



Alnylam Receives European Medicines Agency PRIME Designation for Accelerated Assessment of Lumasiran, an Investigational RNAi Therapeutic for the Treatment of Primary Hyperoxaluria Type 1 (PH1)

March 26, 2018

? Company Intends to Advance Lumasiran to a Phase 3 Study in Late 2018 ?

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 26, 2018-- [Alnylam Pharmaceuticals, Inc.](#) (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today that the European Medicines Agency (EMA) has granted access to its Priority Medicines (PRIME) scheme for lumasiran (ALN-GO1), an investigational RNAi therapeutic targeting glycolate oxidase for the treatment of Primary Hyperoxaluria Type 1 (PH1). The purpose of the PRIME initiative is 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. Lumasiran was recently granted Breakthrough Therapy Designation by the United States Food and Drug Administration (FDA).

Promising [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 2017, formed the basis of the application for PRIME.

"We are very pleased to have lumasiran accepted into the PRIME program. Based on the preliminary clinical data presented to date, we believe lumasiran could potentially be a transformative treatment option for patients with PH1, an ultra-rare, debilitating condition that presents in early childhood and is associated with an enormous disease burden," said Pritesh Gandhi, PharmD., Vice President and General Manager, Lumasiran program at Alnylam. "We look forward to collaborating with the EMA to optimize the development and accelerate the assessment of lumasiran, with the goal of advancing this investigational medicine into a Phase 3 trial in late 2018 and to the market as rapidly as possible."

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, and a Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA). The safety and efficacy of lumasiran have not been evaluated by the FDA, EMA 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.

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](https://twitter.com/Alnylam) or on [LinkedIn](https://www.linkedin.com/company/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 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 regulatory review and Alnylam's global commercialization of lumasiran, if approved, 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 FDA, EMA, 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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Source: Alnylam Pharmaceuticals, Inc.

Alnylam Pharmaceuticals, Inc.

Investors and Media:

Christine Regan Lindenboom, 617-682-4340

or

Investors:

Josh Brodsky, 617-551-8276