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Alnylam Announces New and Enhanced Framework for Value-Based Agreements to Accelerate Patient and Provider Access to GIVLAARI™ (givosiran)

– Framework Ties Payment for GIVLAARI to its Delivery of Patient Outcomes in the Real-World Setting -

– Includes New Approach Designed for Ultra-Rare Diseases that Gives Participating Payers Greater Financial Certainty if Disease Prevalence is Higher Than Anticipated –

- Discussions Underway with Leading Insurers and Agreement in Principle in Place with Harvard Pilgrim -

CAMBRIDGE, Mass., November 20, 2019 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, is announcing today a new and enhanced framework for value-based agreements (VBAs) designed to help patients with acute hepatic porphyria (AHP) – an ultra-rare orphan disease – gain access to GIVLAARI™ (givosiran) injection for subcutaneous use, a first-of-its-kind RNAi therapeutic for the treatment of AHP. Approved today by the U.S. Food and Drug Administration (FDA), GIVLAARI is indicated for the treatment of adults with AHP.

Alnylam is in active discussions with leading payers about VBAs for GIVLAARI and plans to incorporate this new ultra-rare disease framework into these discussions and negotiations. Alnylam has reached an agreement in principle with Harvard Pilgrim covering GIVLAARI.

Under this innovative framework for VBAs, participating government and commercial payers will pay the full value for GIVLAARI only when it delivers patient outcomes in the real-world setting similar to results demonstrated in clinical trials. An additional and newly designed Prevalence-Based Adjustment (PBA) feature will trigger rebates to participating payers if the number of diagnosed patients they cover exceeds current epidemiologic estimates for AHP. There are often uncertainties in diagnosis rates and disease prevalence estimates in ultra-rare diseases, making it challenging for payers to predict the number of patients who will be covered within their plans. This innovative approach offers greater certainty to payers that their overall financial risk will be adjusted if a substantially larger number of patients than currently estimated are identified, diagnosed, and treated with GIVLAARI.

“Patients can sometimes experience lengthy delays waiting for access when a new medicine becomes available, as payers can be challenged to determine both which patients may best respond and the number of potentially undiagnosed patients in their plans,” said Barry Greene, President of Alnylam Pharmaceuticals. “Our proactive approach with VBAs is intended to act as ‘insurance for insurers’ and builds upon our Alnylam Patient Access Philosophy to do everything we can to accelerate patient access to innovative medicines at a sustainable rate to the healthcare system. We are proud of the access achieved in the U.S. for ONPATTRO, and are committed to seeking innovative approaches for patient access with GIVLAARI and each of our approved medicines.”

Currently, the population of AHP patients with diagnosed, active disease in the U.S. and Europe is estimated to be approximately 3,000. Due to the broad, non-specific range of symptoms and comorbidities experienced by AHP patients, the time to diagnosis can be as long as 15 years.

"Harvard Pilgrim applauds Alnylam’s efforts to help us manage plan members’ costs if the number of patients treated exceeds initial forecasts based upon existing prevalence models,” said Michael Sherman, M.D., Chief Medical Officer at Harvard Pilgrim. “This prevalence-based adjustment framework may become a model approach for ultra-rare diseases where few or no therapies have previously existed and where diagnosis rates are uncertain.”

“Express Scripts, Accredo, and Cigna are committed to deliver simpler, more affordable, more predictable ways for patients with rare diseases to receive appropriate care and treatment, said Steve Miller, M.D., Executive Vice President & Chief Clinical Officer at Express Scripts. “The type of agreement Alnylam is proposing helps ensure people living with acute hepatic porphyria have access to breakthrough medicines and that plans will get value for every dollar they pay for these therapies.”

In the absence of GIVLAARI, an AHP patient can cost $400,000 - $650,000 annually for treatment of attacks, including hospitalization, hemin administration, and other medical interventions. GIVLAARI has been shown to reduce the frequency of attacks thereby providing the potential to reduce or avoid the costs of hospitalization and other interventions. Under Alnylam’s new and enhanced VBA framework, payments will be tied to patient clinical outcomes in the real-world setting mirroring those achieved in the ENVISION study in terms of reduced AHP attacks.

Alnylam’s Patient Access Philosophy
The new VBA framework announced today for ultra-rare diseases such as AHP builds upon Alnylam’s Patient Access Philosophy, first released nearly a year ahead of the approval of its first RNAi therapeutic. As part of Alnylam’s Access Philosophy, the Company commits to not increase the price of GIVLAARI by more than the consumer price index for urban consumers (CPI-U), a measure of inflation, in the absence of significant investment associated with a meaningful label expansion. Commercially insured patients are expected to have little-to-no out-of-pocket costs for GIVLAARI. To see Alnylam’s progress as of September 2019, download the report.

Alnylam Assist®
Alnylam is deeply committed to helping patients with AHP get access to GIVLAARI. A comprehensive patient support services program, Alnylam Assist®, will offer an in-house team of Case Managers to assist patients with verification of insurance benefits and financial assistance

for those who qualify. Patients will also be eligible to receive support from Patient Education Liaisons, who can answer questions about disease and treatment. Physicians and patients can learn more about Alnylam's comprehensive patient services by visiting AlnylamAssist.com or call 1-833-256-2478.

Visit GIVLAARI.com for more information, including full Prescribing Information.

GIVLAARI Important Safety Information

Contraindications
GIVLAARI is contraindicated in patients with known severe hypersensitivity to givosiran. Reactions have included anaphylaxis.

Anaphylactic Reaction
Anaphylaxis has occurred with GIVLAARI treatment (<1% of patients in clinical trials). Ensure that medical support is available to appropriately manage anaphylactic reactions when administering GIVLAARI. Monitor for signs and symptoms of anaphylaxis. If anaphylaxis occurs, immediately discontinue administration of GIVLAARI and institute appropriate medical treatment.

Hepatic Toxicity
Transaminase elevations (ALT) of at least 3 times the upper limit of normal (ULN) were observed in 15% of patients receiving GIVLAARI in the placebo-controlled trial. Transaminase elevations primarily occurred between 3 to 5 months following initiation of treatment.

Measure liver function tests prior to initiating treatment with GIVLAARI, repeat every month during the first 6 months of treatment, and as clinically indicated thereafter. Interrupt or discontinue treatment with GIVLAARI for severe or clinically significant transaminase elevations. In patients who have dose interruption and subsequent improvement, reduce the dose to 1.25 mg/kg once monthly. The dose may be increased to the recommended dose of 2.5 mg/kg once monthly if there is no recurrence of severe or clinically significant transaminase elevations at the 1.25 mg/kg dose.

Renal Toxicity
Increases in serum creatinine levels and decreases in estimated glomerular filtration rate (eGFR) have been reported during treatment with GIVLAARI. In the placebo-controlled study, 15% of patients receiving GIVLAARI experienced a renally-related adverse reaction. The median increase in creatinine at Month 3 was 0.07 mg/dL. Monitor renal function during treatment with GIVLAARI as clinically indicated.

Injection Site Reactions
Injection site reactions were reported in 25% of patients receiving GIVLAARI in the placebo-controlled trial. Symptoms included erythema, pain, pruritus, rash, discoloration, or swelling around the injection site. One (2%) patient experienced a single, transient, recall reaction of erythema at a prior injection site with a subsequent dose administration.

Drug Interactions
Concomitant use of GIVLAARI increases the concentration of CYP1A2 or CYP2D6 substrates, which may increase adverse reactions of these substrates. Avoid concomitant use of GIVLAARI with CYP1A2 or CYP2D6 substrates for which minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, decrease the CYP1A2 or CYP2D6 substrate dosage in accordance with approved product labeling.

Adverse Reactions
The most common adverse reactions that occurred in patients receiving GIVLAARI were nausea (27%) and injection site reactions (25%).

For additional information about GIVLAARI, please see full Prescribing Information.

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, GIVLAARI was shown to significantly reduce the rate of porphyria attacks that required hospitalizations, urgent healthcare visits or IV 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, visit GIVLAARI.com.

About AHP
Acute hepatic porphyria (AHP) refers to a family of ultra-rare, genetic diseases characterized by potentially life-threatening attacks and, for some patients, chronic manifestations that negatively impact daily functioning and quality of life. AHP is comprised of four types: 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 deficiency in one of the enzymes of the heme biosynthesis pathway in the liver. 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. The nonspecific nature of AHP signs and symptoms can often lead to misdiagnoses of other more common conditions such as viral gastroenteritis, irritable bowel syndrome (IBS), addiction withdrawal and appendicitis. Consequently, patients with AHP can wait up to 15 years for a confirmed diagnosis. In addition, long-term complications and comorbidities of AHP can include hypertension, chronic kidney disease or liver disease, including fibrosis, cirrhosis and 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, and Switzerland, and GIVLAARI™ (givosiran), approved in the U.S. 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 employs over 1,200 people worldwide and 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 future expectations, plans and prospects, including, without limitation, Alnylam's views with respect to the approval of GIVLAARI™ (givosiran) injection for subcutaneous use, and the implications of such approval for patients and their caregivers, its plans to offer a new and enhanced framework for VBAs designed to help patients with AHP gain access to GIVLAARI and , the status of discussions with leading payers about VBAs for GIVLAARI that would incorporate this framework, expectations regarding the estimated population of AHP patients with diagnosed, active disease in the U.S. and Europe, the potential time to diagnosis for patients and the potential cost to insurers of treatment in the absence of GIVLAARI, expectations regarding the potential for GIVLAARI to reduce the frequency of attacks thereby reducing or avoiding the costs of treatment, its plan to offer comprehensive support services for people prescribed GIVLAARI through Alnylam Assist®, 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, including GIVLAARI, progress in establishing a commercial and ex-United States infrastructure, successfully launching, marketing and selling its approved products globally, including GIVLAARI, 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 and achieve a self-sustainable financial profile in the future, 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, including Regeneron, for development, manufacture and distribution of products, and Ironwood, for assistance with the education about and promotion of GIVLAARI, 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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