Alnylam Receives Orphan Drug Designation from U.S. Food & Drug Administration for ALN-TTR02, an RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis (ATTR)

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 19, 2012-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today that the U.S. Food & Drug Administration (FDA) has provided Orphan Drug Designation to ALN-TTR02 as a therapeutic for the treatment of familial amyloidotic polyneuropathy (FAP), one of the predominant clinical manifestations of transthyretin (TTR)-mediated amyloidosis (ATTR).

"We are very pleased to have received Orphan Drug Designation from the FDA for ALN-TTR02, the lead effort in our 'Alnylam 5x15' product strategy. We believe RNAi therapeutics represent a novel and exciting approach for ATTR patients and have great potential to make a meaningful impact in the treatment of this devastating disease," said Saraswathy (Sara) Nochur, Ph.D., Vice President, Regulatory Affairs and Quality Assurance at Alnylam. "We look forward to sharing Phase I clinical data from our ALN-TTR02 program early in the third quarter, and, assuming continued positive results, we plan to advance to a pivotal trial in 2013. Alnylam is committed to bringing this high impact medicine to patients afflicted with ATTR."

The FDA Office of Orphan Products Development (OOPD) mission is to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. OOPD provides incentives for sponsors to develop products for rare diseases. The Orphan Drug Designation program provides orphan status to drugs and biologics which are defined as those intended for the safe and effective treatment, diagnosis or prevention of rare diseases/disorders that affect fewer than 200,000 people in the U.S.

About Transthyretin-Mediated Amyloidosis

Transthyretin (TTR)-mediated amyloidosis (ATTR) is a hereditary, systemic disease caused by mutations in the TTR gene. TTR protein is produced primarily in the liver and is normally a carrier for thyroid hormones and retinol binding proteins. Mutations in TTR cause abnormal amyloid proteins to accumulate and damage body organs and tissue such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and/or cardiomyopathy. In its severest form, ATTR represents a major unmet medical need with significant morbidity and mortality as an orphan disease; FAP (familial amyloidotic polyneuropathy) affects approximately 10,000 people worldwide and FAC (familial amyloidotic cardiomyopathy) affects at least 40,000 people worldwide. ATTR patients with FAP have a mean life expectancy of five to 15 years from symptom onset and the only treatment options for early stage disease are liver transplantation and tafamidis (approved in Europe); as a result there is a significant need for novel therapeutics to treat patients who have inherited mutations in the TTR gene.

About ALN-TTR Program

ALN-TTR02 is a systemically delivered RNAi therapeutic being developed for the treatment of ATTR. Alnylam has completed enrollment in a Phase I trial with ALN-TTR02 and expects to present data early in the third quarter of 2012. The company recently initiated a Phase II trial in Europe with ALN-TTR02 aimed at evaluating safety, tolerability, and potential clinical activity of multiple once-monthly doses of ALN-TTR02 in ATTR patients. Specifically, the study will evaluate the potential clinical activity of ALN-TTR02 based on measurement of serum levels of TTR, the disease-causing protein in patients with ATTR. ALN-TTR02 is formulated in a proprietary second-generation lipid nanoparticle technology, using the "MC3" lipid. Assuming positive results from the Phase II study, Alnylam expects to start a pivotal trial for ALN-TTR02 in 2013. Alnylam also plans to advance ALN-TTRsc, which utilizes a GalNAc-conjugate delivery approach and subcutaneous dose administration. Alnylam's goal is to advance ALN-TTRsc to an investigational new drug (IND) filing in the second half of 2012 with data in the first half of 2013.

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 leading the translation of RNAi as a new class of innovative medicines with a core focus on RNAi therapeutics for the treatment of genetically defined diseases, including ALN-TTR for the treatment of transthyretin-mediated amyloidosis (ATTR), ALN-PCS for the treatment of severe hypercholesterolemia, ALN-HPN for the treatment of refractory anemia, ALN-APC for the treatment of hemophilia, and ALN-TMP for the treatment of hemoglobinopathies. As part of its "Alnylam 5x15™" strategy, the company expects to have five RNAi therapeutic products for genetically defined diseases in clinical development, including programs in advanced stages, on its own or with a partner by the end of 2015. Alnylam has additional partner-based programs in clinical or development stages, including ALN-RSV01 for the treatment of respiratory syncytial virus (RSV) infection, ALN-VSP for the treatment of liver cancers, and ALN-HTT for the treatment of Huntington's disease. The company's leadership position on RNAi therapeutics and intellectual property have enabled it to form major alliances with leading companies including Merck, Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, and Cubist. In addition, Alnylam and Isis co-founded Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics; Regulus has formed partnerships with GlaxoSmithKline and Sanofi. Alnylam has also formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for applications in biologics manufacturing, including recombinant proteins and monoclonal antibodies. Alnylam's VaxiRNA™ platform applies RNAi technology to improve the manufacturing processes for vaccines; GlaxoSmithKline is a collaborator in this effort. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 100 peer-reviewed papers, including many in the world's top scientific journals such as Nature, Nature Medicine, Nature Biotechnology, and Cell. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit www.alnylam.com.

About "Alnylam 5x15™"

The "Alnylam 5x15" strategy, launched in January 2011, establishes a path for development and commercialization of novel RNAi therapeutics to address genetically defined diseases with high unmet medical need. Products arising from this initiative share several key characteristics including: a genetically defined target and disease; the potential to have a major impact in a high unmet need population; the ability to leverage the existing Alnylam RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of a new drug application (NDA) with a focused patient database and possible accelerated paths for commercialization. By the end of 2015, the company expects to have five such RNAi therapeutic programs in clinical development, including programs in advanced stages, on its own or with a partner. The "Alnylam 5x15" programs include ALN-TTR for the treatment of transthyretin-mediated amyloidosis (ATTR), ALN-APC for the treatment of hemophilia, ALN-PCS for the treatment of severe hypercholesterolemia, ALN-HPN for the treatment of refractory anemia, and ALN-TMP for the treatment of hemoglobinopathies. Alnylam intends to focus on developing and commercializing certain programs from this product strategy itself in the United States and potentially certain other countries; the company will seek development and commercial alliances for other core programs both in the United States and in other global territories.

Alnylam Forward-Looking Statements

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including without limitation, statements regarding Alnylam's views with respect to the potential for RNAi therapeutics, including ALN-TTR02 and ALN-TTRsc, its expectations with respect to the timing

and success of its clinical trials for ALN-TTR02, its expectations regarding the reporting of data from its ALN-TTR02 clinical trials, and Alnylam's expectations regarding its "Alnylam 5x15" product strategy, 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, without limitation, Alnylam's ability to discover and develop novel drug candidates, successfully demonstrate the efficacy and safety of its drug candidates, including ALN-TTR02 and ALN-TTRsc, the pre-clinical and clinical results for these product candidates, which may not support further development of such product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials for such product candidates, obtaining, maintaining and protecting intellectual property, obtaining regulatory approval for products, competition from others using technology similar to Alnylam's and others developing products for similar uses, and Alnylam's ability to establish and maintain strategic business alliances and new business initiatives, 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

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