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Alnylam Initiates Phase 1 Clinical Trial for ALN-TTRsc02, an Investigational RNAi Therapeutic for the Treatment of TTR-Mediated Amyloidosis

- Company Demonstrates Continued Commitment to ATTR Amyloidosis Patients with Potential for Low Volume, Once Quarterly, Subcutaneous Dose Regimen of ALN-TTRsc02 -

- Company Expects to Present Initial Clinical Results in Late 2016 and to Initiate a Phase 3 Study in 2017 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that it has initiated a Phase 1 clinical trial with ALN-TTRsc02, a subcutaneously administered investigational RNAi therapeutic for the treatment of transthyretin (TTR)-mediated amyloidosis (ATTR amyloidosis). The Phase 1 trial will be conducted in normal healthy volunteers. Initiation of this trial is based on encouraging pre-clinical results, including data presented last year at the Oligonucleotide Therapeutics Society (OTS) meeting held October 11 - 14, 2015. The Company has guided that it expects to report initial clinical data from this study in late 2016, and if positive, plans to initiate a Phase 3 study in 2017.

"We believe ALN-TTRsc02 has the potential to become a best-in-class, once-quarterly, subcutaneous treatment regimen for the treatment of ATTR amyloidosis," said Eric Green, Vice President, General Manager, TTR Program. "With just four doses anticipated per year, ALN-TTRsc02 could offer patients with ATTR amyloidosis an important new therapeutic option to manage their disease. In parallel, we continue to make great progress with patisiran and revusiran, with data from both programs expected to be presented at the International Symposium on Amyloidosis meeting next month."

The Phase 1 trial of ALN-TTRsc02 is a randomized, placebo-controlled, single ascending-dose study designed to enroll up to a total of 100 normal healthy volunteers (NHVs). The primary objective of the study is to evaluate safety and tolerability of a single subcutaneous dose of ALN-TTRsc02. Secondary objectives include evaluation of pharmacokinetics and clinical activity for ALN-TTRsc02, as measured by knockdown of serum TTR levels in NHVs, and identification of the appropriate dose and regimen for a pivotal study.

ALN-TTRsc02 utilizes the company's Enhanced Stabilization Chemistry (ESC)-GalNAc-siRNA conjugate delivery platform, which enables high potency and durability with a very wide therapeutic index. Clinical results from other RNAi therapeutic programs in Alnylam's pipeline that utilize ESC-GalNAc technology have demonstrated robust target gene knockdown and durability supportive of the potential for a quarterly and, possibly, bi-annual dosing regimen.

ALN-TTRsc02 Pre-clinical Data
In pre-clinical studies, including those in non-human primates (NHPs), ALN-TTRsc02 achieved potent and highly durable knockdown of serum TTR of up to 99% with multi-month durability achieved after just a single dose at 1 mg/kg, supportive of a potentially once quarterly dose regimen. In 13-week toxicology studies, ALN-TTRsc02, when given monthly for four doses, was generally well-tolerated with no significant adverse events at doses as high as 120 mg/kg in rats or 300 mg/kg in NHPs. There were no effects on platelet counts observed in either study.

About ATTR Amyloidosis
Transthyretin (TTR)-mediated amyloidosis (ATTR amyloidosis) is a progressively debilitating and often fatal disease caused by deposition of TTR in peripheral tissues. TTR protein is produced primarily in the liver and is normally a carrier of vitamin A. In hereditary ATTR amyloidosis (hATTR), 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. hATTR represents a major unmet medical need with significant morbidity and mortality; hATTR with polyneuropathy (hATTR-PN) - also known as familial amyloidotic polyneuropathy (FAP) - affects approximately 10,000 people worldwide and hATTR with cardiomyopathy (hATTR-CM) - also known as familial amyloidotic cardiomyopathy (FAC) - is estimated to affect at least 40,000 people worldwide. hATTR-PN patients have a life expectancy of 5 to 15 years from symptom onset, and the only approved treatment options for early stage disease are liver transplantation and tafamidis (approved in Europe, certain countries in Latin America and Japan, where it is approved for all stages of disease). hATTR-CM is fatal within 2.5 to 5 years of diagnosis and treatment is currently limited to supportive care. Wild-type amyloidosis (wtATTR) - also called senile systemic amyloidosis (SSA) - is a non-hereditary form of TTR cardiac amyloidosis caused by idiopathic deposition of wild-type TTR; its prevalence is generally unknown, but is associated with advanced age. There is a significant need for novel therapeutics to treat patients with ATTR amyloidosis.

Sanofi Genzyme Alliance
In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate and expand the development and commercialization of RNAi therapeutics across the world. The alliance is structured as a multi-product geographic alliance in the field of rare diseases. Alnylam retains product rights in North America and Western Europe, while Sanofi Genzyme obtained the right to access certain programs in Alnylam's current and future Genetic Medicines pipeline in the rest of the world (ROW) through the end of 2019, together with certain broader co-development/co-commercialization rights and/or global rights for certain programs. In the case of patisiran, Alnylam will advance the product in North America and Western Europe, while Sanofi Genzyme will advance the product in the ROW. In the case of revusiran, Alnylam and Sanofi Genzyme will co-develop/co-commercialize the product in North America and Western Europe, while Sanofi Genzyme will advance the product in the ROW. In the case of ALN-TTRsc02, Sanofi Genzyme will have the right to opt into the program with co-development/co-commercialization rights.

About 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 RNA (siRNA), 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. Alnylam's pipeline of investigational RNAi therapeutics is focused in 3 Strategic Therapeutic Areas (STArs): Genetic Medicines, with a broad pipeline of RNAi therapeutics for the treatment of rare diseases; Cardio-Metabolic Disease, with a pipeline of RNAi therapeutics toward genetically validated, liver-expressed disease targets for unmet needs in cardiovascular and metabolic diseases; and Hepatic Infectious Disease, with a pipeline of RNAi therapeutics that address the major global health challenges of hepatic infectious diseases. In early 2015, Alnylam launched its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics as a whole new class of innovative medicines. Specifically, by the end of 2020, Alnylam expects to achieve a company profile with 3 marketed products, 10 RNAi therapeutic clinical programs - including 4 in late stages of development - across its 3 STArs. The company's demonstrated commitment to RNAi therapeutics has enabled it to form major alliances with leading companies including Ionis, Novartis, Roche, Takeda, Merck, Monsanto, The Medicines Company, and Sanofi Genzyme. In addition, Alnylam holds an equity position in Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 200 peer-reviewed papers, including many in the world's top scientific journals such as *Nature, Nature Medicine, Nature Biotechnology, Cell, New England Journal of Medicine,* and *The Lancet*. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information about Alnylam's pipeline of investigational RNAi therapeutics, please visit www.alnylam.com.

Alnylam Forward Looking Statements
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-TTRsc02, patisiran, and revusiran, its expectations regarding the timing of the start of clinical studies for ALN-TTRsc02 and presentation of clinical data for ALN-TTRsc02, patisiran, and revusiran, and its expectations regarding its STAr pipeline growth strategy and its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics, 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 and delivery approaches, successfully demonstrate the efficacy and safety of its drug candidates, the pre-clinical and clinical results for its product candidates, which may not be replicated or continue to occur in other subjects or in additional studies or otherwise support further development of product candidates for a specified indication or at all, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, obtaining regulatory approval for products, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to manage operating expenses, Alnylam's ability to obtain additional funding to support its business activities and establish and maintain strategic business alliances and new business initiatives, Alnylam's dependence on third parties for development, manufacture, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings that Alnylam makes with the SEC. 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 explicitly disclaims any obligation to update any forward-looking statements.

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