Alnylam Provides R&D Updates and Announces 2019 Product and Pipeline Goals at R&D Day

December 6, 2018

− In 2019, Alnylam Will Continue ONPATTRO™ Global Launch and Advance Late-Stage Pipeline of Wholly Owned and Partnered Programs with: Five Phase 3 Programs; Three Phase 3 Program Readouts; and Two New Drug Application (NDA) Filings –

− Initiates Rolling Submission of Givosiran NDA to U.S. Food and Drug Administration (FDA) –

− Initiates HELIOS-A Phase 3 Study of Vutrisiran (ALN-TTRsc02) in Hereditary ATTR Amyloidosis –

− Reviews Next Wave Pipeline of Seven Early-Stage Clinical and Late Pre-Clinical Programs, Including First CNS Development Program: ALN-APP, an Investigational RNAi Therapeutic Targeting Amyloid Precursor Protein (APP) for Cerebral Amyloid Angiopathy –

− Provides Update on RNAi Platform Innovations, Including New Data on CNS and Ocular Delivery Expected to Support Robust and Broadly Distributed Target Gene Silencing with Bi-Annual and Possibly Less Frequent Dosing Regimens –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 6, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, announces it is hosting its R&D Day in New York City today. During the event, the Company plans to discuss its pipeline goals for 2019, focusing on five late-stage investigational programs advancing toward potential commercialization. These programs include the Company's wholly owned programs: givosiran for the treatment of acute hepatic porphyria (AHP), lumasiran for the treatment of primary hyperoxaluria type 1 (PH1), and vutrisiran (*voo-TREE-si-ran*, formerly ALN-TTRsc02) for the treatment of ATTR amyloidosis. The Company will also discuss commercial execution with ONPATTRO™ (patisiran).

Alnylam also announces today a number of commercialization and pipeline updates. In early January 2019, the Company expects to pre-announce global product revenues for ONPATTRO and number of patients on commercial drug for the fourth quarter of 2018. The Company announces today that it has filed regulatory submissions for ONPATTRO in Canada and Switzerland, and expects regulatory decisions in 2019. In addition, Alnylam announces initiation of a rolling submission of an NDA to the FDA for givosiran and initiation of the HELIOS-A pivotal Phase 3 study of vutrisiran in patients with hATTR amyloidosis. Alnylam will also discuss multiple earlier stage clinical and pre-clinical programs and RNAi platform innovations, including its progress on extra-hepatic delivery of RNAi therapeutics. As part of this update, the Company today announces that its first central nervous system (CNS)-targeted development candidate will be ALN-APP, an investigational RNAi therapeutic targeting amyloid precursor protein (APP) for the treatment of cerebral amyloid angiopathy (CAA) associated with intracerebral hemorrhage.

"In the coming year, we plan to continue our commercial execution for ONPATTRO, bringing this much needed medicine to eligible patients around the world, including an upcoming launch expected in Japan, assuming regulatory approval, and potential launches in other global markets. In addition, our continued execution, together with our partners, on our clinical pipeline of five late-stage investigational programs is poised to bring potential approvals of new RNAi therapeutics essentially on an annual basis in each of the coming years, with three expected Phase 3 program data readouts in 2019 alone and two potential NDA filings, one in mid-2019 and one at or around year-end 2019, assuming positive results," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "We believe we are at an unparalleled stage of our company's growth, with a large number of opportunities with transformative potential for patients across both rare and common diseases. We expect our progress will enable achievement of our 'Alnylam 2020' vision of becoming a multi-product, global, commercial-stage biopharma company with a deep and sustainable clinical pipeline and a robust research engine for future innovation and patient impact."

2019 Product and Pipeline Goals

ONPATTRO (patisiran), an approved RNAi therapeutic targeting transthyretin (TTR) for the treatment of polyneuropathy in patients with hATTR amyloidosis. Alnylam plans to:

- Continue global commercial execution, with planned launches in multiple European countries throughout 2019.
- Launch ONPATTRO in Japan and Canada in late 2019, assuming regulatory approvals.
- Announce label expansion plans for ONPATTRO in ATTR amyloidosis patients with cardiomyopathy in early 2019.

Vutrisiran, an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis. Alnylam plans to:

- Continue enrollment in the HELIOS-A Phase 3 study throughout 2019.
- Initiate HELIOS-B Phase 3 study in ATTR amyloidosis patients with cardiomyopathy in late 2019.

Givosiran, an investigational RNAi therapeutic in development for the treatment of acute hepatic porphyria (AHP). Alnylam plans to:

- Report topline results from the ENVISION Phase 3 trial in early 2019.
- Complete submission of an NDA to the FDA in mid-2019.
- File a marketing authorisation application (MAA) with the European Medicines Agency (EMA) in mid-2019.

Lumasiran, an investigational RNAi therapeutic in development for the treatment of primary hyperoxaluria type 1 (PH1). Alnylam plans to:

- Complete enrollment in the ILLUMINATE-A Phase 3 study in mid-2019.
- Initiate ILLUMINATE-B and -C Phase 3 studies in mid-2019.

- Report topline results from the ILLUMINATE-A Phase 3 study in late 2019.

Alnylam also plans to support The Medicines Company's continued efforts with respect to the ORION Phase 3 studies of inclisiran, an investigational RNAi therapeutic targeting PCSK9 in development for the treatment of hypercholesterolemia. Specifically, The Medicines Company has guided to:

- Report topline results from the ORION 9, 10, and 11 LDL-C pivotal studies in mid- and late-2019.
- File an NDA in the U.S. at or around year-end 2019, assuming positive Phase 3 results.

Alnylam also plans to support Sanofi's continued efforts in advancing fitusiran, an investigational RNAi therapeutic in development for the treatment of hemophilia.

In addition, the Company plans to continue advancement of its earlier-stage clinical pipeline, including a Phase 2 study of cemdisiran, a Phase 1/2 study of ALN-AAT02, and, together with its partner Vir Biotechnology, a Phase 1/2 study of ALN-HBV02 (also known as VIR-2218), investigational RNAi therapeutics in development for the treatment of IgA nephropathy, alpha-1 anti-trypsin deficiency-associated liver disease, and hepatitis B virus (HBV) infection, respectively. The Company expects clinical data readouts from each of these programs in 2019. Alnylam also plans to file one or more new clinical trial applications (CTA) in 2019, including for ALN-AGT, an investigational RNAi therapeutic targeting angiotensinogen for the treatment of uncontrolled hypertension. Alnylam will also continue to build on its progress with extra-hepatic delivery, with a newly selected CNS-targeted development candidate, ALN-APP, an investigational RNAi therapeutic for the treatment of CAA.

The Company's R&D Day will be held today, December 6, 2018 from 8:00 am to 1:00 pm ET at the Westin New York at Times Square in New York City and will include a live video stream on the Investors section of the Company's website, www.alnylam.com. A replay will be available on the Alnylam website within 48 hours after the event. Presentations showcased during the event will be featured on Capella.

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 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) 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. Alnylam's first U.S. FDA-approved RNAi therapeutic is ONPATTRO™ (patisiran) lipid complex injection available in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. 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 five 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 1000 people worldwide 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 potential for RNAi therapeutics, including vutrisiran, givosiran, lumasiran, inclisiran, fitusiran, ALN-AAT02, ALN-HBV02, cemdisiran, and ALN-APP, its plans for additional regulatory filings and product launches for ONPATTRO in 2019, including launches in Japan, Canada and multiple EU countries, its expectations about the announcement of plans for potential expansion of the ONPATTRO label, its plans to continue enrollment in its HELIOS-A Phase 3 study of vutrisiran in hATTR amyloidosis throughout 2019 and initiate its HELIOS-B Phase 3 study in ATTR amyloidosis patients with cardiomyopathy in late 2019, its expectations regarding the timing for completion of a rolling NDA submission with the FDA and submission of a MAA for givosiran and the reporting of complete topline results, its expectations regarding the potential timing of ILLUMINATE-A Phase 3 topline study results for lumasiran in late 2019 and its plans to initiate the ILLUMINATE-B Phase 3 study of lumasiran, its plan to initiate the Phase 1/2 study for ALN-AAT02 in alpha-1 liver disease, expectations regarding the timing of study completion and data readouts for inclisiran by The Medicines Company during 2019 and the potential filing of an NDA if such data are positive, its plans to support Sanofi's continued efforts in advancing fitusiran for the treatment of hemophilia, and expectations regarding the progress of multiple early stage clinical programs and its first CNS-targeted development program, ALN-APP, 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 RNAi 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 therapeutics.

View source version on businesswire.com: https://www.businesswire.com/news/home/20181206005360/en/

Source: Alnylam Pharmaceuticals, Inc.

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