May 31, 2017

FDA Grants Breakthrough Therapy Designation for Alnylam's Givosiran for the Prophylaxis of Attacks in Patients with Acute Hepatic Porphyria

- Additional Phase 1 Results to be Presented at the International Congress on Porphyrins and Porphyrias (ICPP), June 25 - 28, 2017 -

- Company Plans to Initiate Phase 3 Clinical Program in Late 2017 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that it has received Breakthrough Therapy designation from the U.S. Food and Drug Administration (FDA) for givosiran (ALN-AS1), an investigational RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) for the prophylaxis of attacks in patients with acute hepatic porphyria (AHP). Breakthrough Therapy designation is granted to expedite the development and review of new drugs that treat serious or life-threatening diseases where preliminary clinical evidence exists in support of substantial benefit over available therapies. The designation is aimed to help ensure that patients with unmet medical needs receive access to new therapies through FDA approval as soon as possible.

"Patients with acute hepatic porphyrias, a family of ultra-rare diseases, suffer from severe neurovisceral attacks often resulting in hospitalization, and chronic, debilitating symptoms that impair daily function. This FDA decision is recognition of both the need for novel therapeutic options and the promising initial results with givosiran," said Jeff Miller, Vice President, General Manager, Givosiran Program at Alnylam. "We believe givosiran could become a transformative treatment for patients with this devastating and potentially life-threatening disease. Accordingly, we look forward to rapidly advancing this program in collaboration with global regulatory authorities, having also received PRIME designation from the European Medicines Agency earlier this year. We plan to initiate the Phase 3 clinical program with givosiran in late 2017."

Promising results from the ongoing Phase 1 study of givosiran demonstrating meaningful reductions in the occurrence of porphyria attacks formed the basis of the Breakthrough application. Updated results from this trial will be provided in an oral presentation on June 26, 2017 at the International Congress on Porphyrins and Porphyrias (ICPP) being held in Bordeaux, France.

About Givosiran Phase 1 Study
The ongoing portion of the Phase 1 study of givosiran (Part C) is being conducted as a randomized, double-blind, placebo-controlled study. Data presented at the 2016 American Society of Hematology (ASH) meeting demonstrated initial evidence for clinical activity with givosiran including meaningful reductions in both the number and frequency of porphyria attacks, as well as meaningful reductions in annualized hemin doses required in patients with acute intermittent porphyria (AIP), the most common and severe form of AHP. In the first two dose cohorts, givosiran was found to be generally well tolerated with no drug-related serious adverse events. In the third dose cohort, which remains blinded, one death due to acute pancreatitis, considered unlikely related to givosiran or placebo, was reported after the data transfer date.

About Givosiran
Alnylam is developing givosiran (formerly known as ALN-AS1), a subcutaneously administered, investigational RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) for the treatment of acute hepatic porphyrias, including acute intermittent porphyria (AIP). AIP is the most common of the porphyrias, an ultra-rare autosomal dominant disease caused by loss of function mutations in porphobilinogen deaminase (PBGD), an enzyme in the heme biosynthesis pathway that can result in accumulation of toxic heme intermediates, including aminolevulinic acid (ALA) and porphobilinogen (PBG). Givosiran is an ESC-GalNAc-siRNA conjugate targeting ALAS1, a liver-expressed, rate-limiting enzyme upstream of PBGD in the heme biosynthesis pathway. Inhibition of ALAS1 is known to reduce the accumulation of heme intermediates that cause the clinical manifestations of AIP. Givosiran has the potential to be a novel treatment approach for the prevention of recurrent attacks. Givosiran has previously been granted PRIME designation which was established by the European Medicines Agency (EMA) to bring treatments to patients faster by enhancing the EMA's support for the development of medicines for diseases where there is an unmet medical need and where early clinical data show potential to benefit patients. Givosiran has also been granted Orphan Drug Designations in both the E.U. and the U.S. for the treatment of acute hepatic porphyrias.

About Acute Hepatic Porphyrias
The porphyrias are a family of rare metabolic disorders with mostly autosomal dominant inheritance predominantly caused

by a genetic mutation in one of the eight enzymes responsible for heme biosynthesis. Acute hepatic porphyrias (AHP) constitute a subset where the enzyme deficiency occurs within the liver, and includes acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), and variegate porphyria (VP). Exposure of AHP patients to certain drugs, dieting, or hormonal changes can trigger strong induction of aminolevulinic acid synthase 1 (ALAS1), another enzyme in the heme biosynthesis pathway, which can lead to accumulation of neurotoxic heme intermediates that precipitate disease symptoms. Patients with AHP can suffer from a range of symptoms that, depending on the specific type, can include acute and/or recurrent life-threatening attacks with severe abdominal pain, peripheral and autonomic neuropathy, neuropsychiatric manifestations, cutaneous lesions and possibly paralysis and death if untreated or if there are delays in treatment. There are no approved treatments for the prevention of attacks; the only approved treatment for acute attacks is hemin for injection (Panhematin® or Normosang®), a preparation of heme derived from human blood. Hemin requires administration through a large vein or a central intravenous line and is associated with a number of complications including thrombophlebitis or coagulation abnormalities. Chronic administration of hemin may result in renal insufficiency, iron overload, systemic infections (due to the requirement for central venous access) and, in some instances, tachyphylaxis.

About RNAi

RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the horizon. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, target the cause of diseases by potently silencing specific mRNAs, thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

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 patients who have limited or inadequate treatment options. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust discovery platform and deep pipeline of investigational medicines, including three product candidates that are in late-stage development or will be in 2017. 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. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam.

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 the potential for RNAi therapeutics, including givosiran, its expectations regarding the timing of clinical studies, including the initiation of a Phase 3 trial for givosiran following interactions with regulatory authorities, its expectations regarding scientific and regulatory support for givosiran from the FDA and EMA and collaborating with these agencies on the accelerated assessment of givosiran, its expectations regarding its STAr pipeline growth strategy, and 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 our 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, 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.

The scientific information referenced in this news release relating to givosiran is preliminary and investigative. Givosiran has not been approved by the U.S. Food and Drug Administration, European Medicines Agency, or any other regulatory authority and no conclusions can or should be drawn regarding its safety or effectiveness.

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