March 17, 2017

The Medicines Company and Alnylam Pharmaceuticals Report Positive Final Results from ORION-1 Phase II Study of Inclisiran

—Inclisiran demonstrated significant and sustained reductions in LDL-C and high standards of safety and tolerability—

—Optimal starting dose regimen (300 mg injection administered on Day-1 and Day-90) lowered LDL-C by average of 52.6% (64 mg/dL) and up to 81% (122 mg/dL) at Day-180, and by time-adjusted mean of > 50% (63 mg/dL) for the six-month period from Day-90 through Day-270; every patient displayed significant response and mean LDL-C reductions over this time period were practically constant—

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

—No material safety issues on inclisiran in ORION-1; overall incidence of adverse events for inclisiran was similar to placebo—

—The Company is actively preparing to advance inclisiran into comprehensive, global Phase III development - initially focused on United States and Europe—

—ORION-1 study presented today in Late-Breaking Clinical Trials session at American College of Cardiology's 66th Annual Scientific Session and published in The New England Journal of Medicine—

—The Company to host conference call at 4:30 p.m., Eastern Time, today—

PARSIPPANY, N.J. & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- The Medicines Company (NASDAQ: MDCO) and Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY) today announced positive final results 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 results are being presented today in the "Late-Breaking Clinical Trials - Featured Clinical Research 1" session at the American College of Cardiology's 66th Annual Scientific Session, ACC.17, and have been published in the March 17, 2017 online issue of *The New England Journal of Medicine.*

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The detailed data from ORION-1 showed that inclisiran delivered significant and sustained reductions of LDL-C and high standards of safety and tolerability. Remarkably, every patient who received the two dose starting regimen displayed a significant response and the mean LDL-C reductions over time were practically constant. Inclisiran was well tolerated and no material safety issue was observed, including no investigational drug-related elevation of liver enzymes and no neuropathy, change in renal function, thrombocytopenia, or anti-drug antibodies.

"The groundbreaking results from ORION-1 are compelling and 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. "We are singularly focused on thoughtfully and aggressively advancing inclisiran into Phase III development, including the initiation of ORION-4, which we expect to include cardiovascular outcomes in high-risk primary and secondary prevention patients with an average baseline LDL-C of approximately 130 mg/dL."

John J.P. Kastelein, M.D., Ph.D., Professor of Medicine and Chairman of the Department of Vascular Medicine at the Academic Medical Center of the University of Amsterdam, continued, "We are pleased to see the complete results from this comprehensive 497 patient Phase II study. 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-C 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."

David Kallend, MBBS, Vice President and Global Medical Director of The Medicines Company, added, "The results from

ORION-1 have the potential to significantly advance the treatment paradigm with robust and durable knockdown of LDL-C and a convincing and highly-reassuring safety and tolerability profile. The data support the selection of 300 mg as the optimal dose, as well as our conclusion that a two dose starting regimen, followed by dosing two times per year, constitutes a highly-differentiated and competitive treatment for patients with hypercholesterolemia. We believe the strength of the data will enable a quick and efficient transition to Phase III development."

John Maraganore, Ph.D., Chief Executive Officer of Alnylam, added, "We are delighted with these final data from the ORION-1 study and impressed by the progress made by investigators and our partner, The Medicines Company. Importantly, as the largest study yet to be performed for an RNAi therapeutic, we believe the results provide compelling support for the positive safety and tolerability profile of our investigational medicines."

In ORION-1, the mean baseline LDL-C was approximately 130 mg/dL among 497 randomized and treated patients. The optimal starting dose regimen (300 mg injection administered on Day-1 and Day-90) achieved a mean LDL-C reduction of 52.6% and up to 81% at Day-180, and a time-adjusted mean of > 50% for the six month period from Day-90 through Day-270. For all dose groups, at all time points, differences in the primary (LDL-C) and secondary (PCSK9) endpoints between inclisiran and placebo were statistically significant ($p < 0.0001$).

The overall incidence of treatment emergent adverse events was 76% in both patients randomized to placebo and patients randomized to inclisiran, with no significant difference between inclisiran doses. Injection site reactions associated with inclisiran were infrequent (observed in 6.5% of patients given the two dose starting regimen and 3.8% of patients given the one dose starting regimen), mild or moderate, and transient.

The results from the Phase II study of inclisiran, published in today's online issue of *The New England Journal of Medicine*, can be found here.

Webcast Information for Late-Breaking Clinical Trial Presentations

Live audio and video of the "Late-Breaking Clinical Trials - Featured Clinical Research 1" presentation by ORION-1's principal investigator, Kausik K. Ray, M.D., MPhil (Cantab), FRCP, Professor of Public Health, Imperial College London, will be webcast over the internet at 1:30 p.m., Eastern Time, today. The live webcast may be accessed from the "Investors-Events/Presentations" section of The Medicines Company website.

Conference Call and Webcast Details

The Medicines Company will host a conference call and webcast today at 4:30 p.m., Eastern Time. The conference call may be accessed as follows:

U.S./Canada: (877) 359-9508
International: (224) 357-2393
Conference ID: 60380330

The live webcast may be accessed in the "Investors-Events/Presentations" section of The Medicines Company website.

A taped replay of the conference call will be archived and available for approximately one week. The replay may be accessed as follows:

U.S./Canada: (855) 859-2056
International: (404) 537-3406
Conference ID: 60380330

A replay of the webcast will also be archived and available after the conference call.

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 compares the effect of different doses of inclisiran and evaluates the potential for an infrequent dosing regimen. The primary endpoint of the study is the percentage change in LDL-C from baseline at Day-180.

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 (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 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 is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is leading the translation of RNAi as a new class of innovative medicines. Alnylam's pipeline of investigational RNAi therapeutics is focused in 3 Strategic Therapeutic Areas (STArs): Genetic Medicines, with a broad pipeline of RNAi therapeutics for the treatment of rare diseases; Cardio-Metabolic Disease, with a pipeline of RNAi therapeutics toward genetically validated, liver-expressed disease targets for unmet needs in cardiovascular and metabolic diseases; and Hepatic Infectious Disease, with a pipeline of RNAi therapeutics that address the major global health challenges of hepatic infectious diseases. In early 2015, Alnylam launched its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics as a whole new class of innovative medicines. Specifically, by the end of 2020, Alnylam expects to achieve a company profile with 3 marketed products, 10 RNAi therapeutic clinical programs - including 4 in late stages of development - across its 3 STArs. The company's demonstrated commitment to RNAi therapeutics has enabled it to form major alliances with leading companies including Ionis, Novartis, Roche, Takeda, Merck, Monsanto, The Medicines Company, and Sanofi Genzyme. In addition, Alnylam holds an equity position in Regulus Therapeutics Inc., a company focused on discovery, development, and commercialization of microRNA therapeutics. Alnylam scientists and collaborators have published their research on RNAi therapeutics in over 200 peer-reviewed papers, including many in the world's top scientific journals such as *Nature, Nature Medicine, Nature Biotechnology, Cell, New England Journal of Medicine,* and *The Lancet*. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information about Alnylam's pipeline of investigational RNAi therapeutics, please visit www.alnylam.com.

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 its 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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