



Press Release

IMM, Cenix and Alnylam Discover New Targets in Malaria Infection with RNAi Technology

- *In Vitro* and *In Vivo* Findings Published in the Journal PLoS Pathogens Identify Novel Host Targets Involved in Malaria Infection -

CAMBRIDGE, Mass., and DRESDEN, Germany, November 11, 2008 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, and Cenix BioScience GmbH, a leading RNAi-focused contract research organization, today announced the publication of a new study in the journal *PLoS Pathogens* demonstrating *in vitro* and *in vivo* RNAi-mediated silencing of novel host factors involved in malaria infection. The work resulted from an ongoing malaria research program started as a collaboration announced in 2005 between the group of Dr. Maria Mota at the Instituto de Medicina Molecular (IMM) in Portugal and Cenix, which was extended to include Alnylam's therapeutic siRNA technology, involving scientists from both Roche Kulmbach GmbH (formerly Alnylam Europe AG), and Alnylam. The new data show the first genomics-driven identification of novel host factors involved in malaria infection and contribute toward a better understanding of host-pathogen interactions, which may help in developing new prophylactic or therapeutic strategies.

"Our collaboration with Dr. Maria Mota's group at the IMM and Cenix has resulted in three peer-reviewed scientific papers that have helped us better understand potential therapeutic opportunities for malaria with RNAi," said Victor Kotelianski, M.D., Ph.D., Senior Vice-President and Distinguished Alnylam Fellow. "In this new work, we have identified several important host kinases that may prove to be clinically relevant targets to treat malaria infection and have demonstrated an RNAi therapeutic to be effective at silencing these targets *in vivo*."

"This study further illustrates the success of the joint efforts between our groups to drive this breakthrough program from initial genomics-enabled discovery of novel targets to *in vivo* validation, and even identification of therapeutic lead molecules," noted Dr. Christophe Echeverri, CEO/CSO of Cenix. "We look forward to making further use of these capabilities to advance the fight against malaria and other parasitic diseases that are similarly devastating to the world's most vulnerable populations."

The World Health Organization estimates that each year 300 to 500 million cases of malaria occur and that more than 1 million people die of malaria. In this new study (Prudêncio et al., *PLoS Pathogens*, 2008 Nov;4(11):e1000201), the team of scientists performed a "kinome-wide" RNAi screen to identify novel host factors involved in malaria infection. The screen led to discovery of five targets clearly implicated in malaria, all of which resulted in significant reductions in infection *in vitro* when silenced with small interfering RNAs (siRNAs), the molecules that mediate RNAi. One of these key targets, PKCzeta, was selected for further evaluation *in vivo*. In mice given a systemically delivered, liposomally formulated anti-PKCzeta RNAi therapeutic, an inhibitory effect on infection was observed. In fact, loss of PKCzeta function *in vivo* by RNAi-mediated silencing led to decreased infection rates by approximately 80%. In addition, certain siRNAs also led to a delay in the appearance of parasites in the blood and a significant reduction in average blood parasitemia.

About RNA Interference (RNAi)

RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as “a major scientific breakthrough that happens once every decade or so,” and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the horizon. RNAi therapeutics target the cause of diseases by potently silencing specific messenger RNAs (mRNAs), thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

About the Instituto de Medicina Molecular

The Instituto de Medicina Molecular (IMM), located on the campus of the University of Lisbon School Of Medicine, has been recognized as a leading research institute in Portugal and thus has acquired the special status of Associate Laboratory of the National Ministry of Science and Higher Education. The mission of the Institute is to foster basic, clinical and translational biomedical research with the aim of contributing to a better understanding of disease mechanisms, developing novel predictive tests, improving diagnostics tools and developing new therapeutic approaches. IMM is a non-profit, private, research Institute mainly supported by national public funds, European Union funds, and private Foundations. Though still a very young institution, IMM has been able to attract international collaborations, foreign researchers and international funds. Dr. Maria Mota is Director of the Malaria Unit at IMM, where she leads a team of 12 researchers whose main objective is to elucidate the molecular and cellular mechanisms underlying host-parasite interaction in malaria infection. Dr. Maria Mota is also Associate Professor at the Lisbon School of Medicine and a Howard Hughes International Scholar. For more information, please visit the IMM’s website: www.imm.ul.pt.

About Cenix BioScience GmbH

Founded in 1999, Cenix BioScience is the first contract research organization specialized in combining advanced applications of RNAi gene silencing with high content phenotypic analyses to enhance and accelerate the discovery and pre-clinical development of novel therapeutics. Now in its 10th year, Cenix has built-up a solid track record, successfully advancing therapeutic programs for numerous major industry and academic partners by addressing the specific needs of each through fully-customized, cutting-edge research offerings covering a wide range of disease fields. The well-established core capabilities in high throughput RNAi and multi-parametric microscopy assays have yielded optimized protocols in a broad and ever-growing collection of cultured mammalian cells, and are now complemented by microRNA-focused experimentation and in vivo applications of synthetic siRNAs. As such, Cenix is a mature and fully-proven industrial research partner, applying the highest of scientific best practices and offering a breadth and depth of expertise second to none world wide. Please contact Cenix or visit the company’s web site www.cenix-bioscience.com for more information.

About Alnylam Pharmaceuticals

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 leading the translation of RNAi as a new class of innovative medicines with peer-reviewed research efforts published in the world’s top scientific journals including *Nature*, *Nature Medicine*, and *Cell*. The company is leveraging these capabilities to build a broad pipeline of RNAi therapeutics; its most advanced program is in Phase II human clinical trials for the treatment of respiratory syncytial virus (RSV) infection. In addition, the company is developing RNAi therapeutics for the treatment of a wide range of disease areas, including liver cancers, hypercholesterolemia, Huntington’s disease, and TTR amyloidosis. 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 Medtronic, Novartis, Biogen Idec, Roche, Takeda, and Kyowa Hakko. To reflect its outlook for

key scientific, clinical, and business initiatives, Alnylam established “*RNAi 2010*” in January 2008 which includes the company’s plan to significantly expand the scope of delivery solutions for RNAi therapeutics, have four or more programs in clinical development, and to form four or more new major business collaborations, all by the end of 2010. Alnylam is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development, and commercialization of microRNA therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, visit www.alnylam.com.

Alnylam Forward-Looking Statement

Various statements in this release concerning Alnylam’s future expectations, plans and prospects, 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, as well as those risks more fully discussed in the “Risk Factors” section of its most recent quarterly 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.

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