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Alnylam Continues Leadership in RNAi Technologies and Delivery with New Pre-Clinical Data Presented on "Enhanced Stabilization Chemistry Plus" (ESC+) GalNAc-siRNA Conjugate Platform at 13th Annual Meeting of the Oligonucleotide Therapeutics Society

- ESC+ Platform Incorporates Novel Design Features, Including Glycol Nucleic Acid (GNA) Modifications, that Confer Greater Specificity, Further Improving Already Wide Therapeutic Index by Over 6-fold -

- First ESC+ Development Candidate, ALN-AAT02, in Development for Treatment of Alpha-1 Antitrypsin (AAT) Deficiency-Associated Liver Disease, Expected to Enter Clinical Trials in 2018 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), the leading RNAi therapeutics company, today announced that the Company presented new pre-clinical data highlighting its next generation "Enhanced Stabilization Chemistry Plus" (ESC+) GalNAc-siRNA conjugate platform at the 13th Annual Meeting of the Oligonucleotide Therapeutics Society (OTS), held September 24 - 27, 2017 in Bordeaux, France.

ESC+ GalNAc conjugates utilize advanced design features to further improve specificity, including a glycol nucleic acid (GNA) modification in the antisense seed region of the siRNA, while maintaining potency and durability. The data presented at OTS indicated that incorporation of GNA destabilizes seed-driven pairing with partially complementary transcripts, thus greatly reducing potential off-target effects while maintaining on-target pairing and activity. Additionally, it was shown that GNA modifications confer enhanced specificity and a greater-than 6-fold improvement in therapeutic index as observed in pre-clinical studies in rodents. The ESC+ design is now being applied to all of Alnylam's pre-clinical programs and has shown successful translation of potency from rodents to non-human primates. Alnylam intends to employ its ESC+ siRNA-conjugate platform in all future development programs.

"At Alnylam, we've been successful in advancing our ESC GalNAc-siRNA conjugate platform with many potent and generally well tolerated investigational RNAi therapeutics in clinical development, including in Phase 3 studies. Nevertheless, we continue to strive to even further optimize our RNAi therapeutics platform to achieve improved target specificity and an even greater therapeutic index. Accordingly, we were pleased to share these new pre-clinical results at this year's OTS meeting, highlighting our ESC+ GalNAc conjugate platform," said Kevin Fitzgerald, Ph.D., Senior Vice President, Research at Alnylam. "Our goal is to employ the ESC+ chemistry in all future development candidates, beginning with ALN-AAT02, which we plan to advance into clinical development in 2018. We believe that by implementing platform improvements that preemptively address potential off-target effects we can further enhance the therapeutic index of our investigational RNAi therapeutics for all future programs in our pipeline."

In addition to new data on the Company's ESC+ platform, Alnylam scientists and collaborators presented additional pre-clinical findings showing continued leadership in RNAi technologies and delivery. First, Alnylam scientists presented further advances toward optimizing the Company's GalNAc-siRNA conjugate platform. These included studies to further improve the mechanistic understanding of conjugate duration of activity as well as the development of advanced ESC designs with significantly improved metabolic stability and *in vivo* efficacy. Further, new data on Alnylam's Reversir™ platform were presented. Specifically, optimizations were implemented that enable rapid reversal of siRNA-mediated mRNA silencing, providing the means to fine-tune the pharmacology of GalNAc-siRNA conjugates. Finally, pre-clinical data demonstrating extra-hepatic siRNA delivery, involving Centyrins, a novel class of highly stable FN3 domain proteins, were also presented as part of a research collaboration with Janssen Research & Development, LLC. Centyrin-siRNA conjugates showed excellent cross-tumor penetration and mediated robust target knockdown in a mouse xenograft tumor model. Also, the generalizability of this approach was demonstrated *in vitro* using Centyrins for a number of different receptors and gene targets.

These results can be viewed on the Capella section of the Alnylam website.

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 Reversir™

Alnylam's Reversir platform utilizes GalNAc-conjugated single-stranded high affinity oligonucleotides complementary to the guide strand of the siRNA to rapidly reverse RNAi-mediated silencing of target transcripts. Reversir provides the means to fine-tune the pharmacology of GalNAc-siRNA conjugates by enabling control of duration of silencing.

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 its ESC+ GalNAc-siRNA-conjugate platform to address potential off-target effects and enhance the specificity of its investigational therapeutics, its plans to employ its ESC+ siRNA-conjugate platform in all future development programs, expectations regarding the timing for initiation of a clinical study for ALN-AAT02, 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.

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