Alnylam Completes Submission of New Drug Application to U.S. Food and Drug Administration (FDA) for Patisiran for the Treatment of Hereditary ATTR (hATTR) Amyloidosis

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– Patisiran Could Become the First in a New Class of Medicines Known as RNAi Therapeutics –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 12, 2017-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today the completion of the rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for patisiran, an investigational RNAi therapeutic targeting transthyretin (TTR) for the treatment of adults with hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis). The rolling submission began on November 15, 2017 with the nonclinical and chemistry, manufacturing and controls components submitted, and now submission of the clinical data completes the filing. Alnylam has requested priority review for the application which, if granted, could result in a six-month review process. Patisiran previously received Fast Track and Breakthrough Therapy designations from the FDA, and recently received an expanded Orphan Drug Designation for ATTR amyloidosis.

“In November, we reported promising results from the APOLLO Phase 3 study of patisiran which showed amelioration of neurological impairment, improved quality of life, and reduced disease symptoms and disability in hATTR amyloidosis patients with polyneuropathy,” said Eric Green, Vice President and General Manager of the TTR program. “In less than 90 days from first reporting the top-line data, the completion of Alnylam’s first NDA submission is an historic event, bringing patisiran one step closer to patients living with hATTR amyloidosis. We look forward to the exciting prospect of introducing the first FDA-approved RNAi therapeutic, marking the arrival of a new class of medicines.”

“People living with hATTR amyloidosis currently have no FDA-approved options to treat this devastating, often fatal disease,” said Isabelle Lousada, President and Chief Executive Officer of the Amyloidosis Research Consortium (ARC). “The ARC applauds this significant milestone for patisiran and we are hopeful this therapy will be approved for patients in the U.S. who are desperately awaiting treatment options.”

Patisiran also has been granted accelerated assessment by the European Medicines Agency. Alnylam, in collaboration with Sanofi Genzyme, intends to file a Marketing Authorization Application in the European Union around year-end. Sanofi Genzyme is currently preparing for regulatory filings for patisiran in Japan, Brazil and other countries, to begin in the first half of 2018. Pending regulatory approvals, Alnylam will commercialize patisiran in the U.S., Canada and Western Europe, with Sanofi Genzyme commercializing the product in the rest of the world, including certain Central and Eastern European countries of the European Union .

About Patisiran
Patisiran is an investigational intravenously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of hereditary ATTR amyloidosis. It is designed to silence specific messenger RNA, potentially blocking the production of TTR protein before it is made. This may help to enable the clearance of TTR amyloid deposits in peripheral tissues and potentially restore function to these tissues. The FDA recently granted a request to amend the Orphan Drug Designation for patisiran to the treatment of transthyretin-mediated amyloidosis (ATTR amyloidosis). The safety and efficacy of patisiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

About APOLLO Phase 3 Study
The APOLLO Phase 3 study (N=225) was a randomized, double-blind, placebo-controlled, global study designed to evaluate the efficacy and safety of patisiran in hATTR amyloidosis patients with symptomatic polyneuropathy. The study was completed in August 2017 and detailed study results were presented at the 1st European ATTR Amyloidosis Meeting for Patients and Doctors on November 2, 2017. All patients completing the APOLLO Phase 3 study are eligible to screen for the global open-label extension study, in which they have the opportunity to receive patisiran on an ongoing basis.

About hATTR Amyloidosis
Hereditary transthyretin (TTR)-mediated (hATTR) amyloidosis is an inherited, progressively debilitating, and often fatal disease caused by mutations in the TTR gene. TTR protein is produced primarily in the liver and is normally a carrier of vitamin A. 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 amyloidosis represents a major unmet medical need with significant morbidity and mortality, affecting approximately 50,000 people worldwide. hATTR amyloidosis patients have a life expectancy of 2.5 to 15 years from symptom onset, and the only approved treatment options are liver transplantation for early stage disease and tafamidis (approved in Europe, Japan and certain countries in Latin America, specific indication varies by region). There is a significant need for novel therapeutics to help treat patients with hATTR amyloidosis.

About LNP Technology
Alnylam has licenses to Arbutus Biopharma LNP intellectual property for use in RNAi therapeutic products using LNP technology.

About RNAi
RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery has been heralded as “a major scientific breakthrough that happens once every decade or so,” and was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. By harnessing the natural biological process of RNAi occurring in our cells, 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, function upstream of today’s medicines by potently silencing messenger RNA (mRNA) – the genetic precursors – that encode for disease-causing proteins, thus preventing them from being made. This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

Alnylam - Sanofi Genzyme Alliance
In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate the advancement of RNAi therapeutics as a potential new class of innovative medicines for patients around the world with rare genetic diseases. The alliance enables Sanofi Genzyme to expand its rare disease pipeline with Alnylam's novel RNAi technology and provides access to Alnylam's R&D engine, while Alnylam benefits from Sanofi Genzyme's proven global capabilities to advance late-stage development and, upon commercialization, accelerate market access for these promising genetic medicine products. In the case of patisiran, Alnylam will advance the product in the United States, Canada and Western Europe, while Sanofi Genzyme will advance the product in the rest of the world.

About Alnylam Pharmaceuticals

Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a whole new class of innovative medicines with the potential to transform the lives of people afflicted with rare genetic, cardio-metabolic, and hepatic infectious diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust discovery platform and deep pipeline of investigational medicines, including four product candidates that are in late-stage development. Looking forward, Alnylam will continue to execute on its "Alnylam 2020" strategy of building a multi-product, commercial-stage biopharmaceutical company with a sustainable pipeline of RNAi-based medicines to address the needs of patients who have limited or inadequate treatment options. Alnylam employs over 600 people in the U.S. and Europe and is headquartered in Cambridge, MA. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam or on LinkedIn.

Alnylam Forward Looking Statements
Various statements in this release concerning Alnylam's future expectations, plans and prospects, including, without limitation, Alnylam's plans for and the expected timing of a regulatory filing seeking approval for patisiran from regulatory authorities in the United States, Europe and ROW countries, its plans for the commercialization of patisiran if approved by regulatory authorities, and expectations regarding 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 and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other 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 product 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 or advice of regulatory agencies, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing, delays, interruptions or failures in the manufacture and supply of its product candidates, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its intellectual property rights against third parties and defend its patent portfolio against challenges from third parties, obtaining and maintaining regulatory approval, pricing and reimbursement for products, progress in establishing a commercial and ex-United States infrastructure, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to manage its growth and operating expenses, 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 and distribution of products, the outcome of litigation, the risk of government investigations, 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, except to the extent required by law, to update any forward-looking statements.

Patisiran has not been approved by the U.S. Food and Drug Administration, European Medicines Agency, or any other regulatory authority and no conclusions can or should be drawn regarding the safety or effectiveness of this investigational therapeutic.

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