Alnylam Reports New Clinical Results from the APOLLO Phase 3 Study of Patisiran at the American Academy of Neurology 2018 Annual Meeting

April 24, 2018

? In New Post-Hoc Analysis, Patisiran Reduced the Composite Rate of All-Cause Hospitalization and Mortality by Approximately 50 Percent, Relative to Placebo ?

? In Addition, Patisiran Demonstrated Improvement in Multiple Quality of Life Measures, Compared to Placebo ?

? Analysis of Alnylam Act™ Genetic Testing Program Shows Identification of Pathogenic Transthyretin (TTR) Mutations in Approximately 7.5 Percent of Samples –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 24, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced new results from the APOLLO Phase 3 study of patisiran, an investigational RNAi therapeutic for the treatment of hereditary ATTR (hATTR) amyloidosis, at the American Academy of Neurology (AAN) 2018 Annual Meeting, being held April 21-27, 2018 in Los Angeles, California. These results were presented at the Clinical Trials Plenary Session on April 24, 2018 by David Adams, M.D., Ph.D., Department of Neurology, Bicêtre Hospital, Greater Paris University Hospitals, AP-HP, and Principal Investigator for the APOLLO trial.

“APOLLO is the largest clinical study of patients with hATTR amyloidosis conducted to date, and we continue to gather and analyze new data to describe the efficacy and safety of patisiran. To that end, we are pleased to share these new results from the APOLLO study, including a post-hoc, exploratory analysis demonstrating a significant decrease in the composite rate of all-cause hospitalization and mortality in patients receiving patisiran compared to placebo. We believe these results, along with previously presented APOLLO data that show halting or reversal of neuropathy progression in a majority of patients treated with patisiran, strengthen the body of evidence demonstrating that patisiran, if approved, has the potential to be a transformative treatment for patients with all forms of hereditary ATTR amyloidosis,” said Eric Green, Vice President and General Manager, TTR Program at Alnylam. “We continue to work collaboratively with the FDA and EMA through patisiran’s review process, with the goal of making this medicine available to patients as quickly as possible, upon approval.”

A new post-hoc, exploratory recurrent event analysis revealed an approximately 50 percent decrease in the composite rate of all-cause hospitalization and mortality over 18 months in patisiran-treated patients, relative to placebo, based upon hospitalizations and deaths designated as serious adverse events (SAEs) within 28 days after last dose of study drug. A similar finding was observed with the composite rate of cardiac hospitalization and all-cause mortality, showing an approximately 45 percent decrease with patisiran, relative to placebo; cardiac hospitalization events were defined as any hospitalizations designated as SAEs within the system organ class designation of cardiac disorder.

Furthermore, based on a quartile analysis of baseline Neurologic Impairment Score (NIS), patisiran demonstrated halting or improvement in the modified NIS+7 (mNIS+7) primary endpoint in patients regardless of baseline neuropathy severity, in contrast to the progression in mNIS+7 seen in placebo-treated patients. While treatment benefit is observed across all stages of disease, these results support the rationale for early treatment with patisiran to potentially halt or improve neuropathy progression or impairment, respectively.

Detailed results regarding patisiran’s effect on quality of life will also be presented in a separate oral presentation on April 25, 2018. Specifically, patisiran treatment was associated with improvement across all domains of the Norfolk Quality of Life-Diabetic Neuropathy (Norfolk QOL-DN) questionnaire at 9 and 18 months, relative to placebo. Significant improvements in disability, gait speed, autonomic neuropathy symptoms, and overall quality of life, as reported by the patient, were also noted at 18 months upon treatment with patisiran compared to placebo, with improvements in disability, gait speed, and overall quality of life observed as early as nine months.

Overall, there were 13 deaths in the APOLLO study; none were considered related to study drug and the frequency of deaths was lower in the patisiran group (4.7 percent) as compared with placebo (7.8 percent). The most commonly reported adverse events (AEs) that occurred more frequently in patisiran-treated patients were peripheral edema and infusion-related reactions (IRRs) and were generally mild to moderate in severity. AEs leading to treatment discontinuation were lower in patisiran-treated patients (4.7 percent) compared with placebo-treated patients (14.3 percent).

Finally, results of an analysis of the utilization of genetic testing through Alnylam Act were also presented, with evidence underscoring the heterogeneous presentation of hATTR amyloidosis symptoms. As of March 2018, Alnylam Act has facilitated testing of approximately 4,600 individuals who may carry gene mutations known to be associated with hATTR amyloidosis. Among these, approximately 350 patients were identified with positive pathogenic TTR mutations, representing approximately 7.5 percent of the patients tested since the Alnylam Act program was initiated in 2014.

All results presented at AAN can be viewed on the Capella section of the Alnylam website.

About the APOLLO Phase 3 Study
The APOLLO Phase 3 trial was 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 was the change from baseline in modified Neurologic Impairment Score +7 (mNIS+7) relative to placebo at 18 months. Secondary endpoints included: the Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN) score; NIS-weakness (NIS-W); Rasch-built Overall Disability Scale (R-ODS); timed 10-meter walk (10-MWT); modified BMI (mBMI); and the composite autonomic symptom score-31 (COMPASS-31). In addition, exploratory cardiac assessments included measurement of N-terminal pro-brain natriuretic peptide (NT-ProBNP) levels and echocardiography. The trial enrolled 225 hATTR amyloidosis patients from 19 countries with 39 genotypes who were randomized 2:1, patisiran:placebo, with patisiran administered at 0.3 mg/kg once every three weeks for 18 months. All patients who completed the APOLLO Phase 3 study were eligible to screen for the Global OLE study, in which they have the opportunity to receive patisiran on an ongoing basis.

About Alnylam Act™
The Alnylam Act™ program was created to reduce barriers to genetic testing and counseling to help people make more informed decisions about their health. While Alnylam provides financial support for this program, all tests and services are performed by independent third parties. At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for health care providers who sign up for this program. Genetic testing service is available in the U.S. and Canada. Genetic counseling is only available in the U.S. Alnylam Act currently offers genetic testing and counseling services in the U.S. for individuals at risk for hereditary ATTR (hATTR) amyloidosis and Acute Hepatic Porphyrias (AHPs).

About Patisiran
Patisiran is an investigational, intravenously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of hereditary ATTR 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

reduce the deposition and facilitate the clearance of TTR amyloid in peripheral tissues and potentially restore function to these tissues. Patisiran is currently under Priority Review as a Breakthrough Therapy with the U.S. Food and Drug Administration (FDA) and under accelerated assessment by the European Medicines Agency (EMA) for the treatment of patients with hATTR amyloidosis. The FDA has set a PDUFA date of August 11, 2018. The safety and efficacy of patisiran have not been evaluated by the FDA, the EMA 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 the TTR gene 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, as well as other disease manifestations. hATTR amyloidosis represents a major unmet medical need with significant morbidity and mortality, affecting approximately 50,000 people worldwide. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy. The only available treatment options for early stage disease are liver transplantation and, in some countries, 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 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 800 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.

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 new data presented for patisiran regarding hospitalizations and mortality and quality of life measurements, and the potential implications of such data for patients, including patients with hATTR amyloidosis with cardiac involvement, its expectations regarding the timing of regulatory reviews and potential regulatory approvals for patisiran in the United States and the EU, its views regarding the implications of an analysis of the utilization of genetic testing through Alnylam Act, 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 Annual Report on Form 10-K 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 FDA, EMA, or any other regulatory authority and no conclusions can or should be drawn regarding the safety or effectiveness of this investigational therapeutic.

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