Alnylam Doses First Patient in Phase 1 Study of ALN-AGT, an Investigational RNAi Therapeutic for the Treatment of Hypertension

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− Initial Results Expected in Late 2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 31, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the first patient has been dosed in the Company's 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 expects to report initial results in late 2019.

"We are pleased to have initiated dosing in this Phase 1 study with the goal of evaluating the safety and preliminary pharmacokinetic and pharmacodynamic activity of ALN-AGT in patients with hypertension," said Lauren Melton, Senior Director, Program Leader, ALN-AGT program at Alnylam. "We believe RNAi-mediated angiotensinogen silencing represents a novel and targeted approach with the potential to offer robust and highly durable control of blood pressure for patients with resistant or refractory hypertension."

The Phase 1 study is a multi-center, randomized, double-blind, placebo-controlled trial designed to evaluate the safety, tolerability, pharmacokinetic, and pharmacodynamic effects of subcutaneously administered ALN-AGT in patients with essential hypertension. The study will be conducted in four parts: Part A: single ascending dose phase in hypertensive patients; Part B: single dose in hypertensive patients with controlled salt intake; Part C: multi-dose phase in hypertensive patients; and Part D: multi-dose phase in hypertensive patients who are obese. In Parts C and D, once daily oral doses of irbesartan (angiotensin II receptor blocker) will be used as the active comparator. Patients will be randomized 2:1 ALN-AGT to placebo or ALN-AGT to irbesartan. The planned enrollment for this study, including optional cohorts, is up to 168 patients.

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 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/ocular diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of diseases with high unmet need. ONPATTRO® (patisiran) is the first-ever RNAi therapeutic approved by the U.S. FDA for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults and by the EMA for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. Alnylam has a deep pipeline of investigational medicines, including six product candidates in Phase 3 studies. 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. Headquartered in Cambridge, MA, Alnylam employs over 1,200 people worldwide. 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, and its expectations regarding the anticipated timing for initial results from the Phase 1 study of ALN-AGT, 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 Quarterly Report on Form 10Q 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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