Alnylam to Report New Clinical Results for Patisiran at the 4th Congress of the European Academy of Neurology

June 15, 2018

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 15, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that additional results from the APOLLO Phase 3 study of patisiran, an investigational RNAi therapeutic for the treatment of hereditary ATTR (hATTR) amyloidosis, will be presented at the 4thCongress of the European Academy of Neurology (EAN), being held June 16-19, 2018 in Lisbon, Portugal.

“The results being presented at EAN add to the wealth of data from the APOLLO Phase 3 study of patisiran that provide evidence for the potential of this investigational RNAi therapeutic for the treatment of hATTR amyloidosis,” said Eric Green, Vice President and General Manager, TTR Program at Alnylam.

Presentations include:

- **Impact of Prior TTR Stabilizer Use in Patients with Hereditary Transthyretin-Mediated Amyloidosis in the APOLLO Phase 3 Study of Patisiran**
  Oral Presentation, Saturday, June 16, 2018, 2:45 to 4:15 pm WET
  Lead Author: Teresa Coelho, Hospital de Santo António, Porto, Portugal.

- **Impact of Patisiran, an Investigational RNAi Therapeutic, on Nutritional Status in Patients with Hereditary Transthyretin-Mediated Amyloidosis**
  Oral Presentation, Saturday, June 16, 2018, 2:45 to 4:15 pm WET
  Lead Author: Laura Obici, Fondazione IRCCS Policlinico San Matteo, Pavio, Italy.

- **Outcomes of Patients with Hereditary Transthyretin-Mediated Amyloidosis with Early Onset V30M versus All Other Mutations in APOLLO, a Phase 3 Study of Patisiran**
  Poster Presentation, Saturday, June 16, 2018, 1:30 to 2:15 pm WET
  Lead Author: Teresa Coelho, Hospital de Santo António, Porto, Portugal.

- **Population Pharmacokinetic (PK)/Pharmacodynamic (PD) Model of Serum Transthyretin (TTR) Following Patisiran-LNP Administration in Healthy Volunteers and Patients with Hereditary TTR-Mediated (hATTR) Amyloidosis with Polyneuropathy**
  Poster Presentation, Saturday, June 16, 2018, 1:30 to 2:15 pm WET
  Lead Author: Varun Goel, Alnylam Pharmaceuticals, Cambridge, USA.

- **Patisiran-LNP Pharmacokinetics (PK), Pharmacodynamics (PD), and Exposure-Response (E-R) Relationship in Patients with Hereditary Transthyretin-Mediated (hATTR) Amyloidosis with Polyneuropathy**
  Poster Presentation, Sunday, June 17, 2018, 1:30 to 2:15 pm WET
  Lead Author: Amy Zhang, Alnylam Pharmaceuticals, Cambridge, USA.

- **Impact of Patisiran on Norfolk Quality of Life Questionnaire Diabetic Neuropathy (QOL-DN) in Patients with Hereditary Transthyretin-Mediated Amyloidosis: Results from the Phase 3 APOLLO Study**
  Poster Presentation, Sunday, June 17, 2018, 1:30 to 2:15 pm WET
  Lead Author: Laura Obici, Fondazione IRCCS Policlinico San Matteo, Pavio, Italy.

In addition, Alnylam and collaborators will give encore presentations of results from the Phase 1 and Phase 1/2 OLE studies of givosiran, an investigational RNAi therapeutic for the treatment of patients with Acute Hepatic Porphyrias (AHPs) with recurrent attacks.

Presentations include:

- **EXPLORE: A Prospective, Multinational Natural History Study of Patients With Acute Hepatic Porphyria With Recurrent Attacks**
  Oral Presentation, Saturday, June 16, 2018, 3:15 pm WET
  Lead Author: Jean-Charles Deybach, Reference Center for Rare Diseases Porphyrias France, European Porphyria Network.

- **Phase 1/2, Randomized, Placebo Controlled and Open Label Extension Studies of Givosiran, an Investigational RNA Interference (RNAi) Therapeutic, in Patients with Acute Intermittent Porphyria**

Oral Presentation, Saturday, June 16, 2018, 2:45 to 4:15 pm WET
Lead Author: Manisha Balwani, Icahn School of Medicine at Mount Sinai, New York, NY.

Alnylam is also sponsoring a Scientific Theatre presentation titled, **"Inherited Metabolic Diseases with Porphyric Neuropathy"** on Saturday, June 16, 4:30 to 4:45 pm WET and Sunday, June 17, 9:30 to 9:45 am WET, with Prof. Jean-Charles Deybach, M.D., Ph.D., Director of the European Porphyria Network and EXPLORE Investigator, as the speaker.

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 APOLLO Phase 3 Study
The APOLLO Phase 3 study (N=225) 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 study was completed in August 2017 and detailed study results were presented at the 1st European ATTR Amyloidosis Meeting for Patients and Doctors on November 2, 2017. All patients who completed the APOLLO Phase 3 study were eligible to screen for the Global OLE study, in which they had the opportunity to receive patisiran on an ongoing basis.

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. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy. 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 Givosiran
Givosiran is an investigational, subcutaneously administered RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) in development for the treatment of acute hepatic porphyrias (AHPs). Monthly administration of givosiran has the potential to significantly lower induced liver ALAS1 levels in a sustained manner and thereby decrease neurotoxic heme intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG) to near normal levels. By reducing accumulation of these intermediates, givosiran has the potential to prevent or significantly reduce the occurrence of severe and life-threatening attacks, control chronic symptoms, and decrease the burden of the disease. Givosiran utilizes Alnylam's Enhanced Stabilization Chemistry ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index. Givosiran has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) and PRIME designation by the European Medicines Agency (EMA). Givosiran has also been granted orphan drug designations in both the U.S. and the EU for the treatment of AHPs. The safety and efficacy of givosiran are currently being investigated in the ENVISION Phase 3 clinical trial and ongoing Phase 1/2 OLE study and have not been evaluated by the FDA, the EMA or any other health authority.

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 data to be presented for patisiran and givosiran, and the potential implications of such data for patients, 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.

Neither patisiran nor givosiran have 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 these investigational therapeutics.

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