia. We also have discovery and development alliances with Isis and Biogen Idec.

We also seek to form or advance new ventures and opportunities in areas outside our primary focus on RNAi therapeutics. For example, during 2009, we established Alnylam Biotherapeutics, an internal effort regarding the

application of RNAi technologies to improve the manufacturing processes for biologics, an approach that has the potential to create new business opportunities. This effort is focused on applying RNAi technologies to the biologics marketplace, which includes recombinant proteins and monoclonal antibodies. In addition, during 2007, we and Isis formed Regulus to capitalize on our technology and intellectual property in the field of microRNA therapeutics. Regulus has formed collaborations with GSK and sanofi-aventis to advance their efforts. Given the broad applications for RNAi technology, in addition to our efforts on Alnylam Biotherapeutics and Regulus, we believe new ventures and opportunities will be available to us.

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To generate revenues from our intellectual property rights, we also grant licenses to biotechnology companies under our InterfeRx program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. 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 January 31, 2011, we had granted such licenses, on both an exclusive and non-exclusive basis, to approximately 20 companies.

Since delivery of RNAi therapeutics remains a major objective of our research activities, we also look to form collaboration and licensing arrangements with other companies and academic institutions to gain access to delivery technologies. For example, we have entered into agreements with Tekmira, the Massachusetts Institute of Technology, or MIT, The University of British Columbia, or UBC, and AlCana Technologies, Inc., or AlCana, among others, to focus on various delivery strategies. We have also entered into license agreements with Isis, Max Planck Innovation GmbH (formerly known as Garching Innovation GmbH), or Max Planck Innovation, Tekmira, MIT, Cancer Research Technology Limited, or CRT, Whitehead Institute for Biomedical Research, or Whitehead, Stanford University, or Stanford, UTSW, as well as a number of other entities, to obtain rights to intellectual property in the field of RNAi.

Finally, we seek funding for the development of our proprietary RNAi therapeutics pipeline from the government and foundations. For example, in 2006, the NIAID awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus.

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, license fees, equity investments, research and development funding, milestone payments and/or royalties or profit sharing based on sales of RNAi therapeutics.

Platform Alliances.

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 up to