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Alnylam Completes Enrollment of Phase II Clinical Trial and Initiates Open-Label Extension (OLE) Study with ALN-TTR02, an RNAi Therapeutic Targeting Transthyretin (TTR) for the Treatment of Transthyretin-Mediated Amyloidosis (ATTR)

— Company to Present Complete Phase II Data at IXth International Symposium on Familial Amyloidotic Polyneuropathy (ISFAP) in November and to Present Initial OLE Study Clinical Endpoint Data in 2014 —

— On Track to Begin Phase III Trial with ALN-TTR02 in Familial Amyloidotic Polyneuropathy (FAP) Patients by End of This Year —

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), a leading RNAi therapeutics company, announced today that it has completed enrollment in its Phase II trial with ALN-TTR02, an RNAi therapeutic targeting the transthyretin (TTR) gene for the treatment of TTR-mediated amyloidosis (ATTR). Recent interim results from this Phase II study showed that ALN-TTR02 achieved up to 93% knockdown of TTR — the disease-causing protein in ATTR. ALN-TTR02 activity was found to be rapid, dose dependent, and durable, with similar levels of TTR knockdown observed toward both wild-type and mutant protein. In addition, ALN-TTR02 was found to be generally safe and well tolerated in this study. Alnylam also announced today that its open-label extension (OLE) study with ALN-TTR02 is open for enrollment. The OLE study will evaluate the long-term safety and tolerability of ALN-TTR02 and will also measure effects of treatment toward a number of clinical endpoints, including a Neuropathy Impairment Score, or "NIS;" the company intends to report clinical data from this study about once per year, with initial data in 2014.

"Our ATTR program is the lead effort in our 'Alnylam 5x15' product development and commercialization strategy, which is focused on advancing RNAi therapeutics toward genetically defined targets for the treatment of diseases with high unmet medical need. We are very encouraged with the clinical activity, safety, and tolerability seen to date with ALN-TTR02 in our Phase II multi-dose study performed in ATTR patients, and look forward to sharing further data at the upcoming ISFAP meeting in November. As we presented at the Peripheral Nerve Society meeting in June, ALN-TTR02 achieved robust knockdown of up to 93% of circulating wild-type and mutant TTR," said Akshay Vaishnaw, M.D., Ph.D., Executive Vice President and Chief Medical Officer of Alnylam. "We are pleased to now be able to provide patients on our Phase II study with the opportunity to continue receiving ALN-TTR02 on our OLE study, which will include clinical endpoint measurements such as NIS. We plan on presenting data from the OLE study about once per year hereafter, with an initial presentation of results in 2014. We also remain on track to initiate our Phase III study of ALN-TTR02 in FAP patients by the end of this year, and have now completed discussions with regulatory authorities regarding our overall development plans to support submissions for product approval."

ATTR is caused by mutations in the TTR gene which cause abnormal TTR amyloid protein deposits to accumulate in various tissues including peripheral nerves and heart, resulting in neuropathy and/or cardiomyopathy. ATTR represents a major unmet medical need with significant morbidity and mortality; familial amyloidotic polyneuropathy (FAP) affects approximately 10,000 people worldwide and familial amyloidotic cardiomyopathy (FAC) affects at least 40,000 people worldwide. ALN-TTR02 is an intravenously administered RNAi therapeutic targeting TTR in development for the treatment of ATTR patients with FAP. Alnylam is also developing ALN-TTRsc, a subcutaneously administered RNAi therapeutic for the treatment of FAC.

The Phase II study is an open-label, multi-center, multi-dose, dose-escalation trial to evaluate the safety and tolerability of two doses of ALN-TTR02 and to demonstrate clinical activity based on serial measurement of circulating serum levels of wild-type and mutant TTR. The study enrolled 29 ATTR polyneuropathy patients with ALN-TTR02 administered at doses of 0.01 to 0.30 mg/kg, using either a once-every-four-week or once-every-three-week dosing regimen. Interim results from the first 19 patients, presented at the 2013 Biennial Meeting of the Peripheral Nerve Society held June 29 — July 3, 2013, showed that multiple doses of ALN-TTR02 led to robust and statistically significant ($p < 0.001$) knockdown of serum TTR protein levels of up to 93% and a mean TTR knockdown of greater than 80%. Knockdown of TTR was found to be rapid, dose dependent, and durable, and similar activity was observed toward both wild-type and mutant protein. In addition, ALN-TTR02 was found to be generally safe and well tolerated in this study. Alnylam will present the final data from this study at the IXth International Symposium on Familial Amyloidotic Polyneuropathy (ISFAP) to be held in Rio de Janeiro, Brazil, November 10 — 13, 2013.

The company has also opened enrollment in an OLE study of ALN-TTR02. Eligible patients treated in the Phase II study can enroll in the study, where they will receive ALN-TTR02 at a dose of 0.3 mg/kg every three weeks for up to two years. The primary objective of this study is to evaluate the long-term safety and tolerability of ALN-TTR02 administration. In addition, the study will measure a number of clinical endpoints at baseline and every six months thereafter. This includes measurement of a modified composite NIS, termed "mNIS+7," which is an evaluation of muscle weakness, sensory and autonomic function, and nerve conductance across a 304-point scale, where neuropathy progression leads to an increased score over time. A number

of additional clinical endpoints will be assessed, including: quality of life; timed 10-meter walk test to evaluate mobility; modified body mass index as a measure of nutritional status; level of disability; and nerve fiber density in skin biopsies. Initial data from the OLE study are expected to be presented in 2014, with periodic updates thereafter approximately once a year.

In addition, Alnylam intends to start a Phase III pivotal trial for ALN-TTR02 in FAP patients by the end of 2013. The primary endpoint will be the difference in the change from baseline in the mNIS+7 score between patients receiving ALN-TTR02 as compared with those receiving placebo. Alnylam has obtained scientific advice for the ALN-TTR02 Phase III study from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) and has completed its End-of-Phase II meeting with the U.S. Food and Drug Administration (FDA). The company will provide further details on the study design upon its initiation.

In 2012, Alnylam entered into an exclusive alliance with Genzyme, a Sanofi company, to develop and commercialize RNAi therapeutics, including ALN-TTR02 and ALN-TTRsc, for the treatment of ATTR in Japan and the broader Asian-Pacific region. Alnylam plans to develop and commercialize the ALN-TTR program in North and South America, Europe, and rest of the world.

About Transthyretin-Mediated Amyloidosis

Transthyretin (TTR)-mediated amyloidosis (ATTR) is an inherited, progressively debilitating, and fatal disease caused by mutations in the TTR gene. TTR protein is produced primarily in the liver and is normally a carrier for retinol binding protein. Mutations in TTR cause abnormal amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart, resulting in intractable peripheral sensory neuropathy, autonomic neuropathy, and/or cardiomyopathy. ATTR represents a major unmet medical need with significant morbidity and mortality; familial amyloidotic polyneuropathy (FAP) affects approximately 10,000 people worldwide and familial amyloidotic cardiomyopathy (FAC) affects at least 40,000 people worldwide. FAP patients have a life expectancy of five to 15 years from symptom onset, and the only treatment options for early stage disease are liver transplantation and tafamidis (approved in Europe). The mean survival for FAC patients is approximately 2.5 years, and there are no approved therapies. There is a significant need for novel therapeutics to treat patients who have inherited mutations in the TTR gene.

About LNP Technology

Alnylam has licenses to Tekmira LNP intellectual property for use in RNAi therapeutic products using LNP technology.

About RNA Interference (RNAi)

RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of 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, target the cause of diseases by potently silencing specific mRNAs, thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

About Alnylam Pharmaceuticals

Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is leading the translation of RNAi as a new class of innovative medicines with a core focus on RNAi therapeutics toward genetically defined targets for the treatment of serious, life-threatening diseases with limited treatment options for patients and their caregivers. These include: ALN-TTR02, an intravenously delivered RNAi therapeutic targeting transthyretin (TTR) for the treatment of TTR-mediated amyloidosis (ATTR) in patients with familial amyloidotic polyneuropathy (FAP); ALN-TTRsc, a subcutaneously delivered RNAi therapeutic targeting TTR for the treatment of ATTR in patients with familial amyloidotic cardiomyopathy (FAC); ALN-AT3, an RNAi therapeutic targeting antithrombin (AT) for the treatment of hemophilia and rare bleeding disorders (RBD); ALN-AS1, an RNAi therapeutic targeting aminolevulinate synthase-1 (ALAS-1) for the treatment of porphyria including acute intermittent porphyria (AIP); ALN-PCS, an RNAi therapeutic targeting PCSK9 for the treatment of hypercholesterolemia; ALN-TMP, an RNAi therapeutic targeting TMPRSS6 for the treatment of beta-thalassemia and iron-overload disorders; ALN-AAT, an RNAi therapeutic targeting alpha-1-antitrypsin (AAT) for the treatment of AAT deficiency liver disease; and ALN-CC5, an RNAi therapeutic targeting complement component C5 for the treatment of complement-mediated diseases, amongst other programs. As part of its "Alnylam 5x15TM" strategy, the company expects to have five RNAi therapeutic products for genetically defined diseases in clinical development, including programs in advanced stages, on its own or with a partner by the end of 2015. Alnylam has additional partnered programs in clinical or development stages, including ALN-RSV01 for the treatment of respiratory syncytial virus (RSV) infection and ALN-VSP for the treatment of liver cancers. The company's leadership position on RNAi therapeutics and intellectual property have enabled it to form major alliances with leading companies including Merck, Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, Cubist,

Ascletis, Monsanto, Genzyme, and The Medicines Company. In addition, Alnylam holds an equity position in Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics. Alnylam has also formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for applications in biologics manufacturing, including recombinant proteins and monoclonal antibodies. Alnylam's VaxiRNA™ platform applies RNAi technology to improve the manufacturing processes for vaccines; GlaxoSmithKline is a collaborator in this effort. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 100 peer-reviewed papers, including many in the world's top scientific journals such as *Nature*, *Nature Medicine*, *Nature Biotechnology*, *Cell*, and the *New England Journal of Medicine*. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit www.alnylam.com.

About "Alnylam 5x15™"

The "Alnylam 5x15" strategy, launched in January 2011, establishes a path for development and commercialization of novel RNAi therapeutics toward genetically defined targets for the treatment of diseases with high unmet medical need. Products arising from this initiative share several key characteristics including: a genetically defined target and disease; the potential to have a major impact in a high unmet need population; the ability to leverage the existing Alnylam RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of a new drug application (NDA) with a focused patient database and possible accelerated paths for commercialization. By the end of 2015, the company expects to have five such RNAi therapeutic programs in clinical development, including programs in advanced stages, on its own or with a partner. The "Alnylam 5x15" programs include: ALN-TTR02, an intravenously delivered RNAi therapeutic targeting transthyretin (TTR) for the treatment of TTR-mediated amyloidosis (ATTR) in patients with familial amyloidotic polyneuropathy (FAP); ALN-TTRsc, a subcutaneously delivered RNAi therapeutic targeting TTR for the treatment of ATTR in patients with familial amyloidotic cardiomyopathy (FAC); ALN-AT3, an RNAi therapeutic targeting antithrombin (AT) for the treatment of hemophilia and rare bleeding disorders (RBD); ALN-AS1, an RNAi therapeutic targeting aminolevulinate synthase-1 (ALAS-1) for the treatment of acute intermittent porphyria (AIP); ALN-PCS, an RNAi therapeutic targeting PCSK9 for the treatment of hypercholesterolemia; ALN-TMP, an RNAi therapeutic targeting TMPRSS6 for the treatment of beta-thalassemia and iron-overload disorders; ALN-AAT, an RNAi therapeutic targeting alpha-1-antitrypsin (AAT) for the treatment of AAT deficiency liver disease; and ALN-CC5, an RNAi therapeutic targeting the C5 component of the complement pathway for the treatment of complement-mediated diseases, amongst other programs. Alnylam intends to focus on developing and commercializing certain programs from this product strategy itself in North and South America, Europe, and other parts of the world; these include ALN-TTR, ALN-AT3, ALN-AS1, and ALN-CC5, amongst other programs.

Alnylam Forward-Looking Statements

Various statements in this press release concerning Alnylam's future expectations, plans and prospects, including without limitation, Alnylam's expectations regarding its "Alnylam 5x15" product strategy, Alnylam's views with respect to the potential for RNAi therapeutics, including ALN-TTR02, its expectations regarding the reporting of data from its ALN-TTR02 clinical trials, its expectations with respect to the timing and success of its clinical trials for ALN-TTR02, and its expectations regarding the potential market opportunity for ALN-TTR02, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important 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 drug candidates, including ALN-TTR02, the pre-clinical and clinical results for its product candidates, which may not support further development of product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, obtaining regulatory approval for products, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to 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, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2013 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 to update any forward-looking statements.

Alnylam Pharmaceuticals, Inc.
Cynthia Clayton
Vice President, Investor Relations and
Corporate Communications
617-551-8207
or
Amanda Sellers (Media)

Spectrum
202-955-6222 x2597

Source: Alnylam Pharmaceuticals, Inc.