



July 10, 2017

Alnylam and Sanofi Genzyme Report Positive Results from Ongoing Phase 2 Open-Label Extension Study with Investigational RNAi Therapeutic Fitusiran in Patients with Hemophilia A and B With or Without Inhibitors

- With up to 20 Months of Dosing, Fitusiran Safety and Tolerability Profile Remains Encouraging -

- Once Monthly, Subcutaneous Fitusiran Achieves Median Annualized Bleeding Rate (ABR) of One for All Patients and Zero for Patients with Inhibitors in Exploratory Post-hoc Analysis -

- New England Journal of Medicine Publishes Phase 1 Clinical Results with Fitusiran in Patients with Hemophilia A and B without Inhibitors -

- Alnylam Management to Discuss New Clinical Data in Webcast Conference Call Monday, July 10, at 11:30 a.m. ET -

CAMBRIDGE, Mass. & PARIS--(BUSINESS WIRE)-- [Alnylam Pharmaceuticals, Inc.](#) (Nasdaq:ALNY), the leading RNAi therapeutics company and [Sanofi Genzyme](#), the specialty care global business unit of [Sanofi](#), announced today new positive results from the ongoing Phase 2 open-label extension (OLE) study with fitusiran in patients with hemophilia A and B, with or without inhibitors (N=33). These results were presented today in an oral presentation at the International Society on Thrombosis and Haemostasis (ISTH) 2017 Congress, being held from July 8 - 13, 2017 in Berlin, Germany. 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 upon activation of the clotting cascade to restore hemostasis and prevent bleeding. The companies also announced that Phase 1 clinical trial results demonstrating an encouraging preliminary safety and tolerability profile and initial evidence that monthly subcutaneously administered fitusiran lowered AT levels and increased thrombin generation in patients with hemophilia A and B without inhibitors were published online today and will appear in the September 7, 2017, print issue of *The New England Journal of Medicine* (NEJM).

The updated clinical results in the fitusiran Phase 2 OLE study showed that the safety and tolerability profile of fitusiran remains encouraging, with no thromboembolic events, including during co-administration of replacement factor or bypassing agents. The majority of adverse events (AEs) were mild or moderate in severity, with the most common AEs consisting of transient, mild injection site reactions (ISRs). In addition, once-monthly subcutaneous (SC) administration of fitusiran achieved lowering of AT, increases in thrombin generation, and, in a post-hoc exploratory analysis, reductions in the median estimated annualized bleeding rate (ABR) in patients with and without inhibitors. Based on these results, the companies announced last week the initiation of the ATLAS Phase 3 program for fitusiran in patients with hemophilia A and B with or without inhibitors.

"With up to 20 months of dosing in patients, we are encouraged by the results from our fitusiran clinical studies presented at the ISTH meeting today, demonstrating what we believe to be promising support for further clinical development," said Akin Akinc, Ph.D., Alnylam's Vice President and General Manager, Fitusiran. "We're also pleased to have announced initiation of our ATLAS Phase 3 program just last week, where the safety and efficacy of fitusiran will be evaluated and where we expect initial results in mid-to-late 2019."

"We've achieved an encouraging safety and tolerability profile and low median ABRs with a monthly subcutaneous dosing regimen, highlighting fitusiran's potential to become a differentiated and innovative treatment option for patients with hemophilia," said Baisong Mei, M.D., Ph.D., Sanofi's Senior Global Project Head, Alnylam Portfolio. "We're now focused on our ATLAS Phase 3 program, a comprehensive set of studies focused on the unmet needs of patients with hemophilia A and B with or without inhibitors, which, if positive, will support global regulatory filings for fitusiran."

The ongoing fitusiran Phase 2 OLE study includes patients (N=33) with hemophilia A (N=27) and hemophilia B (N=6). The study includes 14 patients with inhibitors, including one with hemophilia B. Fitusiran was administered as a low volume (less than 1 mL), monthly, subcutaneous, fixed dose of 50 mg (N=13) or 80 mg (N=20). All results are as of a June 15, 2017 data transfer date.

Patients were treated for up to 20 months in the Phase 2 OLE, with a median of 11 months on study. The majority of AEs were mild or moderate in severity, with the most common non-laboratory AEs consisting of transient, mild ISRs (18 percent of patients). There was one discontinuation due to an AE, an asymptomatic alanine aminotransferase (ALT) elevation in a

patient with chronic hepatitis C virus (HCV) infection. Serious adverse events (SAEs) considered possibly related to drug were reported in two patients: asymptomatic ALT elevation in one patient with chronic HCV infection, as noted above, and seizure with confusion in one patient with a prior history of seizure disorder. Asymptomatic ALT increases greater than 3x the upper limit of normal (ULN), without concurrent elevations in bilirubin greater than 2x ULN, were observed in 11 patients, all of whom were hepatitis C antibody positive; at current follow-up, all ALT elevations are resolved (N=10) or resolving (N=1). No thromboembolic events, laboratory evidence for pathological clot formation, or instances of anti-drug antibody (ADA) formation were reported.

Regarding clinical activity results, treatment with fitusiran resulted in approximately 80 percent lowering of AT with corresponding increases in thrombin generation. Increases in thrombin generation remained within the lower end of the range of values observed in normal healthy volunteers. In an exploratory post-hoc analysis of bleeding events, a median ABR of one (interquartile range [IQR]: 0-3) was achieved for all patients (N=33), and a median ABR of zero (IQR: 0-3) was achieved for the subset of patients with inhibitors (N=14), corresponding favorably to pre-study median ABR values of 20 (IQR: 4-36) in all patients and 38 (IQR: 20-48) in inhibitor patients. There was a high proportion of patients (16 of 33; 48 percent) who remained bleed-free in the observation period, and most patients (22 of 33; 67 percent) experienced zero spontaneous bleeds. All breakthrough bleed events were successfully managed with replacement factor (recombinant factor VIII or recombinant factor IX) or bypassing agents (recombinant factor VIIa or activated prothrombin complex concentrate).

As noted above, the companies also announced today that a paper titled, "Targeting of Antithrombin in Hemophilia A or B with RNAi Therapy," was published online today in [The New England Journal of Medicine](#). Alnylam and its collaborators, including lead author and principal study investigator John Pasi, M.D., Ph.D., Professor of Haemostasis and Thrombosis, Clinical Director of Haemophilia at The Royal London Hospital Barts Health NHS Trust, and Barts and the London School of Medicine and Dentistry, London, UK, provided results from Parts A-C of the Phase 1 multicenter, international, open-label, single- and multiple-ascending dose escalation study in healthy volunteers and patients with hemophilia A and B without inhibitors. This is the first publication of safety, tolerability and initial clinical activity data for fitusiran in patients with hemophilia A and B.

"Current hemophilia management is based on factor replacement therapies that require frequent intravenous infusions to maintain adequate factor trough levels. Significant unmet need remains for additional therapeutic agents," said John Pasi. "The results of our Phase 1 clinical study published in *The New England Journal of Medicine* support the growing body of evidence to continue the clinical development program for fitusiran."

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

Conference Call Details

Management will discuss these results via conference call on Monday, July 10, 2017 at 11:30 a.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 50998303. A replay of the call will be available beginning at 2:30 p.m. ET on July 10, 2017. To access the replay, please dial 855-859-2056 (domestic) or 404-537-3406 (international), and refer to conference ID 50998303.

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 200,000 persons diagnosed worldwide with hemophilia A and hemophilia B.

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, as many as one third of people with severe hemophilia A will develop a neutralizing antibody to their replacement factor - a very serious complication; individuals with these 'inhibitors' become refractory to standard replacement factor therapy.

About Fitusiran

Fitusiran is an investigational, once-monthly, subcutaneously administered RNAi therapeutic targeting antithrombin (AT) 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.

The safety and efficacy of fitusiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

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 revolution in biology, representing a breakthrough in understanding protein synthesis 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, with the goal of preventing disease-causing proteins from being made.

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 patients who have limited or inadequate treatment options. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of 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 three product candidates that are in late-stage development or will be in 2017. 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. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam.

About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Consumer Healthcare. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Sanofi Genzyme focuses on developing specialty treatments for debilitating diseases that are often difficult to diagnose and treat, providing hope to patients and their families. Learn more at www.sanofigenzyme.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 the potential for fitusiran for the treatment of patients with hemophilia A and B, with or without inhibitors, conduct of its ATLAS Phase 3 program for fitusiran, and its 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.

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 the safety or effectiveness of fitusiran.

Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2016. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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