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Alnylam Initiates Phase 2 Clinical Study of Cemdisiran (ALN-CC5) in Patients with Atypical Hemolytic-Uremic Syndrome (aHUS)

- Company Expects to Report Initial Patient Data in 2018 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that it has initiated a Phase 2 clinical study with cemdisiran (formerly known as ALN-CC5), a subcutaneously administered investigational RNAi therapeutic targeting complement component C5 for the treatment of complement-mediated diseases. The trial is being conducted in patients with atypical hemolytic-uremic syndrome (aHUS) and will evaluate the effect of C5 knockdown on hematologic response and renal function, as well as safety and tolerability. The Company expects to report initial clinical proof of concept data from this trial in late 2018.

"C5 is a clinically validated target in patients with aHUS. We believe cemdisiran can potentially offer clinical benefit for patients and physicians with durable maintenance of disease remission with an infrequent subcutaneous injection," said Thomas Hoock, Ph.D., Vice President, Program Lead, Cemdisiran at Alnylam. "We believe that clinical activity for cemdisiran as monotherapy, if demonstrated in the Phase 2 aHUS study, has the potential to open broader opportunities for this investigational RNAi therapeutic in other complement-mediated diseases, and we look forward to initial data in 2018."

Cemdisiran Phase 2 Study Design
The Phase 2 trial will follow an adaptive study design with an initial cohort of 12 aHUS patients who are not currently treated with an anti-C5 monoclonal antibody. Patients will receive a 600 mg dose of cemdisiran once every 4 weeks, with an option of reduced dose level and/or dose frequency in a subsequent cohort. The primary endpoint of the Phase 2 study in aHUS patients is normalization of platelet counts, with secondary endpoints including hematologic and thrombotic microangiopathy (TMA) response, improvement in renal function, safety and tolerability.

About Cemdisiran
Formerly known as ALN-CC5, cemdisiran (pronounced "sem-DEE-si-ran") is an investigational RNAi therapeutic targeting the C5 component of the complement pathway in development for the treatment of complement-mediated diseases. The complement system plays a central role in immunity as a protective mechanism for host defense, but its dysregulation results in life-threatening complications in a broad range of human diseases including paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic-uremic syndrome (aHUS), myasthenia gravis, neuromyelitis optica, and membranous nephropathy, amongst others. Complement component C5, which is predominantly expressed in liver cells, is a genetically and clinically validated target; loss of function human mutations are associated with an attenuated immune response against certain infections and intravenous anti-C5 monoclonal antibody (mAb) therapy has demonstrated clinical activity and tolerability in a number of complement-mediated diseases. A subcutaneously administered RNAi therapeutic that silences C5 represents a novel approach for the potential treatment of complement-mediated diseases. Cemdisiran utilizes Alnylam's ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index.

The safety and efficacy of cemdisiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

About RNAi
RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding protein synthesis in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of 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, target the cause of diseases by potently silencing specific mRNAs, with the goal of preventing disease-causing proteins from being made.

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 patients who have limited or inadequate treatment options. Based on Nobel Prize-

winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of 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. 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 cemdisiran for the treatment of patients with aHUS and potentially other complement-mediated diseases, expectations regarding the timing for initial clinical data from a Phase 2 clinical study of cemdisiran 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.

Cemdisiran 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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