New RNAi Approach for In Vivo Therapeutic Silencing of MicroRNAs is Demonstrated by Alnylam and Rockefeller University Scientists

Findings Published in Nature Show Potential of Targeting MicroRNAs to Treat Diseases

CAMBRIDGE, Mass., October 31, 2005 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today the publication of a novel approach to regulate gene expression through the silencing of microRNAs (miRNAs). miRNAs have been shown to regulate a large number of genes in the human genome through the RNAi pathway. Many of these miRNAs are believed to be involved in disease processes. In a paper published yesterday in *Nature*, scientists from The Rockefeller University and Alnylam describe the rational design of a potential new class of chemically modified RNA-based drugs, called 'antagomirs', that specifically silence miRNAs across multiple tissue types following therapeutically relevant administration in animals. We believe this research creates the opportunity to design antagomirs that target miRNAs in the context of human diseases, such as cancer and viral infection.

"miRNAs are critical for the control of gene expression in all living cells, and appear to play an important role in both normal and disease physiology. There are over 250 genes that encode for miRNAs in the human genome and these appear to regulate as much as one-third of all gene expression," said Markus Stoffel, M.D., Ph.D., Robert and Harriet Heilbrunn Professor of The Rockefeller University's Laboratory of Metabolic Diseases. "Our discovery of antagomirs represents the first-ever demonstration of a pharmacologic strategy to silence miRNAs. These antagomirs have remarkable properties including high potency, high specificity, broad bioavailability, and long-lasting effects, and we believe this may have profound implications for the treatment of many human diseases."

In the *Nature* paper, antagomirs that target miRNA-16, miRNA-122, miRNA-192, and miRNA-194 demonstrated specific *in vivo* silencing of the target miRNA in tissues including liver, lung, kidney, heart, and bone marrow. This silencing was shown to be sustained for over 20 days following a single treatment course. Bioinformatic analyses of gene expression data from antagomir-treated animals revealed a greater degree of gene regulation by miRNAs than previously estimated. Further, efficient silencing of miRNA-122, a liver-specific miRNA recently shown to be required for hepatitis C infection, was achieved without any evidence of adverse effects. This silencing of miRNA-122 was associated with the regulation of a discrete set of genes involved in liver metabolism.

"The opportunity to target miRNAs involved in human disease with antagomirs greatly extends Alnylam's platform for harnessing RNAi for therapeutic applications," said John Maraganore, Ph.D., President and Chief Executive Officer of Alnylam. "This ground-breaking discovery is yet further demonstration of Alnylam's clear scientific leadership in translating RNAi biology into a robust product engine for innovative medicines. We are hopeful that antagomirs will represent an important therapeutic strategy for Alnylam and its partners in the years to come, complementing our near-term focus on development and commercialization of direct RNAi therapeutics targeted toward pulmonary, CNS, and ocular diseases."

Alnylam and The Rockefeller University have a collaboration agreement for research in the field of RNAi. Alnylam has taken an exclusive license to all of The Rockefeller University's interest in antagomir technology.

About RNA Interference (RNAi) RNA interference, or RNAi, is a naturally occurring mechanism within cells for selectively silencing and regulating specific genes. The discovery of RNAi has been widely acknowledged as a major breakthrough in biology, and the technology was recognized for its potential broad impact in medicine with the award of the 2006 Nobel Prize for Physiology or Medicine. 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. RNAi is induced by small, double-stranded RNA molecules. One method to activate RNAi is with chemically synthesized small interfering RNAs, or siRNAs, which are double-stranded RNAs that are targeted to a specific disease-associated gene. The siRNA molecules are used by the natural RNAi machinery in cells to cause targeted gene silencing.

About microRNA (miRNA) RNAi can also be induced by microRNAs, or miRNAs, that occur naturally within all mammalian cells. The miRNA molecules are encoded by the cell's own genes, giving rise to small RNA molecules that are similar in structure to siRNAs. There are believed to be over 250 confirmed miRNA genes in the human genome and there are many other predicted miRNAs. miRNAs are thought to work through RNAi to regulate the activity of an estimated one-third of genes in the genome. The inappropriate absence or presence of specific miRNA molecules in various cells has been shown to be associated with specific human diseases, including cancer and viral infections.

About Alnylam Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi.

The company is applying its therapeutic expertise in RNAi to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Alnylam is building a pipeline of RNAi therapeutics; its lead program is in Phase I human clinical trials for the treatment of respiratory syncytial virus (RSV) infection. RSV infects nearly every child at least once by the age of two and accounts for more than 100,000 hospitalizations annually in the U.S. pediatric population. RSV infection also poses a great risk to the elderly and other adults with compromised immune systems. The company's leadership position in fundamental patents, technology, and know-how relating to RNAi has enabledit to form major alliances with leading companies including Merck, Medtronic, Novartis, and Biogen Idec. The company, founded in 2002, maintains global headquarters in Cambridge, Massachusetts, and has an additional operating unit in Kulmbach, Germany. For more information, visit www.alnylam.com.

Alnylam Forward-Looking Statements Various statements in this release concerning our future expectations, plans and prospects, including without limitation statements related to the potential for miR-181a and other microRNAs, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks related to: Alnylam's approach to discover and develop novel drugs, which is unproven and may never lead to marketable products; Alnylam's ability to fund and the results of further pre-clinical and clinical trials; obtaining, maintaining and protecting intellectual property utilized by Alnylam's products; Alnylam's ability to enforce its patents against infringers and to defend its patent portfolio against challenges from third parties; Alnylam's ability to obtain additional funding to support its business activities; Alnylam's dependence on third parties for development, manufacture, marketing, sales, and distribution of products; the successful development of Alnylam's product candidates, all of which are in early stages of development; obtaining regulatory approval for products; competition from others using technology similar to Alnylam's and others developing products for similar uses; Alnylam's dependence on collaborators; and its short operating history; as well as those risks more fully discussed in the "Risk Factors" section of Alnylam's most recent report on Form 10-K on file with the Securities and Exchange Commission. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam does not assume any obligation to update any forward-looking statements.