Alnylam Submits CTA Application for ALN-AGT, an Investigational RNAi Therapeutic for the Treatment of Hypertension in High Unmet Need Settings

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− Company Expects to Initiate a Phase 1 Study in Mid-2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 11, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), the leading RNAi therapeutics company, announced today that the Company has submitted a clinical trial authorization (CTA) application to The Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom to initiate a Phase 1 study of ALN-AGT, an investigational RNAi therapeutic targeting angiotensinogen (AGT) for the treatment of hypertension in high unmet need populations, including patients with resistant or refractory hypertension, chronic kidney disease or heart failure. The Company plans to initiate a Phase 1 study in mid-2019, upon obtaining MHRA approval.

“We are excited to expand our efforts in the cardiovascular disease setting in pursuit of a novel approach to treat hypertension, particularly given that hypertensive disorders are the leading preventable cause of death in modern society. With RNAi, we believe there’s an opportunity to reimagine the treatment of hypertension in high unmet need settings,” said Lauren Melton, Senior Director, Program Leader, ALN-AGT program at Alnylam. “We believe RNAi-mediated angiotensinogen silencing represents a novel approach with the potential to provide effective and highly durable control of blood pressure for patients with resistant or refractory hypertension, chronic kidney disease or heart failure. Pending feedback from the MHRA, we look forward to evaluating the safety and preliminary pharmacodynamic activity of this molecule in patients with hypertension.”

About ALN-AGT

ALN-AGT is an investigational, subcutaneously administered RNAi therapeutic targeting angiotensinogen (AGT) in development for the treatment of hypertension in high unmet need populations. ALN-AGT utilizes Alnylam's Enhanced Stabilization Chemistry Plus (ESC+) GalNAc-conjugate technology, which enables subcutaneous dosing with increased selectivity and a wide therapeutic index. The safety and efficacy of ALN-AGT have not been evaluated by the FDA, EMA or any other health authority.

About Hypertension

Hypertension is a complex multifactorial disease clinically defined as a systolic blood pressure of above 130 or a diastolic blood pressure of greater than 80 mmHg. Approximately 47 percent of U.S. adults live with hypertension with more than half of patients on medication remaining above the blood pressure target level. Despite the availability of antihypertensive medications, there remains an unmet medical need, particularly given the poor rates of adherence to existing therapies and peak and trough effects. In particular, there are a number of high unmet need settings where novel approaches to hypertension are warranted, including resistant and refractory hypertension, chronic kidney disease, and heart failure.

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 new class of medicines, known as RNAi therapeutics, is now a reality. 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, hepatic infectious, and central nervous system (CNS)/ocular 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. Alnylam’s first U.S. FDA-approved RNAi therapeutic is ONPATTRO® (patisiran) lipid complex injection available in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. In the EU, ONPATTRO is approved for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. Alnylam has a deep pipeline of investigational medicines, including five 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 1,000 people worldwide 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, the potential of RNAi therapeutics, in particular ALN-AGT, Alnylam's filing of a CTA for ALN-AGT and its expectations regarding the anticipated timing for initiation of a Phase 1 study, 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, successfully launching, marketing and selling its approved products globally, Alnylam's ability to successfully expand the indication for ONPATTRO in the future, 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 10K 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-AGT has not been evaluated by the FDA, EMA, 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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