Alnylam Receives Positive Opinion for Orphan Drug Designation in the European Union for ALN-TTRsc02, a Subcutaneously Delivered Investigational RNAi Therapeutic for the Treatment of Transthyretin-Mediated Amyloidosis

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 23, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), the leading RNAi therapeutics company, today announced that the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP) has issued a positive opinion recommending ALN-TTRsc02, an investigational, subcutaneously administered RNAi therapeutic, for designation as an orphan medicinal product for the treatment of transthyretin (TTR)-mediated (ATTR) amyloidosis.

"We are very pleased to have received a positive opinion from the EMA COMP on our application for Orphan Drug Designation for ALN-TTRsc02," said Rena Denoncourt, Program Leader, ALN-TTRsc02 Program at Alnylam. "With potent and durable TTR knockdown, we believe ALN-TTRsc02 holds great promise as an investigational, once-quarterly, low volume, subcutaneously administered RNAi therapeutic for the treatment of a broad spectrum of patients with ATTR amyloidosis. We look forward to advancing ALN-TTRsc02 into Phase 3 later this year."

Orphan Drug Designation by the European Commission provides regulatory and financial incentives for companies to develop and market therapies that treat a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the European Union (EU), and where no satisfactory treatment is available. In addition to a 10-year period of marketing exclusivity in the EU after product approval, Orphan Drug Designation provides incentives for companies seeking protocol assistance from the EMA during the product development phase and direct access to centralized marketing authorization.

About ALN-TTRsc02

ALN-TTRsc02 is an investigational, subcutaneously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of ATTR amyloidosis. It is designed to target and silence specific messenger RNA, potentially blocking the production of TTR protein before it is made. This may help to reduce the deposition and facilitate the clearance of TTR amyloid deposits in peripheral tissues and potentially restore function to these tissues. The safety and efficacy of ALN-TTRsc02 have not been evaluated by the U.S. Food and Drug Administration, European Medicines Agency or any other health authority.

About ATTR amyloidosis

Transthyretin (TTR)-mediated (ATTR) amyloidosis is a rare, progressively debilitating, and often fatal disease caused by misfolded TTR proteins that accumulate as amyloid deposits in multiple tissues including the nerves, heart, and GI tract. TTR protein is primarily produced in the liver and is normally a carrier of vitamin A. Hereditary ATTR (hATTR) amyloidosis is an inherited, progressive disease that occurs when mutations in the TTR gene cause abnormal amyloid proteins to accumulate and damage body organs and tissues, such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and/or cardiomyopathy, as well as other disease manifestations. hATTR amyloidosis represents a major unmet medical need with significant morbidity and mortality, affecting approximately 50,000 people worldwide. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy. Wild-type ATTR (wtATTR) amyloidosis is a nonhereditary, progressive disease of undefined etiology that occurs when misfolded TTR proteins accumulate as amyloid deposits in multiple organs, including the heart, resulting predominantly in cardiomyopathy, leading to heart failure and mortality within 2 to 6 years. Prevalence of wtATTR amyloidosis is uncertain, however estimates suggest fewer than 200,000 patients across the U.S. and Europe.

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.

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 800 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, its expectations as to

the prospects of ALN-TTRsc02, 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 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 Annual Report on Form 10-K 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.

ALN-TTRsc02 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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