Alnylam Obtains Approvals to Initiate Phase I Study with ALN-TTR01 in Patients with TTR-Mediated Amyloidosis (ATTR)

- Phase I Study to Include Approximately 28 ATTR Patients, with Centers in Portugal, Sweden, and United Kingdom -

CAMBRIDGE, Mass., Jun 29, 2010 (BUSINESS WIRE) -- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today that its applications for ALN-TTR01 have been given clearance by Portuguese, Swedish, and British regulatory authorities to begin clinical testing. The trial will begin enrolling patients shortly in a blinded, randomized, placebo-controlled, multicenter Phase I study. ALN-TTR01 is a systemically delivered RNAi therapeutic being developed for the treatment of transthyretin (TTR)-mediated amyloidosis (ATTR), including familial amyloidotic polyneuropathy (FAP) and familial amyloidotic cardiomyopathy (FAC).

ATTR is caused by mutations in the TTR gene, which is expressed predominantly in the liver, that result in the accumulation of pathogenic deposits of mutant and wild-type TTR protein in multiple extra-hepatic tissues, including the peripheral nervous system, heart, and the gastrointestinal tract. Pre-clinical studies in a mouse transgenic model have shown that treatment with ALN-TTR01 results in regression of pre-existing pathogenic TTR deposits in peripheral tissues including dorsal root ganglia, sciatic nerve, stomach, and intestines. Further, ALN-TTR01 administration in non-human primates was found to result in dose-dependent and durable, yet reversible silencing of the TTR gene and plasma levels of TTR.

"We are very excited with our ALN-TTR program, as it holds significant promise as a potential breakthrough therapy for this devastating disease," said Akshay Vaishnaw, M.D., Ph.D., Senior Vice President, Clinical Research at Alnylam. "Having now received approvals for initiation of our Phase I study, we look forward to the next stage of clinical translation in this program with dosing starting in the next few weeks. In particular, we aim to demonstrate safety and tolerability as the study's primary objective. Further, since we can measure plasma levels of TTR in patient plasma samples, we expect to have an opportunity to assess preliminary human proof of concept in this study."

The Phase I trial will be conducted in Portugal, Sweden, and the U.K., and is a randomized, blinded, placebo-controlled dose escalation study designed to enroll approximately 28 patients with ATTR. The primary objective is to evaluate the safety and tolerability of a single dose of intravenous ALN-TTR01, with patients being enrolled into five sequential cohorts of increasing doses of ALN-TTR01 ranging from 0.01 to 0.4 mg/kg. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-TTR01 and assessment of pharmacodynamic activity based on measurements of circulating TTR plasma levels.

ALN-TTR01 is being advanced to clinical development using stable nucleic acid-lipid particles (SNALP) delivery technology developed in collaboration with Tekmira Pharmaceuticals Corporation.

About TTR-Mediated Amyloidosis

TTR-mediated amyloidosis (ATTR) is a hereditary, systemic disease caused by a mutation in the transthyretin (TTR) gene. TTR protein is produced primarily in the liver and is normally a carrier for thyroid hormones and retinol binding proteins. The mutation causes abnormal amyloid proteins to accumulate in and damage body organs and tissue such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and cardiomyopathy. In its severest form, ATTR represents a tremendous unmet medical need with significant morbidity and mortality as an orphan disease; combined, FAP (familial amyloidotic polyneuropathy) and FAC (familial amyloidotic cardiomyopathy) affect approximately 50,000 people worldwide. ATTR patients with FAP have a mean life expectancy of five to 15 years from symptom onset and the only treatment option is liver transplantation; as a result there is a significant need for novel therapeutics to treat patients who have a mutation in the TTR gene.

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. Small interfering RNAs (siRNAs), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic

platform, target the cause of diseases by potently silencing specific 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 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, TTR-mediated amyloidosis (ATTR), hypercholesterolemia, and Huntington's disease. In addition, Alnylam formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for application in manufacturing processes for biotherapeutic products, including recombinant proteins and monoclonal antibodies. 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, Kyowa Hakko Kirin, and Cubist. Alnylam and Isis are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development, and commercialization of microRNA therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit www.alnylam.com.

Alnylam Forward-Looking Statement

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including without limitation, Alnylam's views with respect to the potential for RNAi therapeutics, including ALN-TTR01, its expectations with respect to the timing and success of its clinical and pre-clinical trials, and its plan to initiate a Phase I clinical trial for ALN-TTR01, 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 the company's ability to discover and develop novel drug candidates, such as ALN-TTR01 for the treatment of TTR-mediated amyloidosis (ATTR), and successfully demonstrate efficacy and safety of ALN-TTR01 and other drug candidates in human clinical trials, 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.

SOURCE: Alnylam Pharmaceuticals, Inc.

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