Alnylam Launches ONPATTRO® (patisiran) for the Treatment of Polyneuropathy in hATTR Amyloidosis, the First-Ever RNAi Therapeutic Approved in Canada

July 23, 2019

ONPATTRO® is the Only Treatment that Demonstrated Improvement, Relative to Baseline, in both Polyneuropathy and Quality of Life Measures in Patients[1, 2] with hATTR Amyloidosis

MISSISSAUGA, ON, July 23, 2019 /CNW/ - Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNA interference (RNAi) therapeutics company, today announced the Health Canada approval and immediate availability of ONPATTRO® (patisiran) for the treatment of polyneuropathy in adult patients with hereditary transthyretin-mediated (hATTR) amyloidosis[3]. ONPATTRO is the only treatment in Canada indicated for all stages of polyneuropathy associated with hATTR amyloidosis, a progressive, debilitating, chronic and often fatal disease. ONPATTRO is based on Nobel Prize-winning science and is the first ever RNAi therapeutic to be approved in Canada.

"hATTR amyloidosis can progress quickly becoming severely debilitating, and often leads to premature death," said Dr. Vera Bril, Professor of Medicine at the University of Toronto, Director of Neurology at University Health Network and Mount Sinai Hospital and the Krembil Family Chair in Neurology. "Having a treatment that can potentially reverse the course of this life-threatening disease marks a major advance for my patients, many of whom have crippling neuropathic pain, struggle to walk unaided and suffer from countless other symptoms, like diarrhea and vomiting, that interfere with normal activities of daily living."

hATTR amyloidosis is a multisystemic, progressive disease caused by mutations that interfere with the way the body manufactures a specific protein formed in the liver. Known as gene silencing, RNAi is a new approach to the treatment of the disease, targeting the faulty protein that causes the disease.

"As a cardiologist with several hereditary TTR amyloidosis patients with both polyneuropathy and cardiomyopathy, the approval of ONPATTRO provides a new option for this devastating disease," said Dr. Diego Delgado, Cardiologist at the Peter Munk Cardiac center at the University Health Network. "Many of my patients have significant disease burden not only in their heart, but also the nerves. It is exciting to have an opportunity to halt or even reverse the progression of a disease that my patients have experienced as a slow march to disability and death."

Symptoms of hATTR amyloidosis can vary from person to person, depending on which organs or tissues are affected and can worsen as the disease progresses. Parts of the body that are typically affected are the peripheral nervous (nerves), cardiac (heart) and gastrointestinal (digestive) systems resulting in polyneuropathy and cardiomyopathy. Specifically, neuropathic changes result in sensory-motor issues, with challenges in activities of daily living. Autonomic nerve involvement can lead to low blood pressure, diarrhea, impotence, and bladder disturbances, while cardiac symptoms include heart failure and arrhythmias.[4]

"Imagine looking ahead to a future where your body deteriorates and you are unlikely to survive the next 5 years! No treatment, only symptom management. Until recently, this has been the case for many hATTR patients and their families," said Marsha McWhinnie, Founder of the Canadian Amyloidosis Support Network (CASN) and Anne Marie Carr, Founder of the Hereditary Amyloidosis Canada (HAC) in a joint statement. "Canadian physicians now have another new treatment option to change the future for their patients, to give them meaningful improvement in their lives, to give them hope."

The Health Canada approval was based on results of the APOLLO Phase 3 study, the largest-ever study in patients with hATTR amyloidosis. In the pivotal, placebo-controlled study, 148 patients received 0.3 mg/kg of ONPATTRO and 77 patients received placebo administered once every 3 weeks via intravenous infusion for up to 18 months, with a mean ONPATTRO exposure of 17.7 months. All patients received premedication with a corticosteroid, acetaminophen, and H1 and H2 blockers.[5] The primary endpoint of the APOLLO study was the change from baseline in the modified Neuropathy Impairment Score +7 (mNIS+7), which assesses motor strength, reflexes, sensation, nerve conduction and postural blood pressure. In the APOLLO study, ONPATTRO demonstrated significant improvement versus placebo in polyneuropathy, quality of life, walking, nutritional status and activities of daily living. More than half of ONPATTRO patients improved over their own baseline for polyneuropathy and quality of life with some patients reducing dependence on or no longer requiring walking aids. The mean (±SD) mNIS+7 at baseline was 80.9±41.5 in the patisiran group and 74.6±37.0 in the placebo group; the least-squares mean (±SE) change from baseline was −6.0±1.7 versus 28.0±2.6 (difference, −34.0 points; P<0.001) at 18 months. The mean (±SD) baseline Norfolk QOL-DN score was 59.6±28.2 in the patisiran group and 55.5±24.3 in the placebo group; the least-squares mean (±SE) change from baseline was −6.7±1.8 versus 14.4±2.7 (difference, −21.1 points; P<0.001) at 18 months.[6]

The most frequently occurring adverse reactions reported in ONPATTRO-treated patients (≥ 10% of patients and occurring ≥ 3 percentage points more frequently than in placebo-treated patients) were peripheral edema and infusion-related reactions.[7] ONPATTRO is the only approved treatment in Canada that does not require additional safety monitoring via blood tests.

ONPATTRO was granted Priority Review status by Health Canada, which is intended for new potentially life-saving treatments where there is no existing medicine in the Canadian market or where the new medicine represents a significant improvement in the benefit/risk profile over existing products.[8]

"Health Canada's approval of ONPATTRO underscores our commitment to deliver innovative medicines with the potential to transform the lives of patients suffering from hATTR amyloidosis with polyneuropathy," says Jeff Miller, Country Manager, Alnylam Canada. "It marks a major milestone in Alnylam's history, as the company's first treatment approved in Canada, but we believe this is just the beginning. Our vision is to harness the power of RNAi therapeutics to increase the number of treatment options available for patients with serious, life-threatening rare diseases where there are currently limited or no available treatment options. We take pride in working with the medical and patient community to increase awareness, enable diagnosis and provide important education and support services."

About hATTR amyloidosis[9]
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 a promising and rapidly advancing frontier in biology and drug development that has the potential to transform the care of patients with genetic and other diseases. It was awarded the 2006 Nobel Prize for Physiology or Medicine.

About ONPATTRO (patisiran)
Patisiran is an intravenously administered RNAi therapeutic targeting transthyretin (TTR) for the treatment of hereditary ATTR amyloidosis with polyneuropathy. 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 reverse the progression of the disease.[10]

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. Alnylam has a deep pipeline of investigational medicines, including five product candidates that are in Phase 3 clinical trials and one in registration. 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 1200 people worldwide and is headquartered in Cambridge, MA. Alnylam Canada is headquartered in Mississauga, Ontario with established operations since June 2018.

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Alnylam Forward Looking Statements
Various statements in this release concerning Alnylam's future expectations, plans and prospects, including, without limitation, Alnylam's plans to launch ONPATTRO in Canada, the potential benefits for patients in Canada for whom ONPATTRO is indicated, 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 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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[1] Adams et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. New England Journal of Medicine, 379:11-21, July 5, 2018.

[2] Patisiran Product Monograph, Alnylam Pharmaceuticals Inc, June 7, 2019.

[3] Patisiran Product Monograph, Alnylam Pharmaceuticals Inc, June 7, 2019.

[4] Adams et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. New England Journal of Medicine, 379:11-21, July 5, 2018.

[5] Patisiran Product Monograph, Alnylam Pharmaceuticals Inc, June 7, 2019.

[6] Adams et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. New England Journal of Medicine, 379:11-21, July 5, 2018.

[7] Patisiran Product Monograph, Alnylam Pharmaceuticals Inc, June 7, 2019.

[8] Health Canada https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/prfs_tpfd-eng.pdf Accessed June 17, 2019.

[9] The American Journal of Managed Care https://www.ncbi.nlm.nih.gov/pubmed/28978215/ Accessed June 17, 2019.

[10] Adams et al. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. New England Journal of Medicine, 379:11-21, July 5, 2018.

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