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The Medicines Company and Alnylam Pharmaceuticals Announce Agreement with FDA on Phase III Clinical Program for Inclisiran

— Pivotal trials will enroll approximately 1,500 subjects randomized to inclisiran versus approximately 1,500 subjects randomized to placebo, with a primary endpoint of LDL-C and an 18-month study period —

— NDA submission anticipated at or around the end of 2019 —

PARSIPPANY, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- The Medicines Company (NASDAQ:MDCO) and Alnylam Pharmaceuticals, Inc. (NASDAQ:ALNY) today announced that The Medicines Company has agreed with the U.S. Food and Drug Administration (FDA) on plans for the Phase III clinical program for inclisiran, which is designed to support the submission of a New Drug Application (NDA). The Company has received final, End-of-Phase II meeting minutes from the FDA.

The Phase III program will comprise clinical trials in subjects with atherosclerotic cardiovascular disease (ASCVD) and familial hypercholesterolemia (FH), and will collectively enroll approximately 3,000 subjects randomized to treatment with inclisiran (1,500) or placebo (1,500).

The primary endpoint for all pivotal trials will be LDL-C change from baseline.

Subjects will be studied for 18 months. The dose of inclisiran will be 300 mg given subcutaneously on day-1, day-90 and then every six months thereafter. Subjects will receive a total of four doses of inclisiran during the 18-month study period.

Although not part of the first NDA, The Medicines Company will also perform a cardiovascular outcomes trial in approximately 14,000 subjects with ASCVD and/or risk equivalents, such as diabetes, to determine the effects of LDL-C lowering with inclisiran on cardiovascular outcomes. The design of the outcomes trial has also been agreed with the FDA and the primary efficacy endpoint of the trial will be a composite of coronary heart disease death, non-fatal myocardial infarction and fatal and non-fatal ischemic stroke. These endpoints have been demonstrated to be modifiable in previous, similar outcomes trials. The duration of the outcomes trial will be long enough to accumulate a sufficient number of events to provide overwhelming statistical power to ascertain treatment group differences and maximize the clinical effect size associated with LDL-C lowering. Assuming success, results of the outcomes trial will be submitted to the FDA as a supplemental NDA.

"We are grateful to the FDA for its expertise, advice and support. Cardiovascular disease is a serious threat to the health of Americans, and it is clear that the FDA is committed to facilitating the development and approval of effective and safe drugs to address this important public health problem," said Clive Meanwell, M.D., Ph.D., Chief Executive Officer of The Medicines Company. "Based on data from our Phase II ORION-1 study and the previous Phase I study - both published in *The New England Journal of Medicine* - we are confident that inclisiran reduces LDL-C meaningfully. We have also been highly encouraged by the safety data in these prior studies. Furthermore, inclisiran's highly-differentiated dosing schedule has the potential to transform the burden placed on millions of patients who so badly need to lower LDL-C levels. We anticipate completing the LDL-C lowering program quickly and expect to submit an NDA for ASCVD and FH at or around the end of 2019. We believe our agreement with the FDA on the Phase III clinical development program for inclisiran is highly favorable and adds significantly to inclisiran's strategic value."

Dr. Meanwell added, "Although not required for the NDA, we will also perform an aggressive cardiovascular outcomes trial in high-risk subjects with ASCVD and/or risk-equivalents, such as diabetes. We believe that positive outcomes data, with primary outcome clinical effects greater than those reported for anti-PCSK9 monoclonal antibodies, will drive a high level of competitiveness in the worldwide market - which we expect to become very large."

"The Medicines Company's agreement with the FDA supports a clear path forward for further inclisiran development and regulatory review. Indeed, we're pleased with the excellent progress made by our colleagues at The Medicines Company to advance this potential, innovative medicine to patients in need, and we intend to fully support them in their efforts," said John M. Maraganore, Ph.D., Chief Executive Officer of Alnylam. "Moreover, we believe the planned development path for inclisiran positions this promising potential medicine to contribute meaningfully to our Alnylam 2020 goals."

About Inclisiran

Inclisiran (formerly known as PCSK9si and ALN-PCSsc) is an investigational GalNAc-conjugated RNAi therapeutic targeting PCSK9 - a genetically validated protein regulator of LDL receptor metabolism - being developed for the treatment of hypercholesterolemia. In contrast to anti-PCSK9 monoclonal antibodies that bind to PCSK9 in blood, inclisiran is a first-in-class investigational medicine that acts by turning off PCSK9 synthesis in the liver.

The Medicines Company and Alnylam Pharmaceuticals, Inc. are collaborating in the advancement of inclisiran pursuant to their 2013 agreement. Under the terms of the agreement, Alnylam completed certain pre-clinical studies and the Phase I clinical study, with The Medicines Company leading and funding the development of inclisiran from Phase II forward, as well as potential commercialization.

About The Medicines Company

The Medicines Company is a biopharmaceutical company driven by an overriding purpose - to save lives, alleviate suffering and contribute to the economics of healthcare. The Company's mission is to create transformational solutions to address the most pressing healthcare needs facing patients, physicians and providers in three critical therapeutic areas: serious infectious disease care, cardiovascular care and surgery and perioperative care. The Company is headquartered in Parsippany, New Jersey, with global innovation centers in California and Switzerland.

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 patients who have limited or inadequate treatment options. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of 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 three product candidates that are in late-stage development or will be in 2017. 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. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam.

The Medicines Company Forward-Looking Statements

Statements contained in this press release that are not purely historical may be deemed to be forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates," "expects," "potential," and similar expressions are intended to identify forward-looking statements. These forward-looking statements involve known and unknown risks and uncertainties that may cause the Company's actual results, levels of activity, performance or achievements to be materially different from those expressed or implied by these forward-looking statements. Important factors that may cause or contribute to such differences include whether clinical trials for inclisiran will advance in the clinical process on a timely basis, or at all, or succeed in achieving their specified endpoints; whether physicians, patients and other key decision makers will accept clinical trial results; whether the Company will make regulatory submissions for inclisiran on a timely basis, or at all; whether the Company's regulatory submissions will receive approvals from regulatory agencies on a timely basis, or at all; and such other factors as are set forth in the risk factors detailed from time to time in the Company's periodic reports and registration statements filed with the Securities and Exchange Commission, including, without limitation, the risk factors detailed in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 1, 2017, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

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 inclisiran, its expectations regarding the timing of clinical studies, its expectations regarding scientific and regulatory support for inclisiran, its expectations regarding its STAr pipeline growth strategy, and 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 our 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.

The scientific information referenced in this news release relating to inclisiran is preliminary and investigative. Inclisiran 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 its safety or effectiveness.

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