Alnylam to Report New Clinical Results for ONPATTRO® (patisiran) at Peripheral Nerve Society (PNS) Annual Meeting and the 5th Congress of the European Academy of Neurology (EAN)

June 13, 2019

– Data from Ongoing Open-Label Extension Study Highlight Durable Halting or Reversal of Neuropathy Disease Progression Relative to Baseline and Consistent Safety Profile of ONPATTRO in Patients with hATTR Amyloidosis –

– Alnylam to Share Data Evaluating Treatment with ONPATTRO in Patients Previously Treated with Tafamidis –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 13, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the Company will present new results from the Global Open-Label Extension (OLE) study of ONPATTRO® (patisiran) in patients with hereditary ATTR (hATTR) amyloidosis with polyneuropathy and data from a post-hoc analysis of the APOLLO study, evaluating efficacy of ONPATTRO in patients with previous tafamidis treatment at the Peripheral Nerve Society (PNS) Annual Meeting, June 22-26, in Genoa, Italy. Additional data examining ONPATTRO and hATTR amyloidosis disease burden will be presented at PNS, and at the 5thCongress of the European Academy of Neurology (EAN), June 29-July 2, in Oslo, Norway.

"The results being presented from the ongoing Open-Label Extension study continue to reinforce the long-term ability of ONPATTRO to halt or reverse neuropathy progression and improve quality of life relative to baseline in patients with hATTR amyloidosis with polyneuropathy, while maintaining a safety profile consistent with previous studies," said Eric Green, Senior Vice President and General Manager, TTR Program at Alnylam. "In addition, the data to be presented at the PNS and EAN meetings illustrate the critical need to recognize, properly diagnose, and treat the disease as early as possible."

PNS Data Presentations:

- **Long-Term Safety and Efficacy of Patisiran in Patients with hATTR Amyloidosis: Global OLE Study**
  Lead Author: Michael Polydefkis
  Platform Presentation Session – Monday, June 24,15:30 – 15:45 p.m. (CET)
- **Efficacy of Patisiran in Patients with hATTR Amyloidosis and Prior Tafamidis Use: Analysis of APOLLO**
  Lead Author: Hollis Lin
  Poster Session II – Monday, June 24, 12:00 – 14:00 p.m. (CET)
- **Hereditary Transthyretin-Mediated (hATTR) Amyloidosis: French Perspective on the Patient Journey**
  Lead Author: David Adams
  Poster Session I – Sunday, June 23, 12:00 – 14:00 p.m. (CET)
- **Impact of Patisiran, an RNAi Therapeutic, on Diarrhea Symptoms in Patients with Hereditary Transthyretin-Mediated Amyloidosis**
  Lead Author: Laura Obici
  Poster Session II – Monday, June 24, 12:00 – 14:00 p.m. (CET)
- **Variable Presentation of Hereditary Transthyretin-Mediated (hATTR) Amyloidosis: A Single Center Experience with the Patisiran PAAP**
  Lead Author: Yessar Hussain
  Poster Session II – Monday, June 24, 12:00 – 14:00 p.m. (CET)
- **Indirect Treatment Comparison of the Efficacy of Patisiran and Inotersen for hATTR Amyloidosis with Polyneuropathy**
  Lead Author: Laura Obici
  Poster Session III – Tuesday, June 25, 12:00 – 14:00 p.m. (CET)

EAN Data Presentations:

- **Impact of Baseline Neuropathy State in Patients with Hereditary Transthyretin-Mediated (hATTR) Amyloidosis With or Without Patisiran Treatment**
  Lead Author: Theodoros Kyriakides
  EAN e-Presentation Session – Monday, July 1, 13:30 – 14:15 p.m. (CET)

IMPORTANT SAFETY INFORMATION

ONPATTRO is a medicine that treats the polyneuropathy caused by an illness called hereditary transthyretin-mediated amyloidosis (hATTR

amyloidosis). ONPATTRO is used in adults only.

Infusion-Related Reactions

Infusion-related reactions (IRRs) have been observed in patients treated with ONPATTRO. In a controlled clinical study, 19 percent of ONPATTRO-treated patients experienced IRRs, compared to 9 percent of placebo-treated patients. The most common symptoms of IRRs with ONPATTRO were flushing, back pain, nausea, abdominal pain, dyspnea, and headache.

To reduce the risk of IRRs, patients should receive premedication with a corticosteroid, paracetamol, and antihistamines (H1 and H2 blockers) at least 60 minutes prior to ONPATTRO infusion. Monitor patients during the infusion for signs and symptoms of IRRs. If an IRR occurs, consider slowing or interrupting the infusion and instituting medical management as clinically indicated. If the infusion is interrupted, consider resuming at a slower infusion rate only if symptoms have resolved. In the case of a serious or life-threatening IRR, the infusion should be discontinued and not resumed.

Reduced Serum Vitamin A Levels and Recommended Supplementation

ONPATTRO treatment leads to a decrease in serum vitamin A levels. Supplementation at the recommended daily allowance (RDA) of vitamin A is advised for patients taking ONPATTRO. Higher doses than the RDA should not be given to try to achieve normal serum vitamin A levels during treatment with ONPATTRO, as serum levels do not reflect the total vitamin A in the body.

Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g. night blindness).

Adverse Reactions

The most common adverse reactions that occurred in patients treated with ONPATTRO were respiratory-tract infection (29 percent) and infusion-related reactions (19 percent).

About ONPATTRO® (Patisiran)

ONPATTRO is an RNAi therapeutic that is approved by the U.S. Food and Drug Administration (FDA) for the treatment of the polyneuropathy of hATTR amyloidosis in adults. ONPATTRO is also approved in the European Union for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy. Based on Nobel Prize-winning science, ONPATTRO is an intravenously administered RNAi therapeutic targeting transthyretin (TTR) for the treatment of hereditary ATTR amyloidosis. It is designed to target and silence TTR messenger RNA, thereby blocking the production of TTR protein before it is made. ONPATTRO blocks the production of TTR in the liver, reducing its accumulation in the body's tissues in order to halt or slow down the progression of the disease.

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-motor 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.

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 new class of medicines, known as RNAi therapeutics, is now a reality. 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

Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a new class of innovative medicines with the potential to transform the lives of people afflicted with rare genetic, cardio-metabolic, hepatic infectious, and central nervous system/ocular diseases. Based on Nobel Prizewinning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of diseases with high unmet need. ONPATTRO® (patisiran) is the first-ever RNAi therapeutic approved by the U.S. FDA for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults and by the EMA for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. Alnylam has a deep pipeline of investigational medicines, including six product candidates in Phase 3 studies. 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. Headquartered in Cambridge, MA, Alnylam employs over 1,200 people worldwide. For more information, 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 plans to present additional data concerning ONPATTRO (patisiran), 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, successfully launching, marketing and selling its approved products globally, Alnylam's ability to successfully expand the indication for ONPATTRO in the future, competition from others using technology similar to Alnylam's and others developing or marketing 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.

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