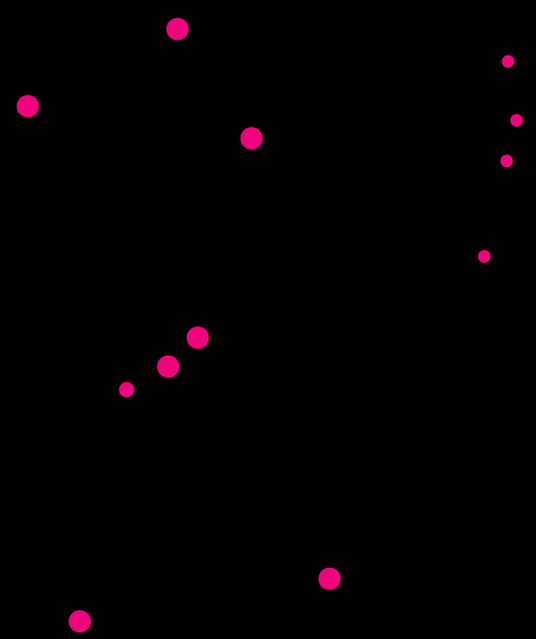
Alnylam Pharmaceuticals

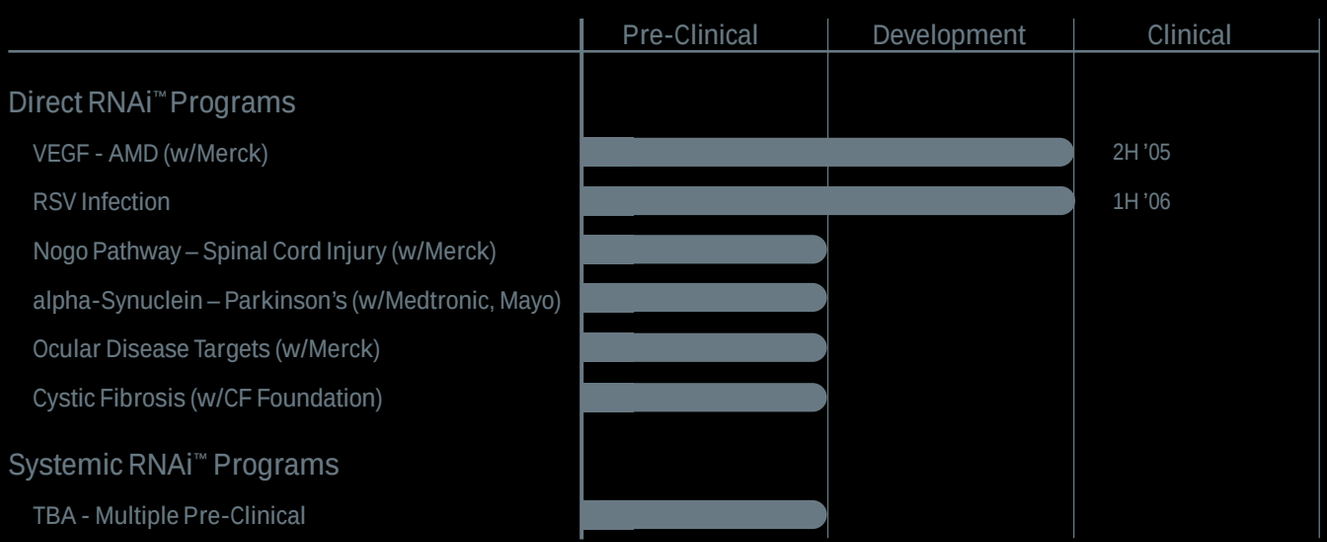


2004 ANNUAL REPORT

ABOUT THE COVER:

The design on the cover depicts the stars of the constellation Orion. The row of three stars in the middle represents Orion's belt. The center star of Orion's belt is Alnilam (al-NIGH-lam). The company Alnylam is developing breakthrough therapeutics based on RNA interference.

Alnylam Pipeline



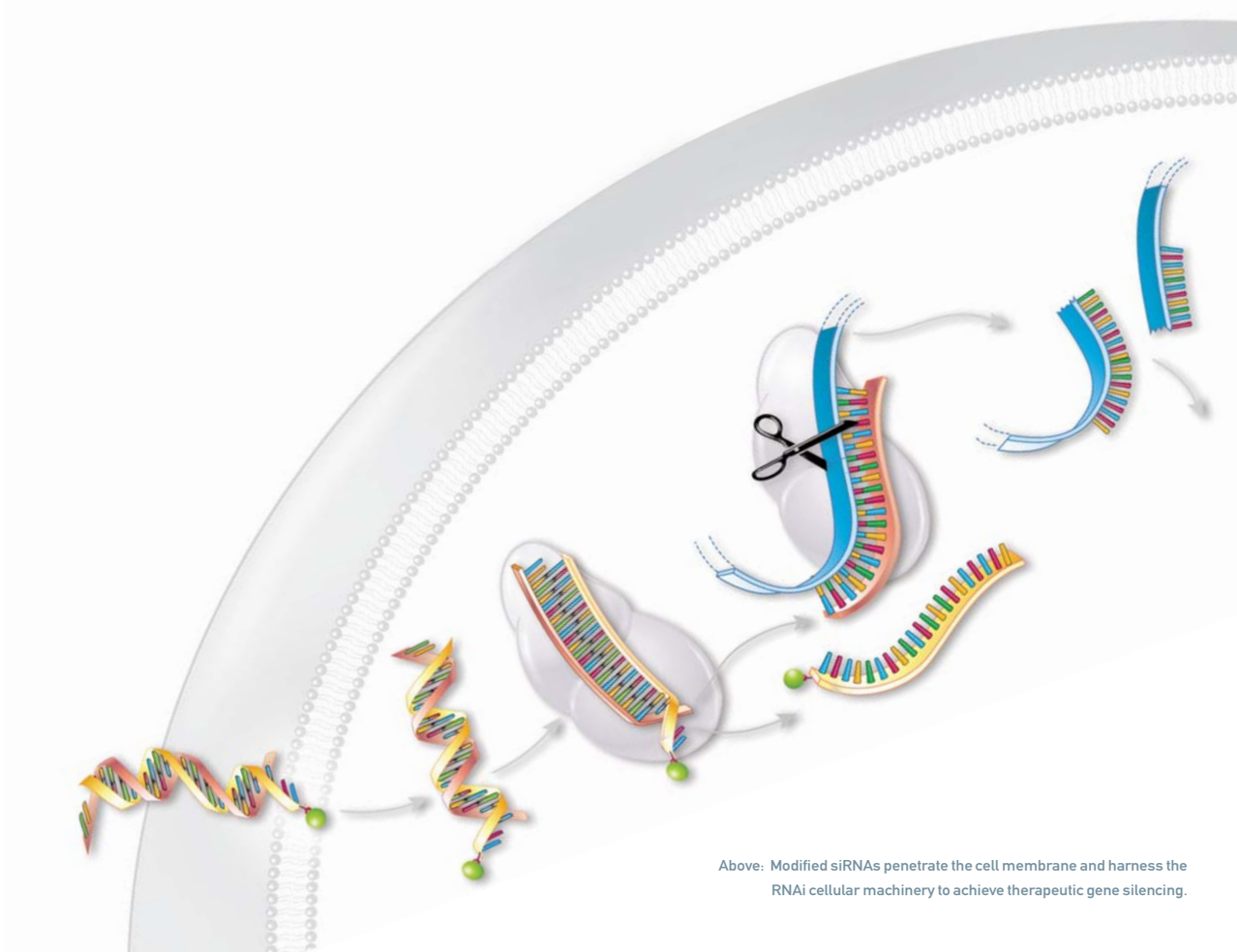
Direct RNAi™ Programs: Therapeutic delivery by direct administration to the site of disease
Systemic RNAi™ Programs: Therapeutic delivery by injection into bloodstream for tissue uptake

Once every decade

there is a breakthrough discovery

that changes the face of medicine.

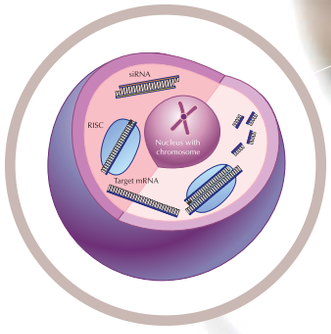
This is ours.



Above: Modified siRNAs penetrate the cell membrane and harness the RNAi cellular machinery to achieve therapeutic gene silencing.

RNA interference (RNAi) is a major discovery in biology that creates the opportunity to develop an entirely new class of medicines designed to "silence" genes that cause disease.

To seize this opportunity, Alnylam has brought together pioneers in RNAi with an experienced team of industry professionals, and is forging strategic relationships with leading companies like Merck and Medtronic. We are passionate about achieving the company's Vision and Mission.



VISION: HARNESSING A REVOLUTION IN BIOLOGY FOR HUMAN HEALTH™

PHILLIP SHARP, PH.D.

"RNAi is one of the most important discoveries in biology in many years. Alnylam was founded with the vision of translating this novel science into important therapeutics for diseases that are difficult, or in some cases impossible, to treat with current drugs. RNAi therapeutics could potentially become a broad and entirely new class of drugs, similar in

Building an RNAi Therapeutic Pipeline

Direct RNAi for Ocular Disease

Age-related macular degeneration (AMD) causes severe deterioration of vision and blindness. To treat the most severe form, "wet" AMD, that affects over 1.5 million people in the U.S., Alnylam is developing an RNAi therapeutic that inhibits production of vascular endothelial growth factor (VEGF), the major culprit behind the disease. Our goal is to develop a best-in-class drug with improved efficacy over current and emerging therapies. We are working with Merck in an alliance that includes two other ocular targets in addition to VEGF.

Direct RNAi for Respiratory Viral Infection

Respiratory syncytial virus (RSV) causes severe lung infections that can be life-threatening in children, the elderly, and people with compromised immune systems. RSV is the leading cause of infant hospitalization and can lead to childhood asthma. There are currently no widely accepted treatments for RSV infection. In a new approach, we are harnessing RNAi to address this need, and have discovered a candidate RNAi therapeutic that potently arrests RSV replication and offers great promise for the treatment of RSV.

Direct RNAi for CNS Disorders

Over 1.5 million people in the U.S. suffer from Parkinson's disease, a debilitating disease of the nervous system, and over 250,000 live with the devastating consequences of spinal cord injury. We are developing RNAi therapeutics to treat these disabling conditions. For Parkinson's disease, we are working with the Mayo Clinic and our development collaborator, Medtronic. For spinal cord injury, we are collaborating with Merck.

Systemic RNAi

To realize the full potential of RNAi therapeutics, Alnylam has made significant progress towards achieving systemic delivery – delivery of siRNAs into tissues following injection into the bloodstream. Our progress was hailed as a landmark by one of the world's leading scientific journals, *Nature*, when it published our results in November 2004. Alnylam's study demonstrated silencing of a previously non-druggable disease-causing gene using modified siRNAs delivered systemically in a clinically relevant manner.

MISSION: BUILD A LEADING PRODUCT COMPANY FOUNDED ON RNAi

importance to monoclonal antibodies and recombinant proteins. I am extremely proud of the accomplishments of Alnylam's scientists who have taken siRNAs, the molecules that trigger RNAi in nature, and found ways to add "drug-like" properties through chemistry solutions. Alnylam is creating a whole new approach to the treatment of disease, and doing so with a commitment to excellence in both science and business."

Product Engine

Alnylam is committed to generating a significant and sustainable product pipeline based on RNAi. To do this, we are developing our "Product Engine": a set of biological and chemical processes applied in a standard fashion to generate promising RNAi therapeutics for a wide range of significant diseases.

To date, we have made considerable progress in rapidly transforming short interfering RNAs (siRNAs), the molecules that induce RNAi, into therapeutic candidates. Our Product Engine allows the selection and optimization of potent molecules to silence specific disease-causing genes. The optimization process includes the application of Alnylam chemistries that instill "drug-like" properties to create stable and efficacious molecules ready for pre-clinical and clinical testing.

Using our current capabilities, we have initiated programs to develop RNAi therapeutics that will be administered directly to diseased parts of the body.

Our current Direct RNAi™ development programs are focused on the ocular disease, age-related macular degeneration (AMD), and on the lung disease caused by infection from human respiratory syncytial virus (RSV). We have additional pre-clinical Direct RNAi programs focused on Parkinson's disease, spinal cord injury and cystic fibrosis.

In addition to these Direct RNAi programs, we are working to extend our capabilities to enable development of Systemic RNAi™ therapeutics that will be administered by injection and travel through the bloodstream to reach diseased parts of the body. We believe Systemic RNAi therapeutics will become important in the treatment of a broad range of diseases, such as cancer, metabolic disorders and autoimmune diseases. One example of our progress toward Systemic RNAi therapeutics is the work we published showing significant reductions in blood cholesterol in mice injected with an optimized siRNA designed to silence an important gene that can contribute to high cholesterol levels.

RNAi IS A NATURAL BIOLOGICAL PROCESS

FOR SILENCING GENES THAT OCCURS IN ALL OF OUR CELLS.

(LEFT TO RIGHT)
THOMAS TUSCHL, PH.D.
PHILLIP ZAMORE, PH.D.

Tom – "To harness the power of RNAi, a natural and catalytic cellular mechanism for gene silencing, we are

RNAi is a natural mechanism used by cells to silence genes. Alnylam is harnessing the power of RNAi by designing synthetic siRNAs that enter cells and interact with cellular proteins to form what is known as the RNA-induced silencing complex (RISC), which then catalytically degrades target messenger RNA.

This mechanism may provide a potent and specific new approach to create medicines that treat disease at its root cause, by halting production of the proteins involved.

RNAi OFFERS THE POTENTIAL TO TREAT DISEASE IN A FUNDAMENTALLY NEW WAY.

continually learning how to add "drug-like" properties to siRNAs without compromising their naturally high potency. To address the challenge of delivering siRNAs, Alnylam has successfully added conjugates, such as cholesterol, that dramatically increase cellular uptake."

Phil – "Alnylam has demonstrated consistent scientific leadership in the RNAi therapeutic field through peer-reviewed publications and presentations. For example, the paper in *Nature* was both a major step forward in harnessing RNAi for therapeutic purposes and the first scientific proof that siRNAs administered to animals trigger RNAi to silence genes."

The field of RNAi is evolving at a rapid pace. Since 1999, our scientific founders have been leaders in showing that the RNAi mechanism is present in mammalian cells, is triggered in nature by siRNAs, and can also be triggered by siRNAs synthesized in the laboratory.

The leadership of our founders is being extended by our scientific team, whose 2004 ***Nature*** article showed that systemically administered siRNAs can be used to trigger RNAi in animals.

THE DISCOVERY OF RNAi HAS BEEN HERALDED AS A MAJOR BREAKTHROUGH IN BIOLOGY, BY LEADING PUBLICATIONS AS DIVERSE AS *SCIENCE* AND *FORTUNE*.

(LEFT TO RIGHT)
PAUL SCHIMMEL, PH.D.
DAVID BARTEL, PH.D.

Paul – "Based on my experience in the biotech sector, Alnylam has a rare combination of quality founders and advisors, and a management team

Business Strategy

Our strategy is to create a leading biopharmaceutical company and build significant long-term value by developing and commercializing a pipeline of innovative medicines.

In parallel with building value from our product pipeline, we are also building value today in additional ways. This includes our continued leadership in intellectual property for RNAi therapeutics and our industry-leading strategic alliances.

We have proactively consolidated what we believe is an unmatched intellectual property (IP) portfolio covering siRNA structure and function, chemical modifications, and target-specific compositions. Alnylam uniquely, owns or holds licenses to the pioneering IP fundamental for RNAi therapeutics. In addition, our agreement with Isis Pharmaceuticals gives us exclusive access to a broad portfolio of issued patents covering chemical modifications of siRNAs.

We are also building value from this IP through multiple revenue-generating collaborations and licensing agreements.

The combination of our strong IP position and our scientific leadership has enabled us to form several major strategic alliances. We currently have two distinct strategic alliances with Merck, one with Medtronic and another with the Cystic Fibrosis Foundation.

Our current and future alliances provide us access to the critical resources necessary to develop and market new innovative medicines.

We expect to continue forming multi-year, multi-million-dollar alliances with pharmaceutical companies that deliver value to our stockholders in the near term.

SCIENTIFIC AND IP LEADERSHIP ARE CREATING VALUE

TODAY THROUGH FORMATION OF MAJOR ALLIANCES.

with significant drug discovery and development experience. Alnylam's intellectual property and scientific credibility have led to a number of collaborations: two separate alliances with Merck, and additional collaborations with Medtronic, Isis, Mayo Clinic, and the Cystic Fibrosis Foundation."

Dave – "Recent discoveries indicate that the RNAi pathway is fundamentally important in humans. At least a third of all our genes appear to be regulated by microRNAs, small RNAs similar to siRNAs that use much of the same cellular machinery. In fact, microRNAs are probably the reason why all cells contain the RNAi machinery that makes siRNAs so powerful in gene silencing."

World Class Team

The most important element of Alnylam's leadership strategy is our people: people who are focused, committed, and passionate about creating a new class of medicines based on the discoveries of RNAi. Our founders are pioneers in the discovery of RNAi and its application towards human therapeutics. As members of our Scientific Advisory Board, our key founders play an ongoing and active role in Alnylam's development. Building on this solid and growing foundation, our scientists have made significant discoveries in their own right in the application of RNAi technology towards development of innovative medicines.

In 2004, we made significant advances in achieving therapeutic gene silencing with RNAi. Our scientific team published these advances in multiple high quality peer-reviewed publications and presentations. We believe that the leadership of our scientists, demonstrating *in vivo* efficacy for RNAi therapeutics, will continue to gain the attention of many key constituents critical to building our business – including academic and clinical opinion leaders, heads of R&D at major pharmaceutical and biotechnology companies, and the media.

The leadership of Alnylam's scientists is paralleled in our business team. The members of our management team have all held leadership positions at top-tier biotechnology companies, bringing the experience needed to advance innovative medicines from drug discovery to development to commercialization and to construct the strategic relationships necessary to build our business. Our employees in the U.S. and Germany are dedicated to developing RNAi therapeutics for the treatment of diseases with high unmet medical need.

THE ACCOMPLISHMENTS OF 2004 COULD NOT HAVE BEEN ACHIEVED WITHOUT THE PASSION AND COMMITMENT OF THE ENTIRE ALNYLAM TEAM.

MANAGEMENT TEAM

BARRY GREENE
Chief Operating Officer

VINCENT MILES, PH.D.
Senior Vice President, Business Development

PATRICIA ALLEN
Vice President, Finance

DAVID KONYS
Vice President, Corporate Development & Operations

With the pharmaceutical industry starved for new innovative approaches to treat human disease, RNAi therapeutics offer a genuinely new approach with the potential to create a broad new class of drugs – a new wave of breakthrough products in biotechnology, not unlike those created in the 80's and 90's from recombinant DNA and monoclonal antibody technologies.

OUR TECHNOLOGY HOLDS PROMISE FOR THE TREATMENT OF DISEASE IN A FUNDAMENTALLY NEW WAY: THERAPEUTIC GENE SILENCING.

VICTOR KOTELIANSKI, M.D., PH.D.
Vice President, Research

ROLAND KREUTZER, PH.D.
Managing Director,
Alnylam Europe AG

STEFAN LIMMER, PH.D.
Managing Director, R&D,
Alnylam Europe AG

MUTHIAH MANOHARAN, PH.D.
Vice President,
Drug Discovery

ROBERT MILLMAN
Chief Intellectual
Property Counsel

To Our Stockholders

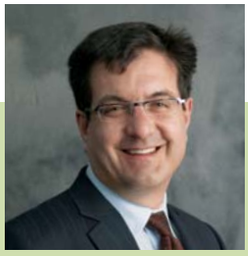
It is with great enthusiasm that I present Alnylam's first Annual Report and review our efforts in advancing a potentially major innovation in medicine based on RNA interference, or RNAi. Our technology holds promise for the treatment of disease in a fundamentally new way: therapeutic gene silencing. We believe RNAi therapeutics will emerge as important treatments for a broad range of diseases where existing medicines have failed to treat the causes of disease, such as ocular disease, viral infections, neurodegenerative disorders, cancer, and autoimmune disease. Reflecting this potential, our bold vision is to harness the revolutionary discovery of RNAi for the betterment of human health, as we aim to achieve our mission of building a leading biopharmaceutical company. The opportunity we have is to develop a broad new class of human therapeutics, perhaps as broad as recombinant proteins and monoclonal antibodies.

By many measures, we enjoyed tremendous success during the past year, our first as a publicly-traded company following our initial public offering in May. Among many accomplishments, we advanced our pipeline of Direct RNAi therapeutics, including our programs in ocular, respiratory infectious, and CNS diseases. At the same time, we made "landmark" advances towards the development of Systemic RNAi therapeutics, as illustrated by the work we published in the world-renowned journal, *Nature*. In addition, on the business side, we continued to execute on our strategies of forming major alliances and strengthening and leveraging our leading IP portfolio. Our new alliances include a second alliance with Merck focused on ocular disease, a drug-device alliance in CNS diseases with Medtronic, and a key IP alliance with Isis Pharmaceuticals, among others.

Our R&D strategy is to build a broadly applicable Product Engine that fuels development of a significant and sustainable product pipeline. At the same time, we are driving certain near-term product opportunities towards clinical trials. Our business strategy is to leverage our scientific leadership and our IP-consolidating position to create significant multi-year strategic alliances that augment our capabilities, technology, and funding. To execute on these strategies, Alnylam has brought together leading scientific experts in the field of RNAi and a management team with deep experience across the entire pharmaceutical value chain. Our scientific and business teams in both the U.S. and Germany are passionate about advancing RNAi therapeutics to treat major diseases, and committed to building Alnylam as a leading biopharmaceutical company.

By harnessing the RNAi mechanism, we believe we can achieve therapeutic gene silencing of virtually any target gene in the genome. Our preferred targets have well-validated roles in human disease, and many are not "druggable" by current methods. The goal for our Product Engine is to achieve therapeutic silencing of such genes across multiple diseases and therapeutic areas. We have reported our progress in various peer-reviewed journals and meetings showing that we can engineer "drug-like" properties into siRNAs and achieve therapeutic silencing of disease-causing genes using clinically relevant modes of administration. These studies have advanced Alnylam significantly closer to our broadest opportunities, namely Systemic RNAi therapeutics for diseases such as cancer, autoimmune diseases and metabolic disorders.

JOHN MARAGANORE, PH.D.
President and Chief Executive Officer



In parallel with our work on Systemic RNAi therapeutics, we are focused on near-term opportunities for Direct RNAi products. We initiated two Direct RNAi therapeutic development programs – the first to treat ocular diseases such as AMD, and the second to treat infection with RSV. AMD is the leading cause of blindness in people over the age of 50. Existing and emerging therapies for AMD leave significant room for improvement, and the growing AMD market offers considerable opportunity for more effective drugs. We and our collaborator Merck believe that a Direct RNAi therapeutic targeting VEGF could become a best-in-class treatment for AMD patients. In our RSV program, we are advancing RNAi therapeutics to treat a major respiratory infectious disease for which there is no widely accepted treatment. Our approach of using RNAi to silence specific viral genes creates a promising new strategy for treating RSV infections.

These two programs are only the beginning of our efforts to bring the innovation of RNAi to patients and make a difference in their lives. In addition to these development programs, we have advanced a number of earlier-stage pre-clinical efforts focused on Parkinson's disease, spinal cord injury, and, most recently, cystic fibrosis. These efforts have been undertaken together with our collaborators at the Mayo Clinic, Medtronic, Merck and the Cystic Fibrosis Foundation.

Alnylam has also taken important steps toward long-term success through execution on our business goals. These include the formation of new major alliances with leading companies such as Merck and Medtronic. These alliances enable us to augment our capabilities, expertise and financial resources so that we can build a clinical pipeline of breakthrough therapies. Such collaborations are an important priority in building our company. In an era when the pharmaceutical industry is starved for innovative medicines, we believe that RNAi therapeutics and Alnylam represent a unique solution for our collaborators.

A key part of our business strategy is the proactive approach we have taken in consolidating the key IP needed for the development and commercialization of RNAi therapeutics. In our view, our IP portfolio is truly unprecedented in this industry as it creates what we believe is a leading position across a whole new class of medicines. It is very satisfying that we are creating value today from this unique asset. For example, our leadership position led to an alliance with Isis that provided Alnylam with chemistries important for developing RNAi therapeutics. Our IP portfolio, together with our scientific leadership, has been a critical component in enabling us to establish major alliances.

Alnylam has a unique opportunity to create a new class of innovative medicines, a business strategy focused on value creation, and a team of people committed to excellence in both science and business. With these core ingredients, we believe that we are well on our way toward making a difference in patients' lives and achieving our Vision and Mission. We thank you for your support as we continue to harness this scientific breakthrough to bring forward RNAi therapeutics, a major new class of medicines.

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

Corporate Information

Officers and Senior Management

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

Barry E. Greene
Chief Operating Officer

Vincent J. Miles, Ph.D.
Senior Vice President, Business Development

Patricia L. Allen
Vice President, Finance

David M. Konys
Vice President, Corporate Development and Operations

Victor E. Kotelianski, M.D., Ph.D.
Vice President, Research

Roland Kreutzer, Ph.D.
Managing Director, Alnylam Europe AG

Stefan Limmer, Ph.D.
Managing Director R&D, Alnylam Europe AG

Muthiah Manoharan, Ph.D.
Vice President, Drug Discovery

Robert Millman
Chief Intellectual Property Counsel

Board of Directors

Peter Barrett, Ph.D.
Senior Partner, Atlas Venture

John E. Berriman
Consultant

John K. Clarke
Managing General Partner, Cardinal Partners
Chairman of the Board, Alnylam Pharmaceuticals, Inc.

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

Phillip A. Sharp, Ph.D.
Institute Professor, Massachusetts Institute of Technology
Nobel Laureate in Physiology or Medicine, 1993

Paul R. Schimmel, Ph.D.
Skaggs Institute for Chemical Biology,
The Scripps Research Institute

Kevin P. Starr
Former Chief Operating Officer, Millennium Pharmaceuticals, Inc.

This document contains forward-looking statements that involve risks and uncertainties. Any statements (including statements to the effect that we "believe" and similar expressions) that are not statements relating to historical matters should be considered forward-looking statements. Actual results could differ materially from those discussed in the forward-looking statements as a result of numerous important factors, including those discussed in "Management's Discussion and Analysis of Financial Condition and Results of Operations – Certain Factors That May Affect Future Results" in our Annual Report on Form 10-K.

Stockholder Information

Corporate Headquarters

Alnylam Pharmaceuticals, Inc.
300 Third Street
Cambridge, Massachusetts 02142
(617) 551-8200

Independent Auditors

PricewaterhouseCoopers LLP, Boston, Massachusetts

Transfer Agent and Registrar

Questions regarding accounts, address changes, stock transfers and lost certificates should be directed to:
EquiServe Trust Company, N.A.
P.O. Box 219045
Kansas City, Missouri 64121-9045
Shareholder Inquiries (877) 282-1168
www.EquiServe.com

Annual Meeting

The 2005 Annual Meeting of Stockholders will be held on June 8, 2005 at 10:00 a.m. at the offices of Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109.

Price Range of Common Stock

Alnylam's common stock began trading on the NASDAQ National 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 closing sales prices per share for our common stock on the NASDAQ National Market for the periods indicated:

	2004	
	High	Low
Second Quarter (May 28 to June 30)	$ 9.50	$5.26
Third Quarter	8.00	3.65
Fourth Quarter	8.60	5.00

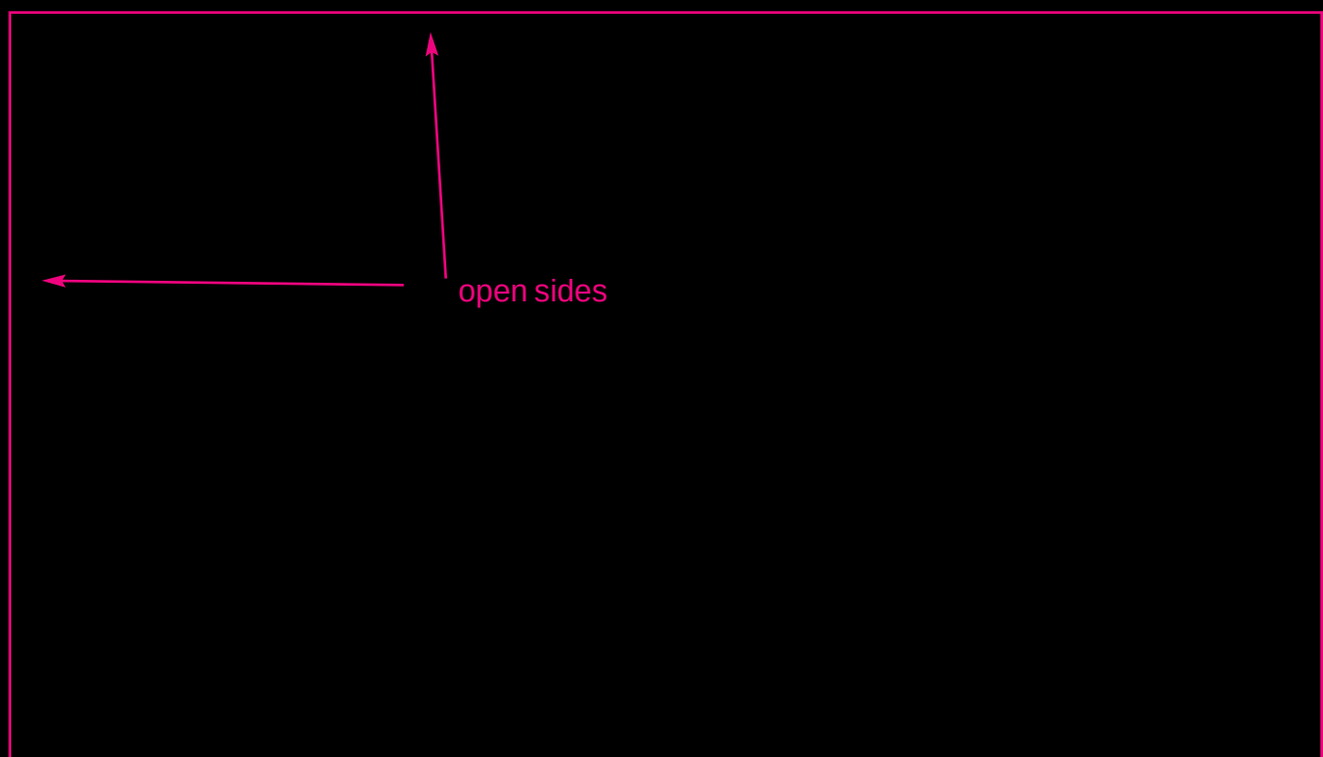
No dividends have been paid on the common stock to date, and the Company does not expect to pay cash dividends on such common stock in the foreseeable future.

SEC Form 10-K

A copy of the Company's Form 10-K for the year ended December 31, 2004, filed with the Securities and Exchange Commission, is available without charge upon written request to:

Investor Relations
Attention: Jennifer Curley
Alnylam Pharmaceuticals, Inc.,
300 Third Street, Cambridge, Massachusetts 02142

or by accessing the Company's web site at www.alnylam.com.



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www.alnylam.com