Alnylam to Report New Clinical Results for Givosiran at the 2019 International Congress on Porphyrins and Porphyrias

August 14, 2019

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 14, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the Company and its collaborators will present at the 2019 International Congress on Porphyrins and Porphyria (ICPP), being held September 8-11, 2019 in Milan, Italy. Presentations will include additional results from the ENVISION Phase 3 study and Phase 1/2 open-label extension study of givosiran, an investigational RNAi therapeutic for the treatment of acute hepatic porphyria (AHP).

Oral presentations:

- **ENVISION, a Phase 3 Study of Safety and Efficacy of Givosiran, an Investigational RNAi Therapeutic, in Acute Hepatic Porphyria Patients**
  Tuesday, September 10, 2019 at 11:30 am CET
  Leading Authors: Gouya L, Sardh E, Rees DC

- **Acute Hepatic Porphyria (AHP) Disease Manifestations and Daily Life Impacts in EXPLORE International, Prospective, Natural History Study**
  Tuesday, September 10, 2019 at 9:15 am CET
  Leading Authors: Anderson K, Ventura P, Balwani M

- **A Drug-Drug Interaction Study to Investigate the Effect of Givosiran on the Activity of Five Major Drug Metabolizing CYP450 Enzymes in Subjects with Acute Intermittent Porphyria (AIP) who are Chronic High Excreters (CHE)**
  Tuesday, September 10, 2019 at 12:00 pm CET
  Leading Authors: Vassiliou D, Sardh E, Harper P

Poster presentations:

- **A Phase 1/2 Open-Label Extension Study of Givosiran, an Investigational RNAi Therapeutic, in Patients with Acute Intermittent Porphyria**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Bonkovsky HL, Bissell DM, Sardh E

- **Overall Health, Daily Functioning, and Quality of Life in Acute Hepatic Porphyria Patients: ENVISION, a Phase 3 Global, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Sardh E, Gouya L, Rees DC

- **Burden of Illness in Acute Hepatic Porphyria (AHP): Insights from Patient and Caregiver Members of the British Porphyria Association**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Gill L, Burrell S, Chamberlayne J

- **Disease Characteristics of Acute Hepatic Porphyria Patients: ENVISION, a Phase 3 Global, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Balwani M, Sardh E, Gouya L

- **The Evolving Diagnosis and Care of Patients with Acute Hepatic Porphyria (AHP) in the UK: from 2006 to 2018**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Gill L, Burrell S, Chamberlayne J

- **A Review of the Predominant Symptoms of Acute Hepatic Porphyria: Pain, Fatigue, and Nausea**
  Monday, September 9, 2019, 10:30 to 11:00 am and 12:45 to 2:00 pm CET
  Leading authors: Ko J, McHorney C, Safikhani S

About Acute Hepatic Porphyria
Acute hepatic porphyria (AHP) refers to a family of rare, genetic diseases characterized by potentially life-threatening attacks and for some patients

chronic debilitating symptoms that negatively impact daily functioning and quality of life. AHP is comprised of four subtypes, each resulting from a genetic defect leading to deficiency in one of the enzymes of the heme biosynthesis pathway in the liver: acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and ALAD-deficiency porphyria (ADP). These defects cause the accumulation of neurotoxic heme intermediates aminolevulinic acid (ALA) and porphobilinogen (PBG), with ALA believed to be the primary neurotoxic intermediate responsible for causing both attacks and ongoing symptoms between attacks. Common symptoms of AHP include severe, diffuse abdominal pain, weakness, nausea, and fatigue. The nonspecific nature of AHP signs and symptoms can often lead to misdiagnoses of other more common conditions such as irritable bowel syndrome, appendicitis, fibromyalgia, and endometriosis, and consequently, patients afflicted by AHP often remain without a proper diagnosis for up to 15 years. In addition, long-term complications of AHP and its treatment can include chronic neuropathic pain, hypertension, chronic kidney disease and liver disease, including iron overload, fibrosis, cirrhosis and hepatocellular carcinoma. Currently, there are no treatments approved to prevent debilitating attacks or to treat the chronic manifestations of the disease.

About Givosiran
Givosiran is an investigational, subcutaneously administered RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) in development for the treatment of acute hepatic porphyria (AHP). Monthly administration of givosiran has the potential to significantly lower induced liver ALAS1 levels in a sustained manner and thereby decrease neurotoxic heme intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG), to near normal levels. By reducing accumulation of these intermediates, givosiran has the potential to prevent or reduce the occurrence of severe and life-threatening attacks, control chronic symptoms, and decrease the burden of the disease. Givosiran utilizes Alnylam's Enhanced Stabilization Chemistry ESC-GalNAc conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index. Givosiran has been granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) and PRIME Designation by the European Medicines Agency (EMA). Givosiran has also been granted Orphan Drug Designations in both the U.S. and the EU for the treatment of AHP. The safety and efficacy of givosiran were evaluated in the ENVISION Phase 3 trial with positive results; these results have not been evaluated by the FDA, the EMA or any other health authority.

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 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 Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of diseases with high unmet need. 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 in Phase 3 studies 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. Headquartered in Cambridge, MA, Alnylam employs over 1,200 people worldwide. 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 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.

Author Disclosures
Dr. Manisha Balwani (Principal Investigator in the ENVISION study) receives financial compensation as an advisory board member for Alnylam (the study sponsor and manufacturer of the study drug givosiran).

The Icahn School of Medicine at Mount Sinai ("ISMMS") holds issued and pending patents related to the study drug givosiran and has licensed these patents to Alnylam. As part of the license to Alnylam, ISMMS will receive payments from Alnylam, including a payment when givosiran entered Phase 3 clinical studies, as well as future payments if givosiran becomes a marketed treatment for acute hepatic porphyria. ISMMS, as well as the ISMMS faculty that are named inventors on the licensed patents, will benefit financially.

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