European Medicines Agency (EMA) Grants Alnylam Accelerated Assessment of Patisiran for Patients with Hereditary ATTR (hATTR) Amyloidosis

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− Company on Track to Submit Marketing Authorization Application (MAA) and New Drug Application (NDA) at Year-End 2017 −

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 13, 2017-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), the leading RNAi therapeutics company, announced today the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has granted an accelerated assessment for patisiran, an investigational RNAi therapeutic targeting transthyretin (TTR) for the treatment of hereditary ATTR (hATTR) amyloidosis. The EMA awards an accelerated assessment to medicines deemed to be of major public health interest and therapeutic innovation, and the award is designed to bring new treatments to patients more quickly. Alnylam intends to file a marketing authorization application (MAA) in the European Union (EU) at year-end 2017. Accelerated assessment potentially provides a reduced review timeline from 210 to 150 days once the MAA is filed and validated.

“We are pleased the CHMP has granted accelerated assessment for patisiran and believe this underscores the urgent need to improve outcomes for patients living with hATTR amyloidosis,” said Eric Green, Vice President and General Manager of the TTR program. “The results from the APOLLO Phase 3 study in hATTR amyloidosis patients with polyneuropathy provide evidence that patisiran has the potential to improve neurologic impairment, quality of life, and cardiac parameters. With this accelerated assessment award from the EMA, we hope to be able to make this promising treatment option available to patients in Europe sooner.”

“The news that patisiran has been accepted for accelerated assessment by the EMA signals to us that everyone involved recognizes the serious impact hereditary ATTR amyloidosis has on the lives of people affected by this devastating, progressive disease,” said Eric Low, Chairman, Amyloidosis Research Consortium UK. “The need for new treatment options is urgent. The patient community really welcomes when everything possible is being done to assess promising new treatments quickly and efficiently to see if patients may benefit earlier.”

Alnylam plans to file a New Drug Application for patisiran in the United States by the end of 2017, where Fast Track Designation has been granted. Sanofi Genzyme is currently preparing for regulatory filings for patisiran in Japan, Brazil and other countries, beginning in the first half of 2018. Pending regulatory approvals, Alnylam will commercialize patisiran in the U.S., Canada and Western Europe, with Sanofi Genzyme commercializing the product in the rest of the world.

About Patisiran

Patisiran is an investigational intravenously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of hereditary ATTR amyloidosis with polyneuropathy. It is designed to target and silence specific messenger RNA, potentially blocking the production of TTR protein before it is made. This may help to enable the clearance of TTR amyloid deposits in peripheral tissues and potentially restore function to these tissues. The safety and efficacy of patisiran have not been evaluated by the U.S. Food and Drug Administration or any other health authority.

About APOLLO Phase 3 Study

The APOLLO Phase 3 study (N=225) was a randomized, double-blind, placebo-controlled, global study designed to evaluate the efficacy and safety of patisiran in hATTR amyloidosis patients with polyneuropathy. Patisiran met its primary endpoint with a 34.0 point mean difference relative to placebo ($p=9.26 \times 10^{-24}$) in the modified neuropathy impairment score (mNIS+7) at 18 months, with 56% of patisiran-treated patients experiencing reductions in mNIS+7 relative to baseline. All secondary endpoints were also met (p less than 0.001), including a 21.1 point mean difference relative to placebo ($p=1.10 \times 10^{-10}$) in the Norfolk Quality of Life-Diabetic Neuropathy score (Norfolk-QOL-DN) at 18 months. 51% of patisiran-treated patients had improvements in Norfolk-QOL-DN relative to baseline. In addition, patisiran treatment was associated with encouraging effects on cardiac biomarker, echocardiographic, and functional parameters in the study's pre-specified cardiac subpopulation.

Patisiran also demonstrated an encouraging safety and tolerability profile. The most commonly reported adverse events (AEs) for patisiran were generally mild to moderate and included peripheral edema (29.7 percent) and infusion-related reactions (IRRs) (18.9 percent), and the frequency of deaths and serious adverse events (SAEs) was similar in the patisiran and placebo groups; no deaths were considered drug-related.

About LNP Technology

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

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 the case of patisiran, Alnylam will advance the product in the United States, Canada and Western Europe, while Sanofi Genzyme will advance the product in the rest of the world.

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 600 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 the complete results from its APOLLO Phase 3 clinical trial for patisiran and the potential implications of such results for patients, its plans for and the expected timing of regulatory filings seeking approval for patisiran from regulatory authorities in the United States, Europe and ROW countries, its expectations regarding the potential for patisiran to improve the lives of hATTR amyloidosis patients with polyneuropathy and their families, its plans for the commercialization of patisiran if approved by regulatory authorities, 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, 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 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.

Patisiran 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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