December 4, 2016

Alnylam Reports Positive Interim Clinical Results for Fitusiran from Ongoing Phase 2 Open Label Extension Study in Patients with Hemophilia A or B without Inhibitors

- Once-Monthly, Subcutaneous Fitusiran Achieves Median Annualized Bleeding Rate (ABR) of 1.0, with Median Observation Period of 5.7 Months -

- Fitusiran Generally Well Tolerated with No Thromboembolic Events -

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

- Management to Discuss New Clinical Data in Webcast Conference Call Today, 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 new positive results from its ongoing Phase 2 open-label extension (OLE) study with fitusiran, an investigational RNAi therapeutic, in patients with hemophilia A or B without 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 consistent lowering of AT and increases in thrombin generation, resulting in a median estimated annualized bleeding rate (ABR) of 1.0 in patients with hemophilia A or B without inhibitors. In addition, fitusiran was generally well tolerated, with no thromboembolic events or laboratory evidence of pathologic clot formation through the data cut-off date.

"We are encouraged by the longer-term tolerability data and clinical activity of fitusiran, with a median ABR of 1.0 in patients with hemophilia A or B with up to 14 months of continuous dosing. These data, combined with positive results we reported yesterday in hemophilia patients with inhibitors, continue to highlight what we believe to be the significant potential of fitusiran as a once-monthly subcutaneous investigational medicine for prevention of bleeding in people with hemophilia and RBD," said Akin Akinc, Ph.D., Vice President and General Manager, Fitusiran. "Going forward, we expect to present data from the ongoing Phase 2 OLE study at least once per year. Meanwhile, we're aiming to initiate our Phase 3 clinical program in early 2017 to generate definitive evidence for fitusiran efficacy and safety in support of potential regulatory approvals."

The Phase 2 OLE study results as of the data cut-off date of October 6, 2016 included 16 hemophilia A or B patients without inhibitors. All patients were previously enrolled in the fitusiran Phase 1 study, receiving 3 weekly or 3 monthly subcutaneous doses ranging from 45 micrograms per kilogram (mcg/kg) to 1800 mcg/kg. In the Phase 2 OLE study, fitusiran was administered subcutaneously once-monthly at two fixed dose levels, 50 mg (N=8) and 80 mg (N=8), with patients receiving up to 14 months of continuous dosing. Both dose levels achieved mean AT lowering of approximately 80 percent and mean increases in thrombin generation levels approaching the lower end of the range observed in normal healthy individuals in Part A of the Phase 1 study. In an exploratory post hoc analysis of bleed events, fitusiran achieved a median overall ABR of 1.0, over a median observation period of 5.7 months, compared to a median pre-study ABR of 4.0. In the study, 8 out of 16 patients (50 percent) reported zero bleeds and 11 out of 16 patients (69 percent) experienced zero spontaneous bleeds.

The data reported from the Phase 2 OLE study also includes the first reported elective surgical procedure in a fitusiran-treated patient. Specifically, a patient with severe hemophilia A receiving 50 mg monthly fitusiran underwent an elective septoplasty procedure. Prior to the surgical procedure, the patient's AT levels were 13 percent relative to baseline. As reported by the investigator via personal communication, the cumulative periprocedural utilization of recombinant factor VIII was approximately 20 percent of that typically used by the investigator for this type of surgery in a severe hemophilia A patient. Based on the International Society of Thrombosis and Haemostasis (ISTH) hemostasis efficacy score, the investigator rated hemostasis control in the intra-operative, 24 hours post-operative, and 7 days post-operative periods as all being "excellent".

Fitusiran was generally well tolerated with the longest period of exposure of up to 14 months of continuous treatment. All adverse events (AEs) were mild or moderate in severity, with the most common AEs consisting of mild injection site reactions (ISRs) in 4 out of 16 patients (25 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 in the OLE study, all of whom have medical history of hepatitis C infection (HCV). All

breakthrough bleeding events were successfully managed with replacement factor. There were no drug-related serious adverse events (SAEs), no discontinuations due to AEs in the OLE study, and no thromboembolic events or laboratory evidence of pathologic clot formation through the data cut-off date.

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 today, 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

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.

View source version on businesswire.com: http://www.businesswire.com/news/home/20161204005038/en/

Alnylam Pharmaceuticals, Inc.
Christine Regan Lindenboom, 617-682-4340
(Investors and Media)
or
Josh Brodsky, 617-551-8276
(Investors)

Source: Alnylam Pharmaceuticals, Inc.