



Alnylam Pharmaceuticals Presents Results Showing Reduction Of Alpha-Synuclein Expression By RNA Interference

Data Reported At Neuroscience Meeting Show Continuing Progress In Preclinical Program In Parkinson's Disease With Mayo Clinic

CAMBRIDGE, Mass., Oct. 27 /PRNewswire-FirstCall/-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading therapeutic RNA interference (RNAi) company, together with its collaborators at the Mayo Clinic, today presented data from cell culture models showing RNA interference (RNAi)- mediated reduction in the expression of alpha-synuclein, a protein whose overexpression is linked to Parkinson's disease, at Neuroscience 2004, the Society for Neuroscience's 34th Annual Meeting in San Diego, California. The preclinical results showed that the use of small interfering RNAs (siRNAs) to target alpha-synuclein gene expression offers hope for the development of RNAi therapeutics to treat Parkinson's disease. The data presented at this meeting were developed by an Alnylam team led by David Bumcrot, Ph.D., Director of Preclinical Research at Alnylam, working collaboratively with the Mayo Clinic research laboratories of Matthew Farrer, Ph.D., and Jada Lewis, Ph.D.

In several in vitro studies, select siRNA molecules were shown to specifically target alpha-synuclein expression, demonstrating effective and sustained reduction of this expression. Further, siRNA molecules were stable, with a long half-life, in both serum and brain extracts, and chemical modifications that increase siRNA stability were successfully developed and tested. These siRNA molecules are now the subject of evaluation in animal models. Mayo Clinic and Alnylam established a collaboration to target Parkinson's disease with RNAi therapeutics in October 2003. As part of this collaboration, researchers at Alnylam developed specific siRNA molecules targeted to alpha-synuclein gene expression and scientists at Mayo Clinic tested these custom siRNAs for efficacy.

"Through our collaboration with Mayo Clinic, we have made important progress in demonstrating how RNAi may be harnessed to treat Parkinson's disease by blocking a recently-identified mechanism underlying the disease" said Vincent Miles, Ph.D., Senior Vice President, Business Development of Alnylam Pharmaceuticals. "Our encouraging results highlight the significant potential of RNAi to create a new class of medicines for important diseases, such as Parkinson's and other diseases of the central nervous system."

Alpha-Synuclein In Parkinson's Disease

Alpha-synuclein is a protein found in various body tissues, primarily in the brain, where scientists believe it may play a role in synaptic vesicle recycling (how nerve cells transmit their signals). Over the last few years, it has been found that mutations in alpha-synuclein appear to cause Parkinson's Disease in a subset of patients. Findings published by Mayo Clinic researchers in Fall 2003 in *Science* highlighted that, in a family with multiple affected members, simple over-expression of normal alpha-synuclein appeared sufficient to cause Parkinson's disease. Previous work by the Mayo Clinic group, published in *Human Molecular Genetics*, demonstrated that over- expression of alpha-synuclein may confer susceptibility to Parkinson's disease in a broader population.

Parkinson's disease is a serious disorder that affects nerve cells (neurons) in the part of the brain controlling muscle movement. Nearly one million Americans currently live with Parkinson's and approximately 50,000 more receive a diagnosis of the disease every year.

About RNAi

RNA interference, or RNAi, is a naturally occurring mechanism within cells for selectively silencing and regulating specific genes that is potentially the basis for a new class of therapeutic products. Since many diseases are caused by the inappropriate activity of specific genes, the ability to silence and regulate such genes selectively through RNAi could provide a means to treat a wide range of human diseases. The discovery of RNAi has been heralded by many as a major breakthrough, and the journal *Science* named RNAi the top scientific achievement of 2002, as well as one of the top ten scientific advances of 2003.

About Alnylam

Alnylam is a biopharmaceutical company seeking to develop and commercialize novel therapeutics based on RNA interference, or RNAi. Growing from its foundation as the world's first company focused on RNAi therapeutics, the company's leadership in the field of RNAi is supported by its preeminent founders and advisors and its strengths in fundamental patents, technology, and know-how that underlie the commercialization of RNAi therapeutics. Alnylam is developing a pipeline of RNAi products using Direct RNAi™ to treat ocular, central nervous system, and respiratory diseases and Systemic RNAi™ to treat a broad range of diseases, including oncologic, metabolic, and autoimmune diseases. The company's global headquarters are in Cambridge, Massachusetts. For additional information, please visit <http://www.alnylam.com>.

Forward-Looking Statements

Various statements in this release concerning our future expectations, plans, prospects and future operating results 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: our approach to discover and develop novel drugs, which is unproven and may never lead to marketable products; our ability to obtain additional funding to support our business activities; our dependence on third parties for development, manufacture, marketing, sales and distribution of our products; the successful development of products, all of which are in early stages of development; obtaining regulatory approval for products; competition from others using technology similar to ours and others developing products for similar uses; obtaining, maintaining and protecting intellectual property utilized by our products; and our short operating history; as well as those risks more fully discussed in the "Certain Factors That May Affect Future Results" section of our Form 10-Q filed with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today and should not be relied upon as representing our views as of any subsequent date. We do not assume any obligation to update any forward-looking statements.

SOURCE Alnylam Pharmaceuticals, Inc.
10/27/2004

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