

# Alnylam and Isis Announce Allowance of First U.S. Patent Covering Human microRNAs

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## - New Patent Strengthens Alnylam and Isis Leadership in microRNA Therapeutic Research -

CAMBRIDGE, Mass. & CARLSBAD, Calif., Mar 01, 2007 (BUSINESS WIRE) -- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that the United States Patent and Trademark Office (USPTO) has allowed claims in a patent application that covers microRNAs (miRNAs) and therapeutic molecules that target these miRNAs. The USPTO issued a "Notice of Allowance" for patent application 10/490,955, which is derived from the "Tuschl III" patent series licensed co-exclusively to Alnylam and Isis for miRNA therapeutics on a world-wide basis through an agreement with Max-Planck-Innovation GmbH, the licensing agent for the Max Planck Society. Following a "Notice of Allowance," the companies would expect final issuance of the patent within six months.

miRNAs have been shown to regulate the expression of a large number of genes in the human genome through the RNAi pathway, and many of these miRNAs are believed to be involved in disease processes including cancer, metabolic disease, and viral infection. The Tuschl III patent series pertains to the discovery of over 120 novel mammalian miRNAs and stems from groundbreaking research performed by Alnylam founder Thomas Tuschl, Associate Professor of RNA Molecular Biology at The Rockefeller University, while at the Max Planck Society (Lagos-Quintana et al., (2001) Science 294, 853-858). The allowed claims cover a disease-associated miRNA, specifically miR-122, which is a liver-specific miRNA that has been shown to be required for hepatitis C virus (HCV) infection (Jopling et al. (2005) Science 309, 1577-81). Isis and Alnylam have demonstrated that in vivo antagonism of miR-122 with antisense drugs is associated with regulation of a discrete set of genes involved in liver metabolism (Krutzfeldt et al. (2005) Nature 438, 685-689; Esau et al. (2006) Cell Metab., 3, 87-98).

"The recent discovery that over 250 human genes encode miRNAs that may control gene expression for as much as one-third of the genome suggests that these small, non-coding RNAs play a major role in human physiology and disease," said C. Frank Bennett, Ph.D., Senior Vice President, Research for Isis. "Scientists at Isis and Alnylam have been performing an exciting line of research to identify novel, antisense-based therapeutic approaches for targeting miRNAs, and our collaborative efforts point to significant opportunities for the future."

"As part of our 2004 agreement with Isis, we have been engaged in consolidating intellectual property in the miRNA field," said Robert Millman, Ph.D., Chief Intellectual Property Counsel for Alnylam. "We believe that, in addition to this first allowed U.S. patent covering isolated miRNAs and molecules that are complementary to the miRNA, several other patents will likely result from the Tuschl III patent series because similar claims to each of the over 120 miRNAs are disclosed in the patent application as well as methods of altering the level of the miRNA in a cell."

### 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, which is the leading cause of hospitalization in infants in the U.S. The company's leadership position in fundamental patents, technology, and know-how relating to RNAi has enabled it 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](http://www.alnylam.com).

### About Isis Pharmaceuticals

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. Isis has successfully commercialized the world's first antisense drug and has 15 drugs in development. Isis' drug development programs are aimed at treating cardiovascular, metabolic and inflammatory diseases. Isis' partners are focused in disease areas such as ocular, viral and neurodegenerative diseases, and cancer. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000 Biosensor System, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

### Alnylam Forward-Looking Statements

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including without limitation, statements relating to the role of miRNAs in human physiology and disease, the possible identification of a novel therapeutic approach for targeting miRNAs and the likelihood that other patents will result from the Tuschl III patent series, 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 Alnylam's 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-Q 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.

#### Isis Forward-Looking Statements

This press release includes forward-looking statements regarding Isis Pharmaceuticals' business, its intellectual property portfolio, and the therapeutic and commercial potential of molecules complementary to microRNAs. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2005, and its quarterly report on Form 10-Q for the quarter ended September 30, 2006, which are on file with the SEC. Copies of these and other documents are available from the Company.

SOURCE: Alnylam Pharmaceuticals, Inc.

Alnylam Pharmaceuticals, Inc.

Investors: □

Patricia Allen, 617-551-8362

or □

Media: □

KMorrisPR □

Kathryn Morris, 845-635-9828

or □

Isis Pharmaceuticals, Inc.

Kate Corcoran, Ph.D., 760-603-2331

or □

William Craumer, 760-603-2331

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