Alnylam Pharmaceuticals and Medison Pharma Partner to Commercialize RNAi Therapeutics in Israel

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ZUG, Switzerland & PETACH TIKVA, Israel--(BUSINESS WIRE)--Jan. 21, 2019-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, and Medison Pharma, Israel's leading commercial partner for innovative pharmaceuticals, announced today an exclusive agreement to commercialize ONPATTRO®, the first-ever commercialized RNAi therapeutic, as well as other investigational therapeutics under development in the Alnylam RNAi portfolio.

"Our partnership with Medison marks an important step in our global commercial expansion and signals our intent to ensure that patients suffering from serious rare diseases have access to our medicines, regardless of location," said Theresa Heggie, SVP and Head of Europe, Middle East and Africa, and Canada, Alnylam Pharmaceuticals. "Medison has a strong organization with a proven track record of commercializing orphan products successfully, together with an infrastructure uniquely suited to supporting patients suffering from rare diseases in Israel and providing access to our potentially transformational therapies. We look forward to partnering with Medison to bring ONPATTRO and potential future therapies to patients."

"We are proud to partner and collaborate with Alnylam in Israel," said Meir Jakobsohn, Founder and CEO, Medison Pharma. "Alnylam's portfolio of ONPATTRO and potentially ground-breaking medicines in late stage development will strengthen our rare disease portfolio, fulfilling Medison's vision to provide innovative treatments to patients in Israel. Patients with hATTR amyloidosis with polyneuropathy in Israel deserve to have the earliest possible access to novel new treatments and we look forward to making this a reality, beginning with ONPATTRO. Patients and physicians in Israel are waiting for potentially disease modifying treatments and we will do everything in our capabilities to secure their access."

The agreement between Alnylam and Medison includes ONPATTRO, approved in the EU in August 2018 for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy; givosiran, a late-stage investigational RNAi therapeutic for the treatment of acute hepatic porphyria (AHP); and lumasiran, a late-stage investigational RNAi therapeutic for the treatment of Primary Hyperoxaluria Type 1 (PH1). These medicines are not currently approved for use in Israel and givosiran and lumasiran have not yet been approved by any regulatory authority.

About ONPATTRO® (patisiran)

Patisiran, based on Nobel Prize-winning science, is an intravenously administered RNAi therapeutic targeting transthyretin (TTR) for the treatment of hereditary ATTR amyloidosis. It is designed to target and silence specific messenger RNA, potentially blocking the production of TTR protein before it is made. Patisiran blocks the production of transthyretin in the liver, reducing its accumulation in the body's tissues in order to halt or slow down the progression of the disease. In August 2018, patisiran received U.S. Food and Drug Administration (FDA) approval for the treatment of the polyneuropathy of hATTR amyloidosis in adults, as well as European Medicines Agency marketing authorization for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy.

Important Safety Information (ISI) for ONPATTRO

Infusion-Related Reactions

Infusion-related reactions (IRRs) have been observed in patients treated with patisiran. In a controlled clinical study, 19% of patisiran-treated patients experienced IRRs, compared to 9% of placebo-treated patients. The most common symptoms of IRRs with patisiran were flushing, back pain, nausea, abdominal pain, dyspnoea, and headache.

To reduce the risk of IRRs, patients should receive premedication with a corticosteroid, paracetamol, and antihistamines (H1 and H2 blockers) at least 60 minutes prior to patisiran infusion. Monitor patients during the infusion for signs and symptoms of IRRs. If an IRR occurs, consider slowing or interrupting the infusion and instituting medical management as clinically indicated. If the infusion is interrupted, consider resuming at a slower infusion rate only if symptoms have resolved. In the case of a serious or life-threatening IRR, the infusion should be discontinued and not resumed.

Reduced Serum Vitamin A Levels and Recommended Supplementation

Patisiran treatment leads to a decrease in serum vitamin A levels. Patients receiving patisiran should take oral supplementation of approximately 2500 IU vitamin A per day to reduce the potential risk of ocular toxicity due to vitamin A deficiency. Doses higher than 2500 IU vitamin A per day should not be given to try to achieve normal serum vitamin A levels during treatment with patisiran, as serum levels do not reflect the total vitamin A in the body. Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g. including reduced night vision or night blindness, persistent dry eyes, eye inflammation, corneal inflammation or ulceration, corneal thickening or corneal perforation).

Adverse Reactions

The most common adverse reactions that occurred in patients treated with patisiran were peripheral oedema (30%) and infusion-related reactions (19%).

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 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

Alnylam (Nasdaq:ALNY) is leading the translation of RNA interference (RNAi) into a new class of innovative medicines with the potential to improve 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 discovery platform. ONPATTRO® (patisiran) lipid complex injection, available in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults, is Alnylam's first U.S. FDA-approved RNAi therapeutic. In the EU, ONPATTRO is approved for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy. Alnylam has a deep pipeline of investigational medicines, including three 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 1,000 people worldwide and is headquartered in Cambridge, MA.

About Medison

Medison, Israel's leading innovative pharmaceutical partner, is an exclusive Israeli partner for global healthcare companies such as Amgen, Biogen, Ipsen, Vertex and more. Backed by three generations of experience in the healthcare industry since 1937, Medison has built and maintained long-standing relations with HMOs, local medical centers and physicians. Medison is uniquely qualified to provide the complete spectrum of integrated services for international companies looking to enter or expand their presence in the Israeli market. Medison runs Medison Ventures, a corporate arm with a dedicated research team boasting deep scientific and commercial backgrounds. Medison Ventures operates a scouting program to cater its partners and is an active investor in life science projects around drug development and digital health.

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 potential for RNAi therapeutics, including without limitation ONPATTRO, givosiran and lumasiran, plans to make ONPATTRO available in additional countries and to continue the filings for regulatory approval and launch of ONPATTRO for hATTR patients with polyneuropathy around the world, 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, successfully launching, marketing and selling its approved products globally, 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, 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.

With the exception of ONPATTRO (patisiran), none of Alnylam's investigational therapeutics have 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 such investigational therapies.

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