Alnylam Launches ONPATTRO™ (patisiran), the First-Ever RNAi Therapeutic, in Germany

October 2, 2018

− ONPATTRO Indicated for Treatment of Hereditary Transthyretin-Mediated (hATTR) Amyloidosis (hATTR Amyloidosis) in Adults with Stage 1 or Stage 2 Polyneuropathy –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 2, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNA interference (RNAi) therapeutics company, today announced that ONPATTRO (patisiran) is now available in Germany. ONPATTRO has been developed to meet a significant unmet need for patients with hereditary ATTR amyloidosis, a devastating, chronic and often fatal disease. ONPATTRO is based on Nobel Prize-winning science and is the first-ever RNAi therapeutic to be approved in the European Union. Alnylam plans to launch ONPATTRO in additional markets in Europe throughout 2018 and 2019.

"The launch of ONPATTRO in Germany, just over a month after being granted approval by the European Medicines Agency, is a demonstration of our commitment to deliver innovative medicines with the potential to transform the lives of patients suffering from hATTR amyloidosis and our recognition of the urgency of unmet medical needs in this patient community," said Hannes Schmeil, Country General Manager, Alnylam Germany. "Up until now, patients in Germany lacked medical treatment options with the potential to halt the progression of their disease. ONPATTRO will provide physicians, patients and their families with a new treatment option that we hope will make a meaningful difference to patients' lives, restoring their hope for the future."

The European Commission decision was based on the evaluation of the effects of patisiran in hATTR amyloidosis patients with polyneuropathy and its safety profile as demonstrated in the APOLLO Phase 3 study, the largest-ever study in hATTR amyloidosis patients with polyneuropathy. Results from the APOLLO study were published in the July 5, 2018, issue of *The New England Journal of Medicine*. The Summary of Product Characteristics (SmPC) includes data from APOLLO on primary and secondary endpoints, as well as exploratory cardiac endpoints. The SmPC allows for the administration of patisiran in the home setting under the supervision of a healthcare professional provided infusions are being tolerated well by the patient. The European Medicines Agency reviewed patisiran under the accelerated assessment procedure that is granted to medicines judged to be of major interest for public health and therapeutic innovation.

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. In Europe, treatment options that can modify the course of the disease are limited and there remains a pressing need for novel medicines 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 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 ONPATTRO™ (patisiran)
Patisiran, based on Nobel Prize-winning science, is an intravenously administered RNAi therapeutic targeting transthyretin (TTR) 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. Patisiran blocks the production of transthyretin in the liver, reducing its accumulation in the body's tissues in order to halt or slow down the progression of the disease. In August 2018, patisiran received U.S. Food and Drug Administration (FDA) approval for the treatment of the polyneuropathy of hATTR amyloidosis in adults, as well as European Medicines Agency marketing authorization for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy.

Important Safety Information for ONPATTRO™

Infusion-Related Reactions
Infusion-related reactions (IRRs) have been observed in patients treated with patisiran. In a controlled clinical study, 19% of patisiran-treated patients experienced IRRs, compared to 9% of placebo-treated patients. The most common symptoms of IRRs with patisiran were flushing, back pain, nausea, abdominal pain, dyspnoea, 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 patisiran 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
Patisiran treatment leads to a decrease in serum vitamin A levels. Patients receiving patisiran should take oral supplementation of approximately 2500

IU vitamin A per day to reduce the potential risk of ocular toxicity due to vitamin A deficiency. Doses higher than 2500 IU vitamin A per day should not be given to try to achieve normal serum vitamin A levels during treatment with patisiran, 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. including reduced night vision or night blindness, persistent dry eyes, eye inflammation, corneal inflammation or ulceration, corneal thickening or corneal perforation).

Adverse Reactions
The most common adverse reactions that occurred in patients treated with patisiran were peripheral oedema (30%) and infusion-related reactions (19%).

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a new class of innovative medicines with the potential to improve the lives of people afflicted with rare genetic, cardio-metabolic, hepatic infectious, and central nervous system (CNS) 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. ONPATTRO™ (patisiran) lipid complex injection, available in the U.S. for the treatment of the polyneuropathy of hATTR amyloidosis in adults, is Alnylam's first U.S. FDA-approved RNAi therapeutic. In the EU, ONPATTRO is approved for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy. Alnylam has a deep pipeline of investigational medicines, including three 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 worldwide and is headquartered in Cambridge, MA.

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 supporting the EC Decision and the potential implications of such data for patients, plans for regulatory filings in other markets in Europe, in 2018 and 2019, and expectations regarding the company's "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 patisiran in the future, 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.

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