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## **Alnylam and Isis Receive Exclusive License to Key microRNA Patents for Therapeutic Applications**

Intellectual Property From Max Planck Society Strengthens Companies' Leadership Positions In RNA-Based Drug Discovery and Development

CAMBRIDGE, Mass., and CARLSBAD, Calif., Oct. 19 /PRNewswire-FirstCall/ — Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), the leading company focused on novel therapeutics targeting RNA, announced today that they have co-exclusively licensed certain core intellectual property relating to all therapeutic uses of microRNA from the Max Planck Society. Garching Innovation GmbH, the Society's technology transfer agency, facilitated the transaction. microRNAs are naturally expressed small RNAs that interact with components shared by the RNA-induced silencing complex (RISC). RISC is an enzyme complex by which the RNA interference (RNAi) pathway operates. It is increasingly believed that microRNAs play a central role in the regulation of gene expression in mammalian cells, and abnormalities in their function may play a role in human disease. This licensing transaction greatly enhances each company's intellectual property portfolio, and its ability to discover and develop RNA therapeutics based on these mechanisms.

Under the terms of the agreement, the Max Planck Society granted rights to patent applications based on the microRNA work of Dr. Thomas Tuschl, a leading scientist in early siRNA research and one of the founders of Alnylam. During his research efforts, Dr. Tuschl discovered more than 100 naturally occurring micro-RNAs that are present in mammalian cells. These microRNAs have the potential to be new drug targets or therapeutic products and are the subjects of the licensed patent applications.

"Alnylam continues to be at the forefront of the science, technology, and intellectual property in the field of RNAi, and is uniquely positioned to develop and commercialize double-stranded RNAi therapeutics," said John Maraganore, Ph.D., President and Chief Executive Officer of Alnylam Pharmaceuticals. "The fundamental cellular importance of microRNAs has the potential to yield new therapeutic products to treat a wide range of human diseases."

"Our license to these Tuschl patents enriches Isis' strong intellectual property position in RNA-based drug discovery. We are enthusiastic about the potential of this new class of drug targets. Our main microRNA research effort is based in our Singapore lab, where we are focused on discovering new miRNA drugs for cancer and blood diseases," said B. Lynne Parshall, Isis' Executive Vice President and Chief Financial Officer of Isis Pharmaceuticals. "Our business strategy has been to participate in all areas of RNA-based drug discovery directly and through collaborations with outstanding companies like Alnylam. Through this alliance, we benefit from Alnylam's high quality focused research efforts on the RNAi mechanism and participate fully in the potential upside of this particular RNA-based mechanism."

**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

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. Isis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Isis 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 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.

**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.