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Alnylam Presents New Data on Fitusiran at EAHAD

- New Phase 1 Results Demonstrate Effective Bleed Management with Replacement Factor and Bypassing Agents During Fitusiran Administration -

- Stability Study Results Support a Greater than Two Year Product Shelf-Life at Room Temperature Storage Conditions -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company today announced new results from an exploratory analysis of its Phase 1 study with fitusiran, an investigational RNAi therapeutic, in patients with hemophilia A or B with or without inhibitors. This analysis of bleed management during fitusiran administration showed that breakthrough bleeds were effectively managed with replacement factors or bypassing agents, with no thromboembolic events. Additionally, results presented from stability studies of fitusiran support a greater than two-year shelf life at room temperature storage conditions and demonstrated resistance to thermal stress, favoring real world handling of the final drug product. These data were presented at the 10th Annual Congress of the European Association of Haemophilia and Allied Disorders (EAHAD) held February 1 - 3, 2017 in Paris, France.

New analyses examined 21 total bleed events in 41 patients treated with fitusiran, after achieving greater than 75 percent antithrombin lowering. This analysis found that dosing of agents was generally within the normal dose range for replacement Factor VIII and Factor IX as well as for the bypassing agent rFVIIa, while at the lower end of the range for the bypassing agent aPCC. Treatment of all breakthrough bleed events resulted in successful hemostasis without any thromboembolic events.

"We are encouraged by this new analysis which provides evidence that breakthrough bleeds occurring in patients treated with fitusiran can be effectively managed with both replacement factor and bypassing agents, with no thromboembolic events. These data, combined with positive recent clinical results, continue to support the potential of fitusiran as a once-monthly subcutaneous investigational medicine for the management of hemophilia," said Akin Akinc, Ph.D., Vice President and General Manager, Fitusiran. "Furthermore, data continue to support the robust stability profile of fitusiran, potentially facilitating treatment in regions where cold chain storage requirements represent a challenge to patients' access to effective therapies. We continue to advance toward the start of our ATLAS Phase 3 clinical program in early 2017."

An evaluation of fitusiran at refrigerated (i.e., 5ºC), customary room temperature (i.e., 25ºC/60 percent relative humidity) and at accelerated aging conditions (i.e., 40ºC) demonstrated a robust stability profile, with all key quality attributes predicted to be retained at both refrigerated and room temperature conditions for at least 24 months. Further, fitusiran has shown resistance to thermal stress and cyclic temperature fluctuations that may occur during real world storage and handling of the drug product. Consequently, the stability profile of fitusiran could enable convenient transportation and storage, including in parts of the world where cold chain delivery is a challenge.

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

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.

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 was 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).

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 ability to successfully manage breakthrough bleeds during fitusiran administration with replacement factors or bypassing agents, with no thromboembolic events, the potential stability, shelf life and resistance to thermal stress of fitusiran, the expected timing of the initiation of Phase 3 studies of fitusiran, its expectations regarding its STAr pipeline growth strategy, 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 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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