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New, One-Year Data from ORION-1 Phase II Study of Inclisiran Extends Excellent Long-Term Efficacy and Safety Profile, Affirming Dose for Phase III Trials

-Inclisiran lowering effects on bad-cholesterol (LDL-C) are robust (mean 56% at Day-150; maximum 81%) and sustained (average 51% across a planned six-month dosing interval), with minimum intra-patient variability-

-Safety data for inclisiran from ORION-1 now include 370 subject-years of observation, including at least 300 subject-years of inclisiran effects; no material safety issues observed on inclisiran - similar to placebo-

-After nine months, with no further inclisiran treatment, LDL-C returns towards pre-treatment levels in a near-linear manner, enabling predictable dose-planning-

-One-year ORION-1 data reaffirm inclisiran's potential to address unmet needs with highly-differentiated, infrequent, low-volume, dosing regimen of two injections per year-

-Inclisiran Phase III development program gearing up-

-New, one-year data from ORION-1 study presented today at ESC 2017-

PARSIPPANY, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- The Medicines Company (NASDAQ: MDCO) and Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY) today announced new, positive data from the ORION-1 Phase II study of inclisiran, an investigational, first-in-class PCSK9 synthesis inhibitor being developed for the treatment of hypercholesterolemia. The data were presented today in the "Hot Line - Late-Breaking Clinical Trials 2" session at the European Society of Cardiology (ESC) Congress 2017, being held in Barcelona, Spain.

Following the presentation of primary results from ORION-1 at ACC.17 in March 2017 and publication of results in *The New England Journal of Medicine* in May 2017, the data presented at ESC 2017 complete an important picture of patient follow-up to one year, including time-averaged LDL-C lowering effects, intra-patient variability and extended safety observations.

Efficacy data affirm inclisiran's significant LDL-C lowering effects following a starting dose of 300 mg given on Day-1 and Day-90, after which the mean LDL-C reduction was 56% at Day-150 and 51% at Day-180. For the subsequent six-month period - from Day-90 to Day-270 - the time-averaged LDL-C reduction was 51% with minimum intra-patient variability over time (all comparisons to placebo $P < 0.0001$). These robust data underscore the selection of a six monthly maintenance dose of 300 mg in Phase III trials, which are now in advanced stages of preparation. The Phase III LDL-C lowering trials in 3,500 patients, which are designed to form the basis for inclisiran approval in the United States and Europe, are expected to test the starting dose of 300 mg given on Day-1 and Day-90, followed by a maintenance dose of 300 mg given every six months for up to 18 months.

With completion of one-year follow-up, safety data for inclisiran from the Phase II ORION-1 study now include 370 subject-years of observation, including at least 300 subject-years of inclisiran effects. As in prior analyses, no material safety issues were observed on inclisiran, which continued to demonstrate an adverse event profile similar to placebo. There were no deaths or serious adverse events during the extended observation period. In particular, in spite of the prolonged LDL-C lowering effects of inclisiran, there were no investigational drug-related elevations of liver enzymes and no neuropathy, change in renal function, thrombocytopenia or anti-drug antibodies during extended follow-up, or at any earlier time periods in the ORION-1 study.

The extended observation also demonstrated that, after nine months, with no further inclisiran treatment, LDL-C returns towards pre-treatment levels in a near-linear manner. This observation also supports dose planning for further trials. One-year ORION-1 data reaffirm inclisiran's potential to address unmet needs with a highly-differentiated, infrequent, low-volume dosing regimen of two injections per year.

"The one-year results from ORION-1 re-affirm inclisiran's unique and highly-differentiated attributes, and its game-changing potential to address the unmet needs of millions of at-risk, often non-adherent, patients worldwide who continue to struggle with high cholesterol given the limitations of available therapies," said Clive Meanwell, M.D., Ph.D., Chief Executive Officer of The Medicines Company. Dr. Meanwell continued, "With scientific advice and regulatory input from the U.S. Food and Drug

Administration (FDA), the European Medicines Agency (EMA) and others, we have made great progress thoughtfully and aggressively advancing inclisiran into Phase III development and look forward to announcing the initiation of patient recruitment into an LDL-C lowering Phase III program, which we believe will provide the data for New Drug Application and Marketing Authorization Application submissions as early as the second half of 2019. These trials aim to study 3,000 subjects with atherosclerotic cardiovascular disease (ASCVD) or their risk-equivalents (ORION-10 and -11 trials), 400 subjects with heterozygous familial hypercholesterolemia (ORION-9 trial) and 60 subjects with homozygous familial hypercholesterolemia (ORION-5 trial). In parallel, we are also advanced in the design and preparation of a highly-efficient cardiovascular outcomes trial of 15,000 subjects with high risk ASCVD (ORION-4), which we believe can provide the necessary proof of outcomes effect and value for inclisiran."

ORION-1 Principal Investigator, Professor Kausik Ray, Professor of Public Health, Imperial College London, United Kingdom, and honorary consultant cardiologist, Imperial College NHS Trust said, "The ease of dosing - small volume subcutaneous injections twice a year, most likely given by healthcare professionals - promises to improve patient adherence to lipid therapy, which has been a real problem with all other approaches. These one-year data extend and affirm the six-month results from ORION-1. The two dose, 300 mg regimen produced the greatest reductions in LDL cholesterol, with an average time-adjusted fall of 51% for the planned dosing interval and 46% for the entire year of the study. The sustained LDL cholesterol lowering effects of inclisiran were achieved with a highly-favorable safety profile and were accompanied by predictable and gradual reversal. The data support dosing twice a year after initial injections on Days-1 and 90." Professor Ray continued, "The novel mechanism of action, which is based on Nobel Prize winning science, enables synthesis of PCSK9 to be reduced and LDL cholesterol to be lowered with low doses of drug. This treatment offers the potential for sustained LDL cholesterol reduction with fewer injections than monoclonal antibodies to PCSK9, which require 12 to 26 injections per year."

Professor John JP Kastelein, Chairman of the ORION 1 study, and Professor of Medicine, and Chairman of the Department of Vascular Medicine, Academic Medical Centre, University of Amsterdam, the Netherlands, said, "We are extremely pleased with these new, extended observations. Inclisiran's universal and practically constant effect is unprecedented in my experience of over 30 years of dyslipidemia clinical trials. The unique dosing regimen virtually eliminates variability in LDL cholesterol levels over time and inclisiran may, therefore, solve one of the most vexing challenges of cardiovascular medicine - namely, how to make sure everyone responds to treatment consistently over the long run."

David Kallend, MBBS, Senior Vice President and Global Medical Director of The Medicines Company, added, "The one-year results from ORION-1 confirm the potential to advance the management of dyslipidemia. Other trials presented here at ESC 2017 underscore the causative link between LDL-C and ASCVD, and demonstrate that, when it comes to LDL-C, lowest levels provide best cardiovascular outcomes. Lowering LDL-C remains a central therapeutic goal for patients with, or at risk of, ASCVD, and we believe that inclisiran can make a very positive contribution to patient care and health system performance."

John Maraganore, Ph.D., Chief Executive Officer of Alnylam, added, "We believe that the extended data from ORION-1 are striking and helpful. Specifically, the study has generated more than 300 subject-years of experience with RNAi effects and safety. We are delighted and impressed by the progress made by investigators and our partner, The Medicines Company, and we look forward to the next steps as inclisiran begins the Phase III program, as planned."

About ORION-1

ORION-1 is a placebo-controlled, double-blind, randomized Phase II study of single or multiple subcutaneous injections of inclisiran in a total of 501 patients with atherosclerotic cardiovascular disease (ASCVD), or ASCVD-risk equivalents (e.g., diabetes and familial hypercholesterolemia), and elevated LDL-C despite maximum tolerated doses of LDL-C lowering therapies. The study compared the effect of different doses of inclisiran and evaluated the potential for an infrequent dosing regimen. The primary endpoint of the study was the percentage change in LDL-C from baseline at Day-180.

About Inclisiran

Inclisiran (formerly known as PCSK9si or 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 (MAbs) 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 the terms of their 2013 agreement. Under the terms of that 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 serious infectious disease care and cardiovascular 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 the timing and success of a commercial launch of inclisiran in the United States; the Company's broader commercial strategy for and competition for inclisiran; whether clinical trials for inclisiran will advance 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 physicians will prescribe and patients will use inclisiran, if it becomes available; whether the Company will make additional 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 9, 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 "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 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.

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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