



September 20, 2017

Alnylam and Sanofi Report Positive Topline Results from APOLLO Phase 3 Study of Patisiran in Hereditary ATTR (hATTR) Amyloidosis Patients with Polyneuropathy

- Investigational RNAi Therapeutic Patisiran Meets Primary and All Secondary Endpoints, with Highly Significant Reduction In Neuropathy Progression and Improvement in Quality of Life at 18 Months Relative to Placebo -

- Alnylam Intends to File New Drug Application (NDA) in Late 2017 and Marketing Authorisation Application (MAA) in Early 2018 -

- Full Results to be Presented at 1st European ATTR Amyloidosis Meeting in November -

- Alnylam to Host Conference Call Today at 8:30 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 that the APOLLO Phase 3 study of patisiran, an investigational RNAi therapeutic being developed for patients with hereditary ATTR amyloidosis with polyneuropathy, met its primary efficacy endpoint and all secondary endpoints. The primary endpoint for the study was the change from baseline in the modified neuropathy impairment score (mNIS+7) at 18 months. The key secondary endpoint was improvement in quality of life assessed by the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN).

"We are very proud to report the first ever positive Phase 3 results for an RNAi therapeutic, marking the potential arrival of an entirely new class of medicines. This moment is the culmination of a 15-year journey of tireless work by countless contributors who have overcome enormous scientific and business challenges to make RNAi therapeutics a reality," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "This is an incredibly exciting milestone for Alnylam and RNAi, and most importantly for patients and their treating physicians and families. We extend our deepest gratitude to all the patients, investigators and study staff who participated in the APOLLO study - they made this important scientific progress possible."

The APOLLO trial enrolled 225 hATTR amyloidosis patients with polyneuropathy, representing 39 genotypes, at 44 study sites in 19 countries around the world. Patients were randomized 2:1 to patisiran or placebo, with patisiran administered intravenously at 0.3 mg/kg once every three weeks for 18 months. For both the mNIS+7 and Norfolk QOL-DN endpoint measures provided below, a lower score indicates a better clinical result.

- | At 18 months, the mean change from baseline in mNIS+7 was significantly lower in the patisiran group as compared with placebo (p less than 0.00001).
 - | The mean and median changes in mNIS+7 impairment scores for patisiran both achieved negative values, indicating an improvement overall and in the majority of patients compared with baseline.
- | Patients in the patisiran group experienced improvement in quality of life compared to placebo, as assessed by the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN) (p less than 0.00001).
 - | The mean and median changes in QOL scores for patisiran also both achieved negative values, indicating an improvement overall and in the majority of patients compared with baseline.
- | All 5 other secondary endpoints also demonstrated statistically significant favorable differences in the patisiran arm compared to placebo (p less than 0.001). These were:
 - | NIS-W, the subdomain of mNIS+7 assessing muscle strength;
 - | Rasch-built Overall Disability Scale (R-ODS), a patient reported outcome measure of daily living and disability;
 - | 10-meter walk test, assessing gait speed;
 - | Modified body mass index (mBMI), assessing nutritional status; and
 - | COMPASS-31, a questionnaire to assess autonomic symptoms.
- | The overall safety profile of patisiran was encouraging.
 - | The patisiran and placebo arms had similar frequencies of adverse events (AEs) (96.6 percent and 97.4 percent, respectively) and serious adverse events (SAEs) (36.5 percent and 40.3 percent, respectively).

- The frequency of deaths in the study was similar in the patisiran (4.7 percent) and placebo (7.8 percent) arms.
- Patisiran treatment was associated with fewer discontinuations from treatment compared with placebo (7.4 percent and 37.7 percent, respectively) and discontinuations from treatment due to AEs (4.7 percent and 14.3 percent, respectively).
- AEs reported in greater than 10 percent of patients and seen more frequently with patisiran compared with placebo were peripheral edema (29.7 percent vs. 22.1 percent, respectively) and infusion-related reactions (18.9 percent vs. 9.1 percent, respectively), both of which were generally mild-to-moderate in severity.

"Patients living with hATTR amyloidosis face an inevitable and painful advancement of their debilitating disease," said Akshay Vaishnav, M.D., Ph.D., Executive Vice President, R&D of Alnylam. "We believe the very encouraging APOLLO data demonstrate the potential for investigational patisiran to help improve the lives of hereditary ATTR amyloidosis polyneuropathy patients. Our immediate objective is now to submit these data to global health authorities."

Based on these positive results, Alnylam expects to file its first New Drug Application in late 2017 and first Marketing Authorisation Application shortly thereafter. Sanofi Genzyme is currently preparing for regulatory filings for patisiran in Japan, Brazil and other countries, to begin in the first half of 2018. Pending regulatory approvals, Alnylam will commercialize patisiran in the U.S., Canada and Western Europe, with Sanofi Genzyme commercializing the product in the rest of the world.

"This is a significant milestone that supports our belief that RNAi therapeutics have the potential to become an innovative new class of medicines for patients with rare genetic diseases," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "The APOLLO data suggest that patisiran could help improve the lives of people living with hATTR amyloidosis with polyneuropathy, a patient population in urgent need of additional treatment options. We look forward to working with Alnylam to make patisiran available around the globe as quickly as possible."

Full results, including data from an exploratory analysis of the subgroup of patients with cardiac involvement, will be presented at the 1st European ATTR Amyloidosis Meeting for Patients and Doctors, on November 2, 2017 in Paris, France.

APOLLO is the largest randomized study ever completed in this disease. Nearly all eligible patients who completed APOLLO have rolled over to the APOLLO-Open Label Extension (OLE) study and continue to receive patisiran.

Conference Call Details

Alnylam management will discuss these results via conference call on September 20, 2017 at 8:30 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 88881001. A replay of the call will be available beginning at 11:30 a.m. ET on September 20, 2017. To access the replay, please dial (855) 859-2056 (domestic) or (404) 537-3406 (international), and refer to conference ID 88881001.

About the APOLLO Phase 3 Study

The APOLLO Phase 3 study is a randomized, double blind, placebo-controlled, global study designed to evaluate the efficacy and safety of patisiran in hATTR amyloidosis patients with polyneuropathy. The primary efficacy endpoint was change from baseline in the mNIS+7 composite neuropathy impairment score at 18 months. Modified NIS+7 is a composite measure of neurologic impairment that evaluates sensorimotor capabilities, nerve conduction, reflexes, and autonomic function. Secondary endpoints included the Norfolk QOL-DN quality of life score as well as measures of motor strength (NIS-W), disability (R-ODS), gait speed (10-meter walk test), nutritional status (mBMI) and autonomic symptoms (COMPASS-31). Exploratory endpoints included cardiac measures in patients with evidence of cardiac involvement at baseline as well as measures of dermal amyloid burden and nerve fiber density in skin biopsies.

About Patisiran

Patisiran is an investigational medicine that uses the body's natural processes to lower the levels of the TTR protein that causes TTR amyloidosis. It is designed to target and silence specific messenger RNA, potentially blocking the production of TTR protein before it is made. This may help to enable the clearance of TTR amyloid deposits in peripheral tissues and potentially restore function to these tissues. The safety and efficacy of patisiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

About hATTR amyloidosis

Hereditary transthyretin (TTR)-mediated (hATTR) amyloidosis is an inherited, progressively debilitating, and often fatal disease caused by mutations in the TTR gene. TTR protein is produced primarily in the liver and is normally a carrier of vitamin A. Mutations in TTR cause abnormal amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and/or cardiomyopathy. hATTR amyloidosis represents a major unmet medical need with significant morbidity and mortality, affecting approximately 50,000 people worldwide. hATTR amyloidosis patients have a life expectancy of 2.5 to 15 years from symptom onset, and the only approved treatment options are liver transplantation for early stage disease and tafamidis (approved in Europe, Japan and certain countries in Latin America, specific indication varies by region). There is a significant need for novel therapeutics to help treat patients with hATTR amyloidosis.

About LNP Technology

Alnylam has licenses to Arbutus Biopharma LNP intellectual property for use in RNAi therapeutic products using LNP technology.

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 the case of patisiran, Alnylam will advance the product in the United States, Canada and Western Europe, while Sanofi Genzyme will advance the product in the rest of the world.

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 potentially 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 topline results from its APOLLO Phase 3 clinical trial for patisiran, its plans for and the expected timing of regulatory filings seeking approval for patisiran from regulatory authorities in the United States, Europe and ROW countries, its expectations regarding the potential for patisiran to improve the lives of hATTR amyloidosis patients with polyneuropathy and their families, its plans for the commercialization of patisiran if approved by regulatory authorities, 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.

Patisiran 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 this investigational therapeutic.

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 regarding the clinical development of and potential marketing approvals for the product. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans", "would be" 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 of the product, 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 the product or biological application that may be filed for the product as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of the product, the absence of guarantee that the product if approved will be commercially successful, risks associated with intellectual property, future litigation, the future approval and commercial success of therapeutic alternatives, and volatile economic conditions, as well as those risks 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.

View source version on [businesswire.com](http://www.businesswire.com/news/home/20170920005628/en/): <http://www.businesswire.com/news/home/20170920005628/en/>

Alnylam Pharmaceuticals, Inc.

Investors and Media
Christine Regan Lindenboom, 617-682-4340
or
Investors
Josh Brodsky, 617-551-8276

Source: Alnylam Pharmaceuticals, Inc.

News Provided by Acquire Media