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Alnylam Announces Approval of GIVLAARI® (givosiran) in Brazil for the Treatment of Acute Hepatic Porphyria (AHP) in Adults

– GIVLAARI is the First Therapy Proven to Prevent AHP Attacks –
– Second RNAi Therapeutic to be Approved in Latin America –

Sao Paulo, July 20, 2020 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that the Brazilian Health Regulatory Agency (ANVISA) has approved GIVLAARI® (givosiran) for the treatment of acute hepatic porphyria (AHP) in adults. AHP refers to a family of rare, genetic diseases characterized by potentially life-threatening attacks and, for some patients, chronic manifestations that negatively impact daily functioning and quality of life. There are approximately 2,000 people living with AHP in Brazil, with less than 25% diagnosed. This milestone marks the second approval for an RNAi therapeutic in Latin America. Alnylam will continue to collaborate with ANVISA and the Ministry of Health in creating a federal protocol for AHP and incorporating GIVLAARI® in the federal program (SUS), to make the drug available to needy patients as soon as possible.

"The approval of GIVLAARI in Brazil is an important milestone and critical advancement for a population in need. AHP can cause debilitating symptoms and potentially life-threatening attacks, and Alnylam is proud to provide a long-sought treatment that has the potential to prevent attacks," said Norton Oliveria, Senior Vice President, Head of Latin America at Alnylam. "Thank you to all of the patients, caregivers, physicians and advocates who had a hand in making this possible. We would not have been able to achieve this milestone without the support of the Brazilian AHP community."

The approval of GIVLAARI is based on positive results from the pivotal ENVISION Phase 3 study, which evaluated the efficacy and safety of givosiran in AHP patients and included data on the reduction in the annualized rate of composite porphyria attacks compared with placebo. Results from the pivotal ENVISION Phase 3 study were published in the June 10, 2020 issue of *The New England Journal of Medicine*.

GIVLAARI was previously granted priority review in Brazil—an accelerated review designation awarded by ANVISA to innovative medicines that treat rare diseases. The therapy was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with AHP in November 2019 and by the European Commission (EC) for the treatment of AHP in adults and

adolescents in March 2020. GIVLAARI was reviewed by the FDA under Priority Review and had previously been granted Breakthrough Therapy and Orphan Drug Designations in the U.S. In the European Union, GIVLAARI was reviewed under accelerated assessment by the European Medicines Agency (EMA), after receiving Priority Medicines (PRIME) Designation and Orphan Drug Designation from the EMA.

About GIVLAARI® (givosiran)

GIVLAARI is an RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) for the treatment of adults 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.

Important Safety Information

The recommended dose of GIVLAARI is 2.5 mg/kg administered via subcutaneous injection once monthly. Dosing is based on actual body weight. Anaphylaxis occurred in one patient with a history of allergic asthma and atopy, monitor for signs and symptoms of anaphylaxis; Transaminase elevations have been observed in patients treated with GIVLAARI, consider interrupting or discontinuing treatment for severe or clinically significant transaminase elevations; Increases in serum creatinine levels and decreases in estimated glomerular filtration rate have been reported during treatment with GIVLAARI, monitor renal function during treatment with GIVLAARI as clinically indicated. There are limited data on the use of GIVLAARI in pregnant and lactating women. This medicine should not be used by pregnant women without the supervision of a doctor or dentist. Caution is recommended when administering narrow therapeutic index drugs that are substrates of CYP1A2 or CYP2D6 while on treatment with GIVLAARI®, as this may increase or prolong their therapeutic effect, or alter their adverse event profiles. GIVLAARI is contraindicated in patients with a history of severe hypersensitivity to givosiran. Adverse reactions with GIVLAARI: very common: nausea, transaminase elevation, rash, serum creatinine increase, injection-site reaction, fatigue; common: hypersensitive; uncommon: anaphylactic reactions.

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 porphyria (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 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 RNAi therapeutics platform. Alnylam's commercial RNAi therapeutic products are ONPATTRO® (patisiran), approved in the U.S., EU, Canada, Japan, Brazil and Switzerland, and GIVLAARI® (givosiran), approved in the U.S., EU and Brazil. Alnylam has a deep pipeline of investigational medicines, including five product candidates that are in late-stage development. Alnylam is executing 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 is headquartered in Cambridge, MA.

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 safety and efficacy of GIVLAARI® (givosiran), its plans to continue to collaborate with ANVISA and the Ministry of Health in creating a federal protocol for AHP and incorporating GIVLAARI® in the federal program, its views regarding the approval of GIVLAARI in Brazil as a critical advancement for a population in need, that can help prevent attacks, and expectations regarding the continued execution on 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: the direct or indirect impact of the COVID-19 global pandemic or a future pandemic, such as the scope and duration of the outbreak, government actions and restrictive measures implemented in response, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by Alnylam products, or in patient enrollment in clinical trials, potential supply chain disruptions, and other potential impacts to Alnylam's business, the effectiveness or timeliness of steps taken by Alnylam to mitigate the impact of the pandemic, and Alnylam's ability to execute business continuity plans to address disruptions caused by the COVID-19 or a future 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, 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, including lumasiran, or its marketed products; obtaining, maintaining and protecting intellectual property; intellectual property matters including potential patent litigation relating to its platform, products or product candidates; obtaining regulatory approval for its product candidates, including lumasiran, and maintaining regulatory approval and obtaining pricing and reimbursement for its products, including ONPATTRO and GIVLAARI; progress in continuing to establish a commercial and ex-United States infrastructure; successfully launching, marketing and selling its approved products globally, including ONPATTRO and GIVLAARI, and achieving net product revenues for ONPATTRO within its revised expected range during 2020; 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 within the ranges of guidance provided by Alnylam through the implementation of further discipline in operations to moderate spend and and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; Alnylam's ability to establish and maintain strategic business alliances and new business initiatives, including completing an agreement for funding by Blackstone of certain R&D activities for vutrisiran and ALN-AGT; Alnylam's dependence on third parties, including Regeneron, for development, manufacture and distribution of certain products, including eye and CNS products, Ironwood, for assistance with the education about and promotion of GIVLAARI, and Vir for the development of ALN-COV and other potential RNAi therapeutics targeting SARS-CoV-2 and host factors for SARS-CoV-2; 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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