Alnylam to Present Full 9-Month Results from the HELIOS-A Phase 3 Study of Vutrisiran at the American Academy of Neurology Virtual Annual Meeting 2021

March 23, 2021

-- Alnylam to Share Additional Data From its RNAi Product Portfolio Including ATTR Amyloidosis and Acute Hepatic Porphyria --

--Company to Host Conference Call April 19th at 4:00 pm ET to Discuss HELIOS-A Results--

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 23, 2021-- Alnylam Pharmaceuticals, Inc., (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the Company will present full 9-month results from the HELIOS-A Phase 3 study of vutrisiran, an investigational RNAi therapeutic in development for the treatment of the polyneuropathy of hereditary ATTR (hATTR) amyloidosis, at the American Academy of Neurology (AAN) Virtual Annual Meeting, being held April 17-22. The Company previously announced positive topline 9-month results from the HELIOS-A study in January. Additional data from Alnylam’s ATTR amyloidosis program, including updates from the ongoing open-label extension study of ONPATTRO (patisiran) in patients with hATTR amyloidosis with polyneuropathy, will also be presented at AAN, along with data from the Phase 3 ENVISION study of GIvlaari in patients with acute hepatic porphyria (AHP).

“The depth and breadth of data that will be presented at AAN from across our RNAi product and pipeline portfolio reinforce the tremendous progress we have made with developing potentially transformative medicines for patients with rare diseases,” said Akshay Vaishnaw, M.D., Ph.D., President of R&D at Alnylam. “In January we announced positive topline results from the HELIOS-A Phase 3 study of vutrisiran, the fifth of our investigational RNAi medicines to reach that significant milestone. We are excited for the upcoming presentation of the full 9-month HELIOS-A results as we believe in the potential of vutrisiran, as a low-dose, once quarterly, subcutaneously administered treatment option for patients living with a progressive, life-threatening, multi-system disease. We look forward to submitting our U.S. regulatory filing for marketing approval of vutrisiran in early 2021 as we continue to make progress towards building what we believe will be an industry-leading franchise of medicines for the treatment of ATTR amyloidosis.”

**hATTR Amyloidosis**

- **HELIOS-A: 9-month Results from the Phase 3 Study of Vutrisiran in Patients with Hereditary Transthyretin-Mediated Amyloidosis with Polyneuropathy**
  - Oral Presentation
  - Monday, April 19, 2021 at 2:00 pm ET
  - Lead Author: David Adams

- **Global Open-label Extension: 24-month Data in Patients with hATTR Amyloidosis**
  - Oral Presentation
  - Wednesday, April 21, 2021 at 4:00 pm ET
  - Lead Author: Michael Polydefkis

- **Impact of Patisiran on Activities of Daily Living and Functional Status in hATTR Amyloidosis**
  - Oral Presentation
  - Wednesday, April 21, 2021 at 4:08 pm ET
  - Lead Author: Amanda Peltier

- **Neurofilament Light Chain (NfL) as a Potential Biomarker of Treatment Response in Hereditary Transthyretin-Mediated Amyloidosis: Data from the Patisiran Global OLE Study**
  - Poster Presentation
  - Available April 17
  - Lead Author: Michael Polydefkis

- **Open-label Study of Patisiran in Patients with hATTR Amyloidosis Post-Orthotopic Liver Transplant**
  - Poster Presentation
  - Available April 17
  - Lead Author: Seth Arum

- **Evaluation of Patisiran With Concomitant or Prior Use of Transthyretin Stabilizers**
  - Poster Presentation
  - Available April 17
  - Lead Author: Madeline Merkel

**Acute Hepatic Porphyria**

- **Reduction in Pain During and Between Attacks in Patients with Acute Hepatic Porphyria Treated with Givosiran: A**
Post-Hoc Analysis of the Phase 3 ENVISION Study
Oral Presentation
Tuesday, April 20, 2021 at 4:24 pm ET
Lead Author: Susana Monroy

- **Disease Burden and Healthcare Utilization Among Patients with Acute Intermittent Porphyria Experiencing Chronic Neuropathy: Analyses from a National Healthcare Database**
  Poster Presentation
  Available April 17
  Lead Author: Angelika Erwin

Conference Call
Alnylam management will discuss the full 9-month results from the HELIOS-A Phase 3 clinical trial via conference call on Monday, April 19th at 4:00 pm ET. A webcast presentation will also be available on the Investors page of the Company’s website, www.alnylam.com. To access the call, please dial 877-312-7507 (domestic) or +1-631-813-4828 (international) five minutes prior to the start time and refer to conference ID 9580096. A replay of the call will be available beginning at 7:00 pm ET on the day of the call. To access the replay, please dial 855-859-2056 (domestic) or +1-404-537-3406 (international) and refer to conference ID 9580096.

**About hATTR Amyloidosis**
Hereditary transthyretin (TTR)-mediated amyloidosis (hATTR) is an inherited, progressively debilitating, and fatal disease caused by variants (i.e., mutations) in the TTR gene. TTR protein is primarily produced in the liver and is normally a carrier of vitamin A. Variants 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 Acute Hepatic Porphyria**
Acute hepatic porphyria (AHP) refers to a family of ultra-rare, genetic diseases characterized by debilitating, potentially life-threatening attacks and, for some patients, chronic manifestations that negatively impact daily functioning and quality of life. AHP is comprised of four subtypes: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and ALA dehydratase-deficiency porphyrinemia (ADP). Each type of AHP results from a genetic defect leading to a lack of certain enzymes needed to produce heme in the liver, which leads to an accumulation of porphyrins in the body to toxic amounts. AHP disproportionately impacts women of working and childbearing age, and symptoms of the disease vary widely. Severe, unexplained abdominal pain is the most common symptom, which can be accompanied by limb, back, or chest pain, nausea, vomiting, confusion, anxiety, seizures, weak limbs, constipation, diarrhea, or dark or reddish urine. AHP is life-threatening due to the possibility of paralysis and respiratory arrest during attacks. The nonspecific nature of AHP signs and symptoms can often lead to misdiagnoses of other more common conditions such as gynecological disorders, viral gastroenteritis, irritable bowel syndrome (IBS), and appendicitis. Consequently, on a global perspective, patients with AHP can wait up to 15 years for a confirmed diagnosis, with the risk of addiction problems. In addition, long-term complications and comorbidities of AHP can include hypertension, chronic kidney disease or liver disease, including hepatocellular carcinoma.

**About Vutrisiran**
Vutrisiran is an investigational, subcutaneously administered RNAi therapeutic in development for the treatment of ATTR amyloidosis, which encompasses both hereditary (hATTR) and wild-type (wtATTR) amyloidosis. It is designed to target and silence specific messenger RNA, blocking the production of wild-type and variant transthyretin (TTR) protein before it is made. Quarterly administration of vutrisiran may help to reduce deposition and facilitate the clearance of TTR amyloid deposits in tissues and potentially restore function to these tissues. Vutrisiran utilizes Alnylam’s Enhanced Stabilization Chemistry (ESC)-GalNAc-conjugate delivery platform, designed for increased potency and high metabolic stability that allows for infrequent subcutaneous injections. The safety and efficacy of vutrisiran have not been evaluated by the U.S. Food and Drug Administration, European Medicines Agency or any other health authority.

**About ONPATTRO® (patisiran)**
ONPATTRO is an RNAi therapeutic that was approved in the United States and Canada for the treatment of the polynuropathy of hATTR amyloidosis in adults. ONPATTRO is also approved in the European Union, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy, and in Japan for the treatment of hATTR amyloidosis with polyneuropathy. ONPATTRO is an intravenously administered RNAi therapeutic targeting transthyretin (TTR). 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 polyneuropathy associated with the disease. For more information about ONPATTRO, including full prescribing information and important safety information, visit ONPATTRO.com.

**About GIVLAARI® (givosiran)**
GIVLAARI is an RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) for the treatment of adults and adolescents with acute hepatic porphyria (AHP). In the pivotal study, givosiran was shown to significantly reduce the rate of porphyria attacks that required hospitalizations, urgent healthcare visits or intravenous hemin administration at home compared to placebo. GIVLAARI is Alnylam’s first commercially available therapeutic based on its Enhanced Stabilization Chemistry ESC-GalNAc conjugate technology to increase potency and durability. GIVLAARI is administered via subcutaneous injection once monthly at a dose based on actual body weight and should be administered by a healthcare professional. GIVLAARI works by specifically reducing elevated levels of aminolevulinic acid synthase 1 (ALAS1) messenger RNA (mRNA), leading to reduction of toxins associated with attacks and other disease manifestations of AHP. For more information about GIVLAARI, including full prescribing information and important safety information, visit GIVLAARI.com.

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 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, 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 RNAi therapeutics platform. Alnylam's commercial RNAi therapeutic products are ONPATTRO® (patisiran), GIVLAARI® (givosiran), and OXLUMO™ (lumasiran) and Leqvîlo® (inclisiran) being developed and commercialized by Alnylam's partner Novartis. Alnylam has a deep pipeline of investigational medicines, including six product candidates that are in late-stage development. Alnylam is executing on its "Alnylam P²x2²" strategy to deliver transformative medicines in both rare and common diseases benefiting patients around the world through sustainable innovation and exceptional financial performance, resulting in a leading biotech profile. Alnylam 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 expectations, plans, aspirations, and goals, including those related to vutrisiran and its potential as a low-dose, once quarterly, subcutaneously administered treatment option for patients, the expected timing of the filing of a NDA for vutrisiran, building an industry-leading franchise in medicines for the treatment of ATTR amyloidosis, becoming a leading biotech company, and the achievement of its "Alnylam P²x2²" strategy, 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: the direct or indirect impact of the COVID-19 global pandemic or any future pandemic on Alnylam’s business, results of operations and financial condition and the effectiveness or timeliness of Alnylam’s efforts to mitigate the impact of the pandemic; Alnylam's ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for its product candidates; actions or advice of regulatory agencies and Alnylam’s ability to obtain and maintain regulatory approval for its product candidates, as well as favorable pricing and reimbursement; successfully launching, marketing and selling its approved products globally; delays, interruptions or failures in the manufacture and supply of its product candidates or its marketed products; obtaining, maintaining and protecting intellectual property; Alnylam’s ability to successfully expand the indication for ONPATTRO in the future; Alnylam's ability to manage its growth and operating expenses through disciplined investment in operations and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; Alnylam’s ability to maintain strategic business collaborations; Alnylam's dependence on third parties for the development and commercialization of certain products, including Novartis, Regeneron and Vir; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and in its other SEC filings. 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.

This release is not intended to convey conclusions about efficacy or safety as to any investigational RNAi therapeutics or investigational uses previously approved therapeutics. There is no guarantee that any investigational therapeutics or expanded uses of commercial products will successfully complete clinical development or gain health authority approval.

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