



Alnylam and Dicerna Form RNAi Therapeutics Collaboration on Alpha-1 Antitrypsin Deficiency-Associated Liver Disease and Complete Cross-License Agreement for Primary Hyperoxaluria Programs

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- Dicerna to Lead Global Clinical Development and U.S. Commercialization of its DCR-A1AT and Alnylam's ALN-AAT02 Investigational Therapeutics for the Treatment of Alpha-1 Liver Disease; Alnylam Retains Post-Phase 3 Opt-in Right for Ex-U.S. Commercialization -

- Companies Complete Non-Exclusive Intellectual Property Cross-License Agreement for the Development and Commercialization of Alnylam's Lumasiran and Dicerna's Nedosiran Investigational Programs for Primary Hyperoxaluria -

CAMBRIDGE, Mass. & LEXINGTON, Mass.--(BUSINESS WIRE)--Apr. 6, 2020-- [Alnylam Pharmaceuticals, Inc.](#) (Nasdaq: ALNY), and [Dicerna Pharmaceuticals, Inc.](#) (Nasdaq: DRNA), both leaders in the field of ribonucleic acid interference (RNAi) therapeutics, announced today the formation of a development and commercialization collaboration on investigational RNAi therapeutics for the treatment of alpha-1 antitrypsin (A1AT) deficiency-associated liver disease (alpha-1 liver disease). In addition, the companies have completed a cross-license of their respective intellectual property for Alnylam's lumasiran and Dicerna's nedosiran investigational programs for the treatment of primary hyperoxaluria (PH). These agreements will enhance and accelerate Alnylam's and Dicerna's ability to bring these orphan product candidates to market.

"We are excited to bring our two leading RNAi therapeutics companies together in our efforts to advance potentially transformative medicines for the treatment of two rare diseases with significant unmet medical need. Specifically, the new agreements allow for Alnylam and Dicerna to join forces in areas of common interest, namely alpha-1 liver disease and primary hyperoxaluria," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "We look forward to collaborating with Dicerna to advance treatments for patients living with alpha-1 liver disease, where Dicerna will lead development and U.S. commercialization while Alnylam retains an ex-U.S. commercialization option, where the company already has the resources and experience to hit the ground running. Moreover, our cross-license agreement for primary hyperoxaluria puts the needs of patients and the patient community first, and ensures freedom to operate for both companies for their respective RNAi therapeutic programs in this ultra-rare orphan disease."

"These agreements between Alnylam and Dicerna represent biopharma collaboration at its best, unifying the strengths of two leaders in RNAi innovation to rally behind the common goal of delivering much-needed new therapies to patients with rare diseases," said Douglas M. Fambrough, Ph.D., President and Chief Executive Officer of Dicerna. "By joining our efforts in alpha-1 liver disease, we believe we can be more strongly assured of bringing forward the therapy with the greatest potential to benefit patients. At the same time, our agreement related to lumasiran and nedosiran clears a path for each company to offer a new and differentiated treatment to patients with PH."

Under the development and commercialization agreement, Alnylam's ALN-AAT02 and Dicerna's DCR-A1AT, investigational RNAi therapeutics, each in Phase 1/2 development, will be explored for the treatment of alpha-1 liver disease. Under the agreement, Dicerna assumes responsibility for both ALN-AAT02 and DCR-A1AT at its cost, and may progress one or both of these investigational medicines through clinical development. Dicerna will select which product candidate(s) to advance in development for the treatment of patients with alpha-1 liver disease. At the completion of Phase 3, Alnylam has the no-cost opportunity to opt-in to commercialize the selected candidate in countries outside the U.S., where it already has a commercialization infrastructure in place. If Alnylam exercises its opt-in right, each party shall pay tiered royalties to the other party based on net product sales generated in its territory at rates dependent on which candidate is commercialized. In the event Alnylam waives its commercialization option, Dicerna will retain worldwide rights to commercialize the selected candidate(s) in exchange for milestones and royalties payable to Alnylam, also at a rate dependent on which candidate is ultimately commercialized.

In a separate agreement, Alnylam and Dicerna granted each other a non-exclusive cross-license to their respective intellectual property related to their PH treatment investigational programs to ensure that each party has the freedom to develop and commercialize its respective product candidate: Alnylam's lumasiran targeting glycolate oxidase (GO) for the treatment of PH type 1 and Dicerna's nedosiran targeting lactate dehydrogenase A (LDHA) for the treatment of PH types 1, 2, and 3. Alnylam's lumasiran has achieved positive Phase 3 results in the ILLUMINATE-A study and is currently the subject of a rolling new drug application (NDA) with the U.S. Food and Drug Administration (FDA). Dicerna's nedosiran is currently being evaluated in the PHYOX™ clinical development program in patients with PH. The cross-license agreement provides for Alnylam to pay mid- to high-single-digit royalties to Dicerna based on global net sales of lumasiran and for Dicerna to pay low-single-digit royalties to Alnylam on global net sales of nedosiran.

The transaction related to alpha-1 liver disease is subject to the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976 and other customary conditions.

About ALN-AAT02 and DCR-A1AT

ALN-AAT02 and DCR-A1AT are investigational, subcutaneously administered RNAi therapeutics targeting alpha-1 antitrypsin (A1AT) in development for the treatment of A1AT deficiency-associated liver disease (alpha-1 liver disease). ALN-AAT02 utilizes Alnylam's enhanced stabilization chemistry plus (ESC+)-GalNAc-conjugate technology, which enables subcutaneous dosing with increased selectivity and a wide therapeutic index. DCR-A1AT utilizes Dicerna's GalXC™ technology, which enables subcutaneous delivery and optimizes the activity of the RNAi pathway so that it operates in the most specific and potent fashion. The safety and efficacy of ALN-AAT02 and DCR-A1AT have not been evaluated by the FDA, EMA or any other health authority.

About Alpha-1 Antitrypsin Deficiency-Associated Liver Disease

Alpha-1 antitrypsin (A1AT) deficiency is an autosomal disorder that results in disease of the lungs and liver. A1AT is a liver-produced serine proteinase inhibitor with the primary function of protecting the lungs from neutrophil elastase and other irritants that cause inflammation. About 95 percent of

people with A1AT deficiency are homozygous and carry two copies of the abnormal Z allele (PiZZ) which expresses the Z-AAT protein. In the liver, misfolding of the mutant Z-AAT protein hinders its normal release into the blood thereby causing it to aggregate in hepatocytes, leading to liver injury, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). There are estimated to be approximately 120,000 individuals with the PiZZ mutation in the U.S. and major European countries, and of these, 10 percent or more have an associated liver pathology (alpha-1 liver disease) caused by the aggregates of the misfolded Z-AAT protein. The only treatment options presently available for alpha-1 liver disease patients are supportive care and, in the case of advanced cirrhosis, liver transplantation. RNAi-mediated inhibition of A1AT in people with alpha-1 liver disease may represent a promising new way to treat this rare disease.

About Lumasiran

Lumasiran is an investigational, subcutaneously administered RNAi therapeutic targeting glycolate oxidase (GO), in development for the treatment of primary hyperoxaluria type 1 (PH1), an ultra-rare life threatening disease. GO is encoded by the hydroxyacid oxidase 1 (HAO1) gene. Thus, by silencing *HAO1* and depleting the GO enzyme, lumasiran inhibits production of oxalate – the metabolite that directly contributes to the pathophysiology of PH1. Lumasiran utilizes Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNac-conjugate technology, which enables quarterly subcutaneous maintenance dosing with increased potency and durability and a wide therapeutic index. Lumasiran has received both U.S. and EU Orphan Drug Designations, a Breakthrough Therapy Designation and pediatric rare disease designation from the U.S. Food and Drug Administration (FDA), and a Priority Medicines (PRIME) designation from the European Medicines Agency (EMA). The safety and efficacy of lumasiran have not been evaluated by the FDA, EMA or any other health authority.

About Nedosiran

Nedosiran (formerly referred to as DCR-PHXC) is the only RNAi drug candidate in development for primary hyperoxaluria (PH) types 1, 2 and 3 and is Dicerna's most advanced product candidate utilizing the proprietary GalXC™ RNAi technology platform. Nedosiran is designed to inhibit the lactate dehydrogenase A (LDHA) enzyme – an enzyme that catalyzes the final step in a common pathway resulting in oxalate overproduction in patients with PH1, PH2 and PH3. Dicerna is evaluating the safety and efficacy of nedosiran in patients with all known forms of PH as part of its PHYOX clinical development program.

About Primary Hyperoxaluria (PH)

PH is an ultra-rare disease with three known types (PH1, PH2 and PH3), each resulting from a mutation in one of three different genes. In patients with PH, 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 and 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, especially in patients with PH1 and PH2, leading to severe illness and death. Current treatment options are very limited and include frequent renal dialysis or combined organ transplantation of liver and kidney, a procedure with high morbidity that is limited due to organ availability. Although a minority of patients are fully responsive to Vitamin B6 therapy, there are no approved pharmaceutical therapies for PH.

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 and Dicerna's RNAi therapeutic platforms, 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, 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 and the EU. Alnylam has a deep pipeline of investigational medicines, including six 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.

About Dicerna Pharmaceuticals, Inc.

Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) is a biopharmaceutical company focused on discovering, developing and commercializing medicines that are designed to leverage ribonucleic acid interference (RNAi) to selectively silence genes that cause or contribute to disease. Using our proprietary RNAi technology platform, GalXC™, Dicerna is committed to developing RNAi-based therapies with the potential to treat both rare and more prevalent diseases. By reducing the level of disease-causing proteins in the hepatocytes of the liver, Dicerna's GalXC platform has the potential to safely target conditions that are difficult to treat with other modalities. Continually innovating, Dicerna is also exploring new applications of RNAi technology beyond the liver, targeting additional tissues and enabling new therapeutic applications. In addition to our own pipeline of core discovery and clinical candidates, Dicerna has established collaborative relationships with some of the world's leading pharmaceutical companies, including Novo Nordisk A/S, Roche, Eli Lilly and Company, Alexion Pharmaceuticals, Inc. and Boehringer Ingelheim International GmbH. Between Dicerna and our collaborative partners, we currently have more than 20 active discovery, preclinical or clinical programs focused on rare, cardiometabolic, viral-infectious, chronic-liver and complement-mediated diseases, as well as neurodegeneration and pain. At Dicerna, our mission is to interfere – to silence genes, to fight disease, to restore health. For more information, please visit www.dicerna.com.

Alnylam Forward Looking Statements

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including, without limitation, Alnylam's views and plans with respect to the potential for RNAi therapeutics, including ALN-AAT02, lumasiran, DCR-A1AT and nedosiran, the development and potential commercialization of ALN-AAT02 and/or DCR-A1AT and its potential to opt-in to such program(s) in the future to commercialize outside of the U.S., expectations regarding the rolling submission of an NDA for lumasiran and the potential benefit of lumasiran and nedosiran for patients with PH, 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: potential risks to Alnylam's business, activities and prospects as a result of the COVID-19 pandemic, or delays or interruptions resulting therefrom; Alnylam's ability to discover and develop novel drug candidates; its ability to successfully demonstrate the efficacy and safety of its product candidates, including ALN-AAT02; the pre-clinical and clinical results for its product candidates, including ALN-AAT02, 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 or its marketed products, including ALN-AAT02 or lumasiran; 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 achieve net product revenues for ONPATTRO within its 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 its expected guidance 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 Vir, for development of candidates for the treatment of infectious diseases, including COVID-19, and commercialization of any infectious disease product resulting therefrom, Regeneron, for development, manufacture and distribution of certain products, including eye and CNS products, and Ironwood, for assistance with the education about and promotion of GIVLAARI in the U.S.; 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.

Dicerna Forward-Looking Statements

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