Alnylam Reports Preclinical Data Demonstrating Central Nervous System (CNS) Delivery of RNAi Therapeutics

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− Novel siRNA Conjugates Achieve Robust, Durable, and Broadly Distributed Silencing of CNS Gene Transcripts Following a Single Intrathecal Injection –

− Company Expects First CNS-Targeted Development Candidate in 2018, First IND in Late 2019/Early 2020, and Capacity for Sustained Pipeline of One or More CNS INDs per Year Thereafter −

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 8, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the Company has achieved delivery of novel small interfering RNA (siRNA) conjugates to the central nervous system (CNS) and is planning to advance a pipeline of investigational RNAi therapeutics into clinical development. RNAi therapeutics have the potential to prevent or reverse neurodegenerative diseases caused by dominantly inherited genes, such as in Alzheimer's, Huntington's, Parkinson's, and amyotrophic lateral sclerosis (ALS), where there are limited to no treatment options. The Company plans to complete selection of its first CNS-targeted development candidate (DC) in 2018, and then expects to file its first investigational new drug (IND) or IND equivalent in late 2019/early 2020, with the potential for one or more INDs per year thereafter. Alnylam's planned emerging pipeline of CNS-directed investigational RNAi therapeutics is in addition to the Company's continued advancement of GalNAc-conjugated siRNAs toward a broad range of liver-expressed disease targets for the Company's Genetic Medicine, Cardiometabolic Disease, and Hepatic Infectious Disease Strategic Therapeutic Areas (STArs).

"Over the past 15 years, Alnylam has advanced conjugate-based delivery of investigational RNAi therapeutics with multiple transformative discoveries, paving the way for development of a whole new class of innovative medicines. We have now applied our learnings, including additional chemistry advances, to enable delivery of siRNAs beyond the liver to the CNS, where there are a large number of unmet needs well suited for RNAi therapeutics. As we begin to advance our CNS pipeline, initial efforts are focused on genetically validated CNS targets, use of biomarkers for initial proof-of-concept, and disease settings with high unmet need and a definable path to regulatory approval and patient access," said Kevin Fitzgerald, Ph.D., Senior Vice President, Research at Alnylam. "We believe the robust potency, durability, and tolerability of liver-targeted RNAi therapeutics in Alnylam's broader clinical pipeline set a strong foundation for the future development of investigational CNS-targeted RNAi therapeutics, where we expect to select our first development candidate later this year."

Alnylam presented initial results from preclinical studies at the TIDES: Oligonucleotide and Peptide Therapeutics 2018 Annual Meeting being held May 7-10 in Boston, MA., as part of a plenary talk entitled "Delivering on RNAi Therapeutics: Patisiran and Beyond." In a rat preclinical study, a single intrathecal injection of a novel siRNA conjugate resulted in broad distribution across the brain and spinal cord regions. Robust and highly durable silencing of a disease target gene transcript was seen in all key anatomical regions of the brain and spinal cord. Specificity of the silencing effect was confirmed with a second siRNA conjugate targeting an independent gene transcript ubiquitously expressed in the CNS. The novel siRNA conjugates utilize Alnylam's enhanced stabilization chemistry (ESC) platform with further modifications to enable broad CNS delivery and efficient uptake in neuronal cells.

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, Alnylam's views with respect to the potential for CNS-targeted investigational RNAi therapeutics, the expected timelines for identification of a CNS-targeted development candidate, as well as expected potential CNS-targeted IND or IND equivalent filings, and expectations regarding "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.

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