November 2, 2017

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

- Patisiran Meets Primary Endpoint with a 34.0 Point Mean Difference Relative to Placebo and a Negative 6.0 Point Mean Change (Improvement) Relative to Baseline in Modified Neuropathy Impairment Score (mNIS+7) at 18 Months -

- Patisiran Meets All Secondary Endpoints, Including a 21.1 Point Mean Difference Relative to Placebo and a Negative 6.7 Point Mean Change (Improvement) Relative to Baseline in Norfolk-Quality of Life-Diabetic Neuropathy (QOL-DN) Score at 18 Months -

- Significant Effects Observed on Certain Exploratory Cardiac Biomarker and Echocardiographic Endpoints in Pre-Specified Cardiac Subpopulation Relative to Placebo at 18 Months -

- Encouraging Safety Profile with up to 18 Months of Dosing -

- Alnylam to Host Conference Call Today at 12:30 p.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 positive complete results from the APOLLO Phase 3 study of patisiran, an investigational RNAi therapeutic being developed for patients with hereditary ATTR (hATTR) amyloidosis with polyneuropathy. These clinical data were presented today in an oral presentation at the 1st European ATTR Amyloidosis Meeting for Patients and Doctors being held November 2-3, 2017 in Paris, France. Based on these results, Alnylam intends to file a new drug application (NDA) in the United States for patisiran by end-2017 and a marketing authorization application (MAA) in the European Union shortly thereafter.

The full APOLLO results showed improvement with patisiran relative to placebo in the primary endpoint of modified Neuropathy Impairment Score +7 (mNIS+7) and additional secondary endpoints encompassing sensory, motor, and autonomic neuropathy symptoms, as well as in exploratory cardiac endpoints, at 18 months. Patients exhibited improved quality of life, activities of daily living, nutritional status, motor strength, and ambulatory ability, with reduced disease symptoms and disability. Favorable effects of patisiran relative to placebo were observed across subgroups defined by demographic and baseline hATTR amyloidosis disease characteristics. In a pre-specified cardiac subpopulation, significant positive effects were observed for patisiran on certain exploratory cardiac biomarker and echocardiographic endpoints.

The most commonly reported adverse events (AEs) that occurred more frequently in patisiran-treated patients were generally mild to moderate and included peripheral edema and infusion-related reactions (IRRs). The frequency of deaths and serious adverse events (SAEs) was similar in the patisiran and placebo groups. These data support the potential of patisiran to stabilize and even improve the cardinal, multi-system disease manifestations of hATTR amyloidosis, including improvement in patients' quality of life.

"We are very pleased for patients and families living with hATTR amyloidosis as we believe these results from APOLLO offer new hope for the treatment of this devastating disease. Indeed, patisiran holds the potential to halt or improve neurological impairment and broader disease features in patients with hATTR amyloidosis. We also view these results as a landmark achievement for the field of RNAi therapeutics, as we believe they demonstrate the transformational potential of this novel class of innovative medicines," said Akshay Vaishnaw, M.D., Ph.D., Executive Vice President of R&D at Alnylam. "Alnylam is indebted to all the patients, investigators, and study staff who took part in the APOLLO study, making this important and notable milestone possible. We're also grateful to the caregivers and family members whose support of APOLLO patients was such an important contribution. With these promising APOLLO data in hand, we intend to start filing our results with regulatory authorities in late 2017 with the goal of achieving approval in mid-2018."

Overall Efficacy Results

Patisiran met the primary endpoint of mNIS+7 change from baseline at 18 months relative to placebo, and all secondary study endpoints. Specifically:

- Patisiran treatment (N=148) resulted in a negative 6.0 point mean change (improvement) in mNIS+7 score from baseline at 18 months as compared to a 28.0 point mean increase (worsening) reported for the placebo group (N=77), resulting in a 34.0 point mean difference relative to placebo ($p=9.26 \times 10^{-24}$).
  - The results were found to be consistent across all sub-components of the mNIS+7 scale.
  - Improvement in mNIS+7 from patisiran treatment was also consistently observed across all defined patient subgroups, including age, sex, race, geographic region, baseline neuropathy impairment, genotype, prior TTR stabilizer use, baseline Familial Amyloid Polyneuropathy (FAP) stage, and inclusion in the pre-specified cardiac subpopulation.
- Patisiran treatment resulted in a negative 6.7 point mean change (improvement) in Norfolk-Quality of Life-Diabetic Neuropathy (Norfolk QOL-DN) score from baseline at 18 months as compared to a 14.4 point mean increase (worsening) reported for the placebo group, resulting in a mean 21.1 point difference relative to placebo ($p=1.10 \times 10^{-10}$).
- Improvements in mNIS+7 and Norfolk QOL-DN with patisiran were also seen at nine months, the earliest time point for these measurements in the study, with a mean 16.0 and a mean 15.0 point difference observed, respectively, relative to placebo.
- In a pre-specified binary analysis of neurological improvement, 56 percent (95 percent CI: 48.1, 64.1) of patisiran patients had an improvement in mNIS+7 (less than 0 point change compared to baseline at 18 months), while 4 percent (95 percent CI: 0.0, 8.2) of placebo patients had an improvement ($p=1.82 \times 10^{-15}$).
- Similarly, 51 percent (95 percent CI: 43.3, 59.4) of patisiran patients had an improvement in Norfolk QOL-DN (less than 0 point change compared to baseline at 18 months), versus 10 percent (95 percent CI: 3.6, 17.2) for placebo ($p=1.95 \times 10^{-10}$).
- Patisiran also demonstrated statistically significant and clinically meaningful improvements over placebo in all other secondary endpoints at 18 months, including: NIS-W ($p=1.40 \times 10^{-13}$), the subdomain of mNIS+7 assessing muscle strength; Rasch-built Overall Disability Scale (R-ODS) ($p=4.07 \times 10^{-16}$), a patient reported outcome measure of daily living and disability; timed ten-meter walk test (10-MWT) ($p=1.88 \times 10^{-12}$), assessing ambulatory ability and gait speed; modified body mass index (mBMI) ($p=8.83 \times 10^{-11}$), assessing nutritional status; and, COMPASS-31 ($p=0.0008$), a patient questionnaire assessing autonomic disease symptoms.

Cardiac Subpopulation Results

Favorable and significant changes in several exploratory cardiac measures, including N-terminal pro b-type natriuretic peptide (NT-proBNP), certain echocardiographic parameters, and 10-MWT were reported in patisiran-treated patients in the pre-specified cardiac subpopulation*. Specifically:

- Patisiran treatment resulted in a median decrease (improvement) of 49.9 pg/ml in NT-proBNP levels as compared to a median increase (worsening) of 320 pg/ml reported for the placebo arm at 18 months (nominal $p=7.74 \times 10^{-8}$, based on analysis of log-transformed values).
- Regarding echocardiographic measures, patisiran treatment resulted in a mean 0.93 mm reduction (improvement) in left ventricular (LV) wall thickness (nominal $p=0.0173$) and a mean absolute 1.37 percent improvement in longitudinal strain (nominal $p=0.0154$) relative to placebo.
- Regarding functional measures in the cardiac subpopulation, patisiran treatment resulted in a 0.35 m/sec increase (improvement) in 10-MWT (nominal $p=7.42 \times 10^{-9}$) relative to placebo at 18 months.
- Changes relative to baseline were also measured for troponin-I, LV mass, and LV ejection fraction but were not statistically significant.

"Patients with hATTR amyloidosis are afflicted with an aggressive, rapidly progressing, debilitating and fatal disease, and have a profound need for effective and safe treatment options," said David Adams, M.D., Ph.D., Department of Neurology, Bicetre hospital, Greater Paris University Hospitals, AP-HP, and Principal Investigator for the APOLLO trial. "The exciting APOLLO data that were released today demonstrate the potential of patisiran to alleviate the multiple neurological, cardiac, and autonomic manifestations of the disease. If approved, I believe that patisiran could have a tremendous impact for patients and physicians in the amyloidosis community. As a clinician, it has been deeply rewarding to see the potential impact patisiran may have on the lives of hATTR patients."

Safety and Tolerability

Patisiran showed an encouraging safety and tolerability profile relative to placebo with up to 18 months of dosing. Specifically:

- The most commonly reported AEs that occurred more frequently in patisiran patients were peripheral edema (29.7 percent versus 22.1 percent in placebo) and IRRs (18.9 percent versus 9.1 percent in placebo). These were generally mild to moderate in severity and only one patient discontinued due to an IRR (0.7 percent).
- Compared to placebo, patisiran treatment was associated with fewer treatment discontinuations (4.7 versus 14.3 percent) and fewer study withdrawals (4.7 versus 11.7 percent) due to AEs.
- The incidence of SAEs across the patisiran (36.5 percent) and placebo (40.3 percent) groups was similar.
  - SAEs reported in 2 or more patients in the patisiran group included: diarrhea (5.4 percent), cardiac failure, congestive cardiac failure, orthostatic hypotension, pneumonia, and atrioventricular block complete (2 percent each). These were all considered unrelated to patisiran, except for one SAE of diarrhea. SAEs occurred with similar frequency in the placebo group, except for diarrhea (1.3 percent in placebo group).
- Deaths were recorded with a similar incidence across the patisiran (4.7 percent) and placebo (7.8 percent) treatment groups.
  - No deaths were considered related to study drug.
- There were no safety signals with regard to hepatic or renal function, or evidence of thrombocytopenia, due to patisiran.
- Patisiran also showed an encouraging tolerability profile in the pre-specified cardiac subpopulation, with a similar frequency of AEs in the patisiran and placebo arms and a numerically lower incidence of SAEs (34.4 percent for patisiran versus 50.0 percent for placebo). The frequency of deaths was 5.6 percent for patisiran versus 11.1 percent for placebo.

"The APOLLO data presented in Paris provide robust evidence supporting the potential of RNAi as a novel therapeutic approach for patients with hATTR amyloidosis," said Elias Zerhouni, M.D., President, Global R&D, Sanofi. "In this study, patisiran's effect in helping to alleviate neurological impairment and improve the quality of life for people living with this debilitating rare disease is a remarkable accomplishment. Sanofi looks forward to coordinating global regulatory submissions with Alnylam on an expedited basis."

Phase 2 Open-Label Extension (OLE) Study Results Over 36 Months

Alnylam and Sanofi Genzyme also announced today 36 month results from patients originally on the patisiran Phase 2 OLE study. Specifically:

- Nearly all patients who were originally treated in the Phase 2 OLE study have continued to receive patisiran in the Global OLE study.
- 25 patients who received 24 months of treatment in the Phase 2 OLE were followed for an additional mean 16.2 months in the Global OLE study.
  - There were no new safety concerns with additional dosing.
  - The majority of AEs were mild or moderate in severity.
  - Related AEs in two or more patients were IRRs (8.0 percent).
- For the 24 patients who have completed 36 months of treatment, the clinical activity of patisiran was maintained, with a negative 4.1 point mean change (improvement) in the mNIS+7 score relative to baseline.

To view the results presented by Alnylam at the 1st European ATTR Amyloidosis Meeting, please visit www.alnylam.com/capella.

*Pre-specified cardiac subpopulation: patients with evidence of pre-existing cardiac amyloid involvement and without confounding medical conditions, i.e., patients with baseline left ventricular wall thickness greater than or equal to 1.3 cm and no aortic valve disease or hypertension in medical history.

Conference Call Details

Alnylam management will discuss these results via conference call on November 2, 2017 at 12:30 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 2354344. A replay of the call will be available beginning at 3:30 p.m.

ET on November 2, 2017. To access the replay, please dial (855) 859-2056 (domestic) or (404) 537-3406 (international), and refer to conference ID 2354344.

About the APOLLO Phase 3 Study

The APOLLO Phase 3 trial 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 endpoint of the study is the difference in the change in mNIS+7 between patisiran and placebo at 18 months. Secondary endpoints include: the Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN) score; NIS-weakness (NIS-W); Rasch-built Overall Disability Scale (R-ODS); modified BMI (mBMI); timed 10-meter walk (10-MWT); and the COMPASS-31 autonomic symptom score. The trial enrolled 225 hATTR amyloidosis patients that were randomized 2:1, patisiran:placebo, with patisiran administered at 0.3 mg/kg once every three weeks for 18 months. The study was designed with 90 percent power to conservatively detect as little as a 37.5 percent difference in change in mNIS+7 between treatment groups, with a two-sided alpha of 0.05. The placebo mNIS+7 progression rate was derived from an Alnylam analysis of natural history data from 283 hATTR amyloidosis patients. All patients completing the APOLLO Phase 3 study are eligible to screen for the Global OLE study, in which they have the opportunity to receive patisiran on an ongoing basis.

About Patisiran

Patisiran is an investigational intravenously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of hereditary ATTR amyloidosis with polyneuropathy. 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 amyloidosis (hATTR) is an inherited, progressively debilitating, and often fatal disease caused by mutations in the TTR gene. TTR protein is primarily produced 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 for early stage disease are liver transplantation and tafamidis (approved in Europe, Japan, and certain countries in Latin America, specific indication varies by region). As such, 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 natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. By harnessing the natural biological process of RNAi occurring in our cells, 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, function upstream of today's medicines by potently silencing messenger RNA (mRNA) - the genetic precursors - that encode for disease-causing proteins, thus preventing them from being made. This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

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 people afflicted with rare genetic, cardio-metabolic, and hepatic infectious diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and 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 four product candidates that are in late-stage development. 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 to address the needs of patients who have limited or inadequate treatment options. Alnylam employs over 600 people in the U.S. and Europe and is headquartered in Cambridge, MA. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam or on LinkedIn.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions. With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe. Sanofi, Empowering Life. 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 complete results from its APOLLO Phase 3 clinical trial for patisiran and the potential implications of such results for patients, 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.

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