Alnylam to Report New Clinical Results from the APOLLO Phase 3 Study of Patisiran at the 16th International Symposium on Amyloidosis

March 14, 2018

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 14, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq:ALNY), the leading RNAi therapeutics company, today announced that additional results from the APOLLO Phase 3 study of patisiran, an investigational therapeutic for the treatment of hereditary ATTR (hATTR) amyloidosis, will be presented at the 16th International Symposium on Amyloidosis (ISA), being held March 26-29, 2018 in Kumamoto, Japan. In addition, new data from the Phase 1 trial of ALN-TTRsc02, an investigational, subcutaneously administered RNAi therapeutic for the treatment of ATTR amyloidosis, will also be presented.

“The data being presented at ISA will further demonstrate the potential of patisiran to alleviate multiple neurological, cardiac, and autonomic manifestations of hATTR amyloidosis, a progressively disabling, rare disease with significant unmet medical need. Nine presentations will provide additional safety and efficacy data from clinical studies with patisiran, including the relationship of TTR knockdown to clinical efficacy and the effects of patisiran on cardiac manifestations of disease,” said Eric Green, Vice President and General Manager, TTR Program at Alnylam. “We also plan on presenting additional clinical data for ALN-TTRsc02, which is on track to enter Phase 3 development in late 2018.”

All presentations will be held on **Wednesday, March 28, 2018 from 1:00 to 2:00 pmJST** and include:

- *Title:* Long-term use of patisiran, an investigational RNAi therapeutic, in patients with hereditary transthyretin-mediated amyloidosis: Baseline demographics and preliminary data from global open label extension study

  *Presenter:*Ole Suhr, Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden

- *Title:* Patisiran, an investigational RNAi therapeutic for patients with hereditary transthyretin-mediated amyloidosis: Regional and genotypic subgroup analyses from the APOLLO study

  *Presenter:*Teresa Coelho, Hospital de Santo Antonio, Porto, Portugal.

- *Title:* Patisiran, an investigational RNAi therapeutic for patients with hereditary transthyretin-mediated (hATTR) amyloidosis: Phase 3 APOLLO study subanalysis of Japanese patients

  *Presenter:*Taro Yamashita, Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

- *Title:* APOLLO, a phase 3 study of patisiran for the treatment of hereditary transthyretin-mediated amyloidosis: 18-month safety and efficacy in subgroup of patients with cardiac involvement

  *Presenter:*Arnt Kristen, Heidelberg University Hospital, Heidelberg, Germany

- *Title:* Relationship between transthyretin knockdown and change in mNIS+7: Findings from the patisiran phase 2 open-label extension and phase 3 APOLLO studies for patients with hereditary transthyretin-mediated amyloidosis

  *Presenter:*Michael Polydefkis, Johns Hopkins Bayview Medical Center, Baltimore, United States

- *Title:* Changes in neuropathy stage in patients with hereditary transthyretin-mediated amyloidosis following treatment with patisiran, an investigational RNAi therapeutic: An analysis from the phase 3 APOLLO study

  *Presenter:*Alejandra Gonzalez-Duarte, Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán, (INCMNSZ), Mexico City, Mexico

- *Title:* Home infusion administration of patisiran, an investigational RNAi therapeutic in patients with hereditary transthyretin-mediated amyloidosis: An analysis of safety and adherence

  *Presenter:*Julian Gillmore, University College London Medical School, London, United Kingdom

- *Title:* Impact of hereditary transthyretin-mediated amyloidosis on daily living and work productivity: Baseline results from APOLLO

  *Presenter:*John Berk, Boston University, Boston, United States

- *Title:* Impact of hereditary transthyretin-mediated amyloidosis on use of health care services: An analysis of the APOLLO Study

  *Presenter:*Hartmut Schmidt, Universitatsklinikum Munster, Munster, Germany

- *Title:* Phase 1 study of ALN-TTRsc02, a subcutaneously administered investigational RNAi therapeutic for the treatment of

transthyretin-mediated amyloidosis

*Presenter:*John Vest, Alnylam Pharmaceuticals

About Patisiran

Patisiran is an investigational, intravenously administered RNAi therapeutic targeting transthyretin (TTR) in development 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. 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 ALN-TTRsc02

ALN-TTRsc02 is an investigational, subcutaneously administered RNAi therapeutic targeting transthyretin (TTR) in development for the treatment of ATTR amyloidosis. 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 ALN-TTRsc02 have not been evaluated by the U.S. Food and Drug Administration or any other health authority. ALN-TTRsc02 utilizes Alnylam's ESC-GalNAc-siRNA conjugate technology, which enables subcutaneous dosing with increased potency and durability. The significance of this technology is under investigation.

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. The study was completed in August 2017 and detailed study results were presented at the 1st European ATTR Amyloidosis Meeting for Patients and Doctors on November 2, 2017. All patients who completed the APOLLO Phase 3 study were eligible to screen for the Global OLE study, in which they had the opportunity to receive patisiran on an ongoing basis.

About hATTR amyloidosis

Hereditary transthyretin (TTR)-mediated (hATTR) amyloidosis is an inherited, progressively debilitating, and often fatal disease caused by mutations in the TTR gene. TTR protein is produced primarily in the liver and is normally a carrier of vitamin A. 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. hATTR amyloidosis represents a major unmet medical need with significant morbidity and mortality, affecting approximately 50,000 people worldwide. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy. The only approved treatment options are liver transplantation for early stage disease and tafamidis (approved in Europe, Japan and certain countries in Latin America, specific indication varies by region). There is a significant need for novel therapeutics to help treat patients with hATTR amyloidosis.

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 January 2018, Alnylam and Sanofi Genzyme restructured their alliance, providing Alnylam with global rights to develop and commercialize products for the treatment of ATTR amyloidosis, including investigational therapeutics patisiran and ALN-TTRsc02, and Sanofi Genzyme with global rights to develop and commercialize fitusiran, an investigational RNAi therapeutic for the treatment of hemophilia and other rare bleeding disorders. Sanofi Genzyme continues to have the right to opt into other Alnylam rare genetic disease programs for development and commercialization in territories outside of the United States, Canada and Western Europe, as well as one right to a global license.

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 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 data to be presented for patisiran and ALN-TTRsc02, and the potential implications of such data for patients, 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 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.

Neither patisiran nor ALN-TTRsc02 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 these investigational therapeutics.

View source version on businesswire.com: http://www.businesswire.com/news/home/20180314005074/en/

Source: Alnylam Pharmaceuticals, Inc.

Alnylam Pharmaceuticals, Inc.
Christine Regan Lindenboom, 617-682-4340
(Investors and Media)
or
Josh Brodsky, 617-551-8276
(Investors)