Alnylam Retains Global Rights to Lumasiran, an Investigational RNAi Therapeutic for the Treatment of Primary Hyperoxaluria Type 1 (PH1)

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− Company Plans to Accelerate Development with Phase 3 Start in Late 2018 −

− Lumasiran Granted Breakthrough Therapy Designation by the United States Food and Drug Administration −

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 12, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that Sanofi Genzyme has declined its opt-in for the development and commercialization of lumasiran (ALN-GO1), an investigational RNAi therapeutic for the treatment of Primary Hyperoxaluria Type 1 (PH1). Based on this decision, Alnylam intends to rapidly advance lumasiran into a Phase 3 pivotal study in late 2018, and to commercialize lumasiran globally, assuming product approval. In addition, the Company also announced that lumasiran has been granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration (FDA), representing the third BTD the Company has received to date for programs in its pipeline. BTD is intended to expedite the development and review of investigational drugs for the treatment of serious or life-threatening conditions based on preliminary clinical evidence indicating that the drug may demonstrate substantial improvement on clinically significant endpoint(s) over available therapies.

"We are extremely pleased to retain worldwide development and commercialization rights for lumasiran, expanding the number of global rare disease opportunities for Alnylam. Based on Phase 1/2 clinical data presented to date, we believe lumasiran could be a transformative treatment for patients with PH1, an ultra-rare disease with no approved therapies, in which excess oxalate production leads to kidney failure and significant morbidity and mortality," said Yvonne Greenstreet, MBChB, MBA, Chief Operating Officer of Alnylam. "We are also thrilled with FDA's decision to grant Breakthrough Therapy Designation to lumasiran. We believe this is a testament to the drug's potential to address the severe unmet medical need that PH1 represents for patients and their families. Alnylam is now poised to advance lumasiran into Phase 3 in late 2018 and, assuming approval, to commercialize lumasiran globally."

The clinical dataset informing the Sanofi Genzyme decision consisted of results from Parts A and B of the ongoing Phase 1/2 study of lumasiran, recently presented at the American Society of Nephrology (ASN) Kidney Week 2017 Annual Meeting in November. Through the end of 2019 and, potentially for up to two years thereafter, Sanofi Genzyme retains the right to opt into other Alnylam rare genetic disease programs for development and commercialization in territories outside of the United States, Canada, and Western Europe, as per the terms of the 2014 collaboration, as well as one right to a global license for a rare disease program.

About Lumasiran
Lumasiran (formerly known as ALN-GO1) is an investigational RNAi therapeutic targeting glycolate oxidase (GO) in development for the treatment of Primary Hyperoxaluria Type 1 (PH1). Lumasiran is designed to reduce the hepatic levels of the GO enzyme, thereby depleting the substrate necessary for oxalate production, which directly contributes to the pathophysiology of PH1. Lumasiran utilizes Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNAc-conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index. Lumasiran has received both U.S. and EU Orphan Drug Designations. The safety and efficacy of lumasiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

About Primary Hyperoxaluria Type 1 (PH1)
PH1 is an ultra-orphan disease in which excessive oxalate production results in the deposition of calcium oxalate crystals in the kidneys and urinary tract and can lead to the formation of painful and recurrent kidney stones or nephrocalcinosis. Renal damage is caused by a combination of tubular toxicity from oxalate, calcium oxalate deposition in the kidneys, and urinary obstruction by calcium oxalate stones. Compromised kidney function exacerbates the disease as the excess oxalate can no longer be effectively excreted, resulting in subsequent accumulation and crystallization in bones, eyes, skin, and heart, leading to severe illness and death. About 50 percent of patients will have kidney failure by age 15, and about 80 percent will have end stage renal disease by age 30. Current treatment options for advanced disease are very limited and include frequent renal dialysis or combined organ transplantation of liver and kidneys, a procedure with high morbidity that is limited due to organ availability. Although a small minority of patients respond to Vitamin B6 supplementation, there are no approved pharmaceutical therapies for PH1.

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 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, 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.

Alnylam – Sanofi Genzyme Alliance
In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate the advancement of RNAi therapeutics as a potential new class of innovative medicines for patients around the world with rare genetic diseases. The alliance enables Sanofi Genzyme to expand its rare disease pipeline with Alnylam's novel RNAi technology and provides access to Alnylam's R&D engine, while Alnylam benefits from Sanofi Genzyme's proven global capabilities to advance late-stage development and, upon commercialization, accelerate market access for these promising genetic medicine products.

In January 2018, Alnylam and Sanofi Genzyme restructured their alliance, providing Alnylam with global rights to develop and commercialize products for the treatment of ATTR amyloidosis, including investigational RNAi therapeutics patisiran and ALN-TTRsc02, and Sanofi Genzyme with global rights

to develop and commercialize fitusiran, an investigational RNAi therapeutic for the treatment of hemophilia and potentially other rare bleeding disorders. Sanofi Genzyme continues to have the right to opt into other Alnylam rare genetic disease programs for development and commercialization in territories outside of the United States, Canada, and Western Europe, as well as one right to a global license.

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, and hepatic infectious 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 discovery platform and deep pipeline of investigational medicines, including four product candidates that are in late-stage development. 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. Alnylam employs over 700 people in the U.S. and Europe 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 potential for lumasiran to be a transformative treatment for patients with PH1, the plans and timing to advance lumasiran into a pivotal study, expectations regarding Alnylam’s global commercialization of lumasiran, if approved, the continuing option rights of Sanofi Genzyme through 2019 and potentially beyond, and expectations regarding "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, 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 Annual Report on Form 10-K 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.

Lumasiran 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 the safety or effectiveness of this investigational therapeutic.

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