December 3, 2016

Alnylam Reports Positive Interim Phase 1 Results for Fitusiran in Hemophilia A and B Patients with Inhibitors

- Once-Monthly, Subcutaneous Fitusiran Achieves Median Annualized Bleeding Rate (ABR) of Zero in this Hemophilia Patient Segment with Highest Unmet Need -

- Fitusiran Generally Well Tolerated with No Thromboembolic Events, Including with Co-Administration of Bypassing Agents -

- Alnylam On Track to Initiate Phase 3 Program in Early 2017 -

- Management to Discuss New Clinical Data in Webcast Conference Call Tomorrow, Sunday, December 4, at 1:00 p.m. ET -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced positive interim results from Part D of its ongoing Phase 1 study with fitusiran, an investigational RNAi therapeutic, in patients with hemophilia with inhibitors. These results were presented today in a poster at the 58th Annual Meeting of the American Society of Hematology (ASH), held December 3 - 6, 2016 in San Diego, California.

New clinical data showed that once-monthly subcutaneous administration of fitusiran achieved lowering of AT and increases in thrombin generation, resulting in a median estimated annualized bleeding rate (ABR) of zero in patients with hemophilia A or B with inhibitors (N=16). In addition, fitusiran was generally well tolerated through the data cut-off date, October 6, 2016, with no thromboembolic events, including in circumstances when bypassing agents were administered to treat breakthrough bleeding events. Additional data on longer-term administration of fitusiran in patients without inhibitors will be presented in a separate poster presentation at ASH tomorrow, Sunday, December 4.

"As many as one-third of severe hemophilia A patients will develop inhibitors, one of the most serious treatment-related complications of hemophilia. We believe that achievement of a median ABR of zero in this study population is very encouraging, as the prophylactic treatment options for patients with inhibitors are limited and may be suboptimal for many patients," said Akin Akinc, Ph.D., Vice President and General Manager, Fitusiran. "We look forward to continuing to study fitusiran in hemophilia patients with and without inhibitors, and plan to initiate our Phase 3 program in early 2017."

New results as of an October 6, 2016 data cut-off date were presented from Part D of the ongoing fitusiran Phase 1 study, which included patients with hemophilia A or B with inhibitors who were enrolled in two separate dose cohorts of 50 mg, once-monthly (N=6) or 80 mg, once-monthly (N=10). Treatment with fitusiran resulted in potent and dose-dependent lowering of AT and increases in thrombin generation. In an exploratory analysis of bleeding events, a median ABR of zero was achieved for patients in combined dose cohorts in the observation period, compared to the pre-study median ABR of 31. The majority of patients treated in both cohorts (9 of 16; 56 percent) were bleed-free and most patients (11 of 16; 69 percent) experienced zero spontaneous bleeds. In the 80 mg cohort, 70 percent (7 out of 10) of patients were bleed-free and 90 percent (9 out of 10) of patients experienced zero spontaneous bleeds.

Fitusiran was generally well tolerated in the study. All adverse events (AEs) were mild or moderate in severity, with the most common AEs consisting of mild injection site reactions (ISRs) in 8 out of 16 patients (50 percent). Asymptomatic and reversible alanine aminotransferase (ALT) increases greater than 3 times the upper limit of normal (ULN), without concurrent elevations in bilirubin greater than 2 times ULN, were observed in three patients, all of whom have medical history of hepatitis C infection (HCV). Non-clinically significant increases in D-dimer were observed in some patients; none were associated with laboratory signs of pathologic clot formation. There were no drug-related serious adverse events (SAEs), no discontinuations due to AEs, and no thromboembolic events through the data cut-off date. All breakthrough bleed events were successfully managed with bypassing agents (recombinant factor VIIa and/or activated prothrombin complex concentrate). As of the data cut-off date, seven inhibitor patients have transitioned to the Phase 2 open-label extension (OLE) study, and continued dosing with fitusiran for up to seven months has been generally well tolerated.

To view the fitusiran clinical results described in this press release, please visit www.alnylam.com/capella.

Conference Call Information
Alnylam management will discuss these clinical data in a webcast conference call tomorrow, Sunday, December 4, at 1:00 p.m. ET. A slide presentation will also be available on the Investors page of the company's website, www.alnylam.com, to

accompany the conference call. To access the call, please dial 877-312-7507 (domestic) or 631-813-4828 (international) five minutes prior to the start time and refer to conference ID 28671881. A replay of the call will be available beginning at 4:00 p.m. ET. To access the replay, please dial 855-859-2056 (domestic) or 404-537-3406 (international), and refer to conference ID 28671881.

About Fitusiran Phase 1 Study
The ongoing Phase 1 trial of fitusiran is being conducted in the United States, Bulgaria, Russia, Switzerland, and the U.K. as a single- and multi-dose, dose-escalation study comprised of four parts. Part A - which is complete - was a randomized, single-blind, placebo-controlled, single-dose, dose-escalation study (N=4 per cohort; 3:1 randomization of fitusiran:placebo) in healthy volunteers. This part of the study was completed after the first dose cohort received a single subcutaneous dose of fitusiran at 30 mcg/kg. Part B of the study - which is also complete - was an open-label, multi-dose, dose-escalation study that enrolled 12 patients with severe hemophilia A or B. Patients in Part B received three weekly subcutaneous injections of fitusiran at doses of 15, 45, or 75 mcg/kg. Part C of the study - which has completed dosing - is an open-label, multi-dose, dose escalation study that enrolled 18 patients with moderate or severe hemophilia A or B without inhibitors. Twelve patients in Part C received three monthly subcutaneous doses of fitusiran at doses of 225, 450, 900, or 1800 mcg/kg. In addition, six patients in Part C received three fixed monthly subcutaneous doses of fitusiran at 80 mg. Part D of the study is designed to enroll up to 18 patients with inhibitors. Patients in Part D received 3 fixed monthly subcutaneous doses of fitusiran at 50 mg or 80 mg. The primary objective of Parts B, C, and D of the study is to evaluate the safety and tolerability of multiple doses of subcutaneously administered fitusiran in patients with hemophilia, with and without inhibitors. Secondary objectives include assessment of clinical activity as determined by lowering of circulating AT levels and increase in thrombin generation at pharmacologic doses of fitusiran. In addition, exploratory analyses of bleeding are being performed. In the U.K., enrollment has been aided by the Southern Academic Coagulation Consortium (SACC).

About Fitusiran
Fitusiran is a subcutaneously administered, investigational RNAi therapeutic targeting antithrombin (AT) for the treatment of hemophilia A and B and rare bleeding disorders (RBD) currently in early stage clinical development. Fitusiran is designed to lower levels of AT with the goal of promoting sufficient thrombin generation to restore hemostasis and prevent bleeding in patients with hemophilia and RBD. AT, also known as "antithrombin III" and "SERPINC1" is a liver-expressed plasma protein and member of the "serpin" family of proteins that acts by inactivating thrombin and other coagulation factors. AT plays a key role in normal hemostasis by helping to limit the process of fibrin clot formation. However, in hemophilia, insufficient thrombin generation results in impaired fibrin clot formation. Lowering AT in the hemophilia setting may promote the generation of sufficient levels of thrombin needed to form an effective fibrin clot and prevent bleeding. This rationale is supported by human genetic data suggesting that co-inheritance of thrombophilic mutations, including AT deficiency, may ameliorate bleeding in hemophilia. Lowering of AT is a unique and innovative strategy for restoring hemostasis in people with hemophilia. Fitusiran utilizes Alnylam's ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index.

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 through the end of 2019, together with certain broader co-development/co-commercialization rights and global rights for certain products. 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 rest of world 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 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 fitusiran, its expectations regarding the timing of clinical studies and the presentation of clinical data, including for its studies of fitusiran, 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 pursuit of pre-clinical programs 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 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 fitusiran is preliminary and investigative. Fitusiran 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 its safety or effectiveness.

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