Alnylam Announces Filing for Marketing Authorization of ONPATTRO® (patisiran) in Brazil for the Treatment of Hereditary ATTR Amyloidosis with Polyneuropathy

October 10, 2019

– Filing Marks the First RNAi Therapeutic to be Submitted for Potential Approval in Latin America –

– Submission Made Under the Accelerated Regulatory Pathway for Rare Diseases –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 10, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that the marketing authorization application of patisiran for the treatment of patients with hereditary transthyretin-mediated (hATTR) amyloidosis with polyneuropathy has been filed with the Brazilian Health Regulatory Agency (ANVISA). Patisiran has been granted priority review by ANVISA which is awarded to innovative medicines that treat rare diseases under this accelerated regulatory pathway. Alnylam expects a decision from ANVISA in the first half of 2020.

Patisiran – which will be commercialized following regulatory approval under the brand name ONPATTRO® – is Alnylam's first investigational drug submitted for review in Brazil. If approved, it will be the first product to be launched and marketed by Alnylam in the country and the first ever RNAi therapeutic to be approved in Latin America.

"The filing of our registration submission for patisiran in Brazil is an important step forward in our continued commitment to bring RNAi therapeutics to people around the world," said Norton Oliveira, Senior Vice President, Head of Latin America at Alnylam. "hATTR amyloidosis is a rare progressive condition that is considered endemic in Brazil, affecting more than 5,000 people. Symptoms can manifest throughout the entire body and have a devastating impact on patients. We look forward to working closely with ANVISA to bring patisiran to these patients in need as quickly as possible."

The registration submission is based on positive data from the APOLLO Phase 3 study, which evaluated the efficacy and safety of patisiran 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*.

ONPATTRO 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 for this indication in Canada and Japan, and is approved in the European Union and Switzerland for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy.

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 and Switzerland for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy, in Canada for the treatment of hATTR amyloidosis with polyneuropathy by Health Canada, and in Japan for the treatment of hATTR amyloidosis with polyneuropathy by the Japanese Ministry of Health, Labour and Welfare (MHLW). Patisiran is also being investigated in patients with ATTR amyloidosis (hereditary [hATTR] or wild type [wtATTR]) with cardiomyopathy in the APOLLO-B study. 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.

Important Safety Information for ONPATTRO

The most common adverse reactions observed with ONPATTRO included infusion-related reactions (IRRs) such as flushing, back pain, nausea, abdominal pain, dyspnea, and headache. To reduce the risk of IRRs, patients should receive premedication with a corticosteroid, acetaminophen, and antihistamines prior to ONPATTRO infusion. If an IRR occurs, consider slowing or interrupting the infusion and instituting medical management as clinically indicated. In the case of a serious or life-threatening IRR, the infusion should be discontinued and not resumed. Because ONPATTRO reduces serum vitamin A levels, patients should be advised to take the recommended daily allowance (RDA) of vitamin A, and referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g. night blindness).

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 whole 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 (CNS)/ocular 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. Alnylam's first commercial RNAi therapeutic is ONPATTRO ® (patisiran), approved in the U.S., EU, Canada, and Japan. Alnylam has a deep pipeline of investigational medicines, including five 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 1,200 people worldwide 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 expectations regarding the review of its filing for marketing approval for patisiran in Brazil by ANVISA and the expected timing of a decision from ANVISA, the potential size of the patient population in Brazil that could benefit from patisiran, if approved, 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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