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Alnylam Presents Initial 2017 Pipeline Goals at R&D Day with Focus on Alnylam 2020 Strategy

- Three Mid- to Late-Stage Programs Advancing Toward Potential Commercialization -

- In Addition, Company Announces Positive Preliminary Results from Phase 1 Study of ALN-TTRsc02 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, is hosting its R&D Day in New York City today. During the event, the Company will discuss its pipeline goals for 2017, focusing primarily on three mid- to late-stage programs advancing toward potential commercialization and on the path to achieving its *Alnylam 2020* goals. The highlighted programs, all of which are expected to be in Phase 3 trials or in registration in 2017, include patisiran in development for the treatment of hereditary ATTR amyloidosis (hATTR) with polyneuropathy, fitusiran in development for the treatment of hemophilia and rare bleeding disorders, and givosiran (formerly ALN-AS1) in development for the treatment of acute hepatic porphyrias. Alnylam believes that all three investigational RNAi therapeutics have the potential to become transformative medicines for patients afflicted with these rare and ultra-rare orphan diseases with high unmet medical need. In addition, Alnylam will present preliminary positive Phase 1 study results for ALN-TTRsc02, an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis.

"In the coming year, we look forward to the advancement of our mid- to late-stage pipeline and the continued evolution of our organization, as we prepare to make the planned transition from a development-stage company toward a multi-product, commercial-stage biopharmaceutical company," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "As we near 2020, we continue to be focused on pipeline execution and the building of capabilities that we believe will enable us to achieve our *Alnylam 2020* goals, bringing RNAi therapeutics to patients in need around the world."

2017 Pipeline Goals
Patisiran, an investigational RNAi therapeutic in development for the treatment of hATTR with polyneuropathy. Alnylam plans to:

- Complete APOLLO Phase 3 study in 2017.
  - The Company expects to report top-line data from the APOLLO Phase 3 trial in mid-2017 and additional results in late 2017.
  - Assuming positive Phase 3 data, Alnylam plans to submit a New Drug Application (NDA) and Marketing Authorisation Application (MAA) for patisiran at year-end 2017.
- Present 36-month data from patients originally enrolled in the patisiran Phase 2 Open-Label Extension (OLE) study in late 2017.

Fitusiran, an investigational RNAi therapeutic for the treatment of hemophilia and rare bleeding disorders. Alnylam plans to:

- Initiate the ATLAS Phase 3 program in early 2017.
  - The ATLAS program is expected to consist of three separate Phase 3 trials: ATLAS-INH in severe hemophilia A and B patients with inhibitors; ATLAS-A/B in severe hemophilia A and B patients *without* inhibitors; and, ATLAS-PPX in severe hemophilia A and B patients with or without inhibitors, switching from prophylactic factor or bypassing agent therapy to fitusiran prophylaxis.
- Present data from ongoing fitusiran trials in mid- and late 2017.

Givosiran, an investigational RNAi therapeutic for the treatment of acute hepatic porphyrias. Alnylam plans to:

- Present additional data from the ongoing randomized, double-blind, placebo-controlled Phase 1, Part C study in recurrent attack acute intermittent porphyria (AIP) patients in mid-2017.
- Initiate a givosiran Phase 3 trial in late 2017.

Alnylam also plans to continue support of The Medicines Company's advancement of inclisiran (formerly ALN-PCSsc) into

Phase 3 studies in early and mid-2017. In addition, the Company plans to continue advancement of its earlier-stage clinical pipeline programs with multiple data read-outs expected throughout 2017.

ALN-TTRsc02 Preliminary Phase 1 Data
The Company also announced preliminary clinical data from its Phase 1 study of ALN-TTRsc02, an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis. The Phase 1 trial is a randomized, placebo-controlled, single ascending-dose study in healthy volunteers receiving fixed subcutaneous doses ranging from 5 mg to 300 mg.

New results (N=48) showed:

- Single subcutaneous doses of ALN-TTRsc02 achieved robust transthyretin (TTR) knockdown of up to 98.4 percent (mean max of 97.1 ± 0.5 percent), with durability for well over four months. At a dose of 50 mg, ALN-TTRsc02 achieved a mean knockdown at day 90 of 86.2%. Based on these results, the Company believes that a once-quarterly, fixed dose of 25 to 50 mg of ALN-TTRsc02 could achieve clamped and potentially clinically meaningful reductions exceeding 80% of TTR, the disease-causing protein in hATTR amyloidosis.
- In addition, ALN-TTRsc02 was generally well tolerated in healthy volunteers, with no serious adverse events and no discontinuations due to adverse events. All adverse events reported were mild or moderate in severity and included transient injection site reactions (redness and pain), pruritus, cough, nausea, fatigue and abdominal pain. No significant changes were reported in hematologic or laboratory parameters (e.g., liver function tests), vital signs or physical exams.

"At Alnylam, we remain committed to the goal of bringing RNAi therapeutics to hATTR amyloidosis patients. We are encouraged by these initial results from ALN-TTRsc02 and the broader advances of our Enhanced Stabilization Chemistry (ESC) platform that have enabled an over 100-fold improvement of potency and a meaningful improvement in durability in our GalNAc-siRNA conjugate efforts," said Eric Green, Vice President, General Manager of the TTR Program. "Pending positive results from the APOLLO Phase 3 study of patisiran, we plan to engage regulators to align on a development path for ALN-TTRsc02. With potent TTR knockdown and durability supportive of once-quarterly dosing, we believe ALN-TTRsc02 has the potential to be a best-in-class therapeutic for patients with all forms of ATTR amyloidosis."

Sanofi Genzyme Alliance
In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate and expand the development and commercialization of RNAi therapeutics across the world. The alliance is structured as a multi-product geographic alliance in the field of rare diseases. Alnylam retains product rights in the United States, Canada and Western Europe, while Sanofi Genzyme obtained the right to access certain programs in Alnylam's current and future Genetic Medicines pipeline in the rest of the world (ROW) through the end of 2019, together with certain broader co-development/co-commercialization rights and global rights for certain products. In the case of patisiran, Alnylam will advance the product in the United States, Canada and Western Europe, while Sanofi Genzyme will advance the product in the ROW. In the case of fitusiran, Sanofi Genzyme has elected to opt in to co-develop (through Sanofi R&D) and co-commercialize fitusiran in the United States, Canada and Western Europe, in addition to developing and commercializing fitusiran in its ROW territories.

About RNAi
RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off 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, thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

About LNP Technology
Alnylam has licenses to Arbutus LNP intellectual property for use in RNAi therapeutic products using LNP technology.

About Alnylam Pharmaceuticals
Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is leading the translation of RNAi as a new class of innovative medicines. Alnylam's pipeline of investigational RNAi therapeutics is focused in 3 Strategic Therapeutic Areas (STArs): Genetic Medicines, with a broad pipeline of RNAi therapeutics for the treatment of rare diseases; Cardio-Metabolic Disease, with a pipeline of RNAi therapeutics toward genetically validated, liver-expressed disease targets for unmet needs in cardiovascular and metabolic diseases; and Hepatic Infectious Disease, with a pipeline of RNAi therapeutics that address the major global health challenges of hepatic

infectious diseases. In early 2015, Alnylam launched its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics as a whole new class of innovative medicines. Specifically, by the end of 2020, Alnylam expects to achieve a company profile with 3 marketed products, 10 RNAi therapeutic clinical programs - including 4 in late stages of development - across its 3 STArs. The company's demonstrated commitment to RNAi therapeutics has enabled it to form major alliances with leading companies including Ionis, Novartis, Roche, Takeda, Merck, Monsanto, The Medicines Company, and Sanofi Genzyme. In addition, Alnylam holds an equity position in Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 200 peer-reviewed papers, including many in the world's top scientific journals such as *Nature, Nature Medicine, Nature Biotechnology, Cell, New England Journal of Medicine,* and *The Lancet*. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information about Alnylam's pipeline of investigational RNAi therapeutics, please visit www.alnylam.com.

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 RNAi therapeutics, including patisiran, fitusiran, givosiran, and ALN-TTRsc02, its expectations regarding the timing of clinical studies and the presentation of clinical data, its expectations regarding the filing of an NDA and MAA for patisiran, its expectations regarding its STAr pipeline growth strategy, its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics, and its plans regarding the 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 our 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.

The scientific information referenced in this news release relating to Alnylam's investigational therapeutics is preliminary and investigative. None of Alnylam's investigational therapeutics have 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 these therapeutics.

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