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Alnylam Announces Successful Outcome Following FDA Type A Meeting to Discuss Fitusiran Program in Hemophilia

− Alignment Reached with FDA on Amended Safety Measures and Risk Mitigation Strategy to Enable Resumption of Fitusiran Clinical Program −

− Reinitiation of Dosing Targeted Around Year-End −

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today a successful Type A meeting with the U.S. Food and Drug Administration (FDA) where alignment was achieved on safety measures and a risk mitigation strategy to enable resumption of dosing in clinical studies with fitusiran, including the Phase 2 open-label extension (OLE) study and the ATLAS Phase 3 program. With the completion of the Type A meeting, the FDA will now consider removal of the clinical hold upon final review of the amended protocols and other trial materials. Fitusiran is an investigational RNAi therapeutic targeting antithrombin (AT) for the treatment of patients with hemophilia A and B, that is designed to lower levels of AT with the goal of promoting sufficient thrombin generation to restore hemostasis and prevent bleeding.

"We are pleased with the outcome of our meeting with the FDA regarding next steps for the fitusiran clinical program and remain committed to reinitiating the Phase 2 OLE and the Phase 3 ATLAS program around year-end," said Akin Akinc, Ph.D., Vice President and General Manager, Fitusiran. "Further, we look forward to continuing our partnership with physicians and nurses to support education efforts on fitusiran safety, which we believe are a critical step when introducing a new therapeutic modality with the potential to address important unmet needs in hemophilia."

The Company and the FDA reached alignment on new clinical risk mitigation measures, including protocol-specified guidelines and additional investigator and patient education concerning reduced doses of replacement factor or bypassing agent to treat any breakthrough bleeds in fitusiran studies.

About Fitusiran
Fitusiran is an investigational, once-monthly, subcutaneously administered RNAi therapeutic targeting antithrombin (AT) in development for the treatment of hemophilia A and B, with and without inhibitors. Fitusiran also has the potential to be used for rare bleeding disorders. Fitusiran is designed to lower levels of AT with the goal of promoting sufficient thrombin generation to restore hemostasis and prevent bleeding. Fitusiran utilizes Alnylam's ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability. The clinical significance of this technology is under investigation. In September 2017, Alnylam temporarily suspended dosing in all ongoing studies of fitusiran following the observation of a fatal thrombotic serious adverse event that occurred in a patient with hemophilia A without inhibitors who was receiving fitusiran in the Phase 2 OLE study. All ongoing studies were placed on clinical hold. Alnylam and fitusiran study investigators and the FDA have now aligned on safety measures and a risk management strategy for further advancement of fitusiran. Following regulatory and institutional review and approval of amended study protocols and other clinical materials implementing these measures, Alnylam intends to resume fitusiran studies as soon as possible.

Fitusiran has not been approved by the FDA, EMA or any other regulatory authority for any indication and no conclusions can or should be drawn regarding the safety or effectiveness of this investigational therapeutic.

About Hemophilia
Hemophilia is a hereditary bleeding disorder characterized by an underlying defect in the ability to generate adequate levels of thrombin needed for effective clotting, thereby resulting in recurrent bleeds into joints, muscles, and major internal organs. There are approximately 400,000 people living with hemophilia A and hemophilia B worldwide.

Standard treatment for people with hemophilia currently involves replacement of the deficient clotting factor either as prophylaxis or "on-demand" therapy, which can lead to a temporary restoration of thrombin generation capacity. However, with current factor replacement treatments people with hemophilia are at risk of developing neutralizing antibodies or ‘inhibitors' to their replacement factor, a very serious complication affecting as many as one third of people with hemophilia A and a smaller fraction of people with hemophilia B. People who develop inhibitors become refractory to replacement factor therapy and are twice as likely to be hospitalized for a bleeding episode.

Alnylam - Sanofi Genzyme Alliance

In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate the advancement of RNAi therapeutics as a potential new class of innovative medicines for patients around the world with rare genetic diseases. The alliance enables Sanofi Genzyme to expand its rare disease pipeline with Alnylam's novel RNAi technology and provides access to Alnylam's R&D engine, while Alnylam benefits from Sanofi Genzyme's proven global capabilities to advance late-stage development and, upon commercialization, accelerate market access for these promising genetic medicine products.

In November 2016, Sanofi Genzyme elected to co-develop (through Sanofi R&D) and co-commercialize fitusiran in the United States, Canada and Western Europe, in addition to commercializing fitusiran in its rest of world territories.

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 600 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 fitusiran for the treatment of people with hemophilia, expectations regarding the timing for resumption of dosing in the Phase 2 OLE study and Phase 3 ATLAS studies of fitusiran following regulatory and institutional review and approval of amended study protocols and other clinical materials implementing these measures, 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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