November 15, 2016

The Medicines Company and Alnylam Pharmaceuticals Present Positive Results from ORION-1 Phase 2 Study of Inclisiran (formerly PCSK9si)

—Study meets all interim analysis goals—

—A single injection of inclisiran (300 mg) lowered 'bad cholesterol' (LDL-C) by an average of 51%, and up to 76%—

—Two injections of inclisiran (300 mg) lowered LDL-C by an average of 57% and up to 81%—

—Significant LDL-C reductions were sustained out to 180 days following a single dose—

—Potential for highly-differentiated, infrequent, low volume dosing regimen of 2 or 3 injections per year affirmed—

—Inclisiran demonstrated highly encouraging safety and tolerability—

—Based on the strength of the ORION-1 data, The Medicines Company expects to advance inclisiran aggressively in a global Phase 3 development program—

—Conference call to be held at 3:00 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 results from the analysis of Day 90 data for 497 patients, as well as analysis of preliminary Day 180 data for 189 patients, enrolled in the ORION -1 Phase 2 study of inclisiran. Data from ORION-1 were presented today in a Late-Breaking Clinical Trials session at the American Heart Association Scientific Sessions 2016 in New Orleans.

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.

Inclisiran was generally well tolerated and no material safety issue was observed, including no elevations of liver enzymes considered related to study medication and no neuropathy or change in renal function. Overall incidence of treatment emergent adverse events was 54% both in patients randomized to placebo and in patients randomized to inclisiran, with no differences between inclisiran doses. Injection site reactions (ISRs) with inclisiran were infrequent (observed in 3.2% of patients), mild or moderate, and transient - in only 2.4% of patients, the reported ISR started or was still present 4 or more hours after dosing.

Baseline LDL-C was approximately 130 mg/dL among 497 randomized and treated patients. Among these patients, one 300 mg subcutaneous injection of inclisiran achieved mean LDL-C reductions of 51% at Day 60, which were durable to Day 90 (mean 45% and up to 76%). All differences relative to placebo in these 497 patients were statistically significant ($p < 0.0001$).

Among 189 randomized and treated patients who had been followed for 180 days or more by the interim data cut-off date of October 25, 2016, one 300 mg subcutaneous injection of inclisiran achieved mean LDL-C reductions of 59% at Day 60, which were durable to Day 90 (mean 50%) and Day 180 (mean 43% and up to 81%). Two 300 mg injections of inclisiran - one given on Day 1 and one on Day 90 - achieved a mean LDL-C reduction of 57% at Day 120, which was durable to Day 180 (mean 52% and up to 81%). All differences relative to placebo in these 189 patients were statistically significant ($p < 0.0001$).

"The remarkable strength and consistency of the data from ORION-1 provide compelling support for the medical and commercial potential of inclisiran and drive our decision to move into Phase 3 with what we believe could be a highly-competitive and potentially transformational medicine," said Clive Meanwell, M.D., Ph.D., Chief Executive Officer of The Medicines Company. "We will focus our resources on inclisiran for aggressive Phase 3 development to ensure that this promising agent is investigated thoroughly and rapidly in Phase 3, submitted to worldwide regulatory agencies and, if approved, made available to millions of at-risk, often non-adherent, patients worldwide who continue to grapple with the

realities and risks of high LDL-C."

David Kallend, MBBS, Vice President and Global Medical Director of The Medicines Company, added, "These positive results from ORION-1 showed robust and durable knockdown of LDL-C and a very encouraging safety and tolerability profile at this stage of development. The data strengthen our earlier findings in Phase 1 - published recently in the *New England Journal of Medicine* - that an infrequent, low volume dosing regimen of 2 or 3 injections per year could constitute a highly-differentiated and competitive treatment for patients with hypercholesterolemia. Inclisiran also has the potential to open new care approaches linking the temporal cycle of LDL-C monitoring with counseling and administration of therapy. The ORION-1 data have enabled us to select an optimal dose of 300 mg, and the data presage a quick and efficient transition to Phase 3 development."

John J.P. Kastelein, M.D., Ph.D., Professor of Medicine and Chairman of the Department of Vascular Medicine at the Academic Medical Center (AMC) of the University of Amsterdam, said, "Elevated LDL-C remains a major risk factor for coronary artery disease, and new therapies are needed for patients who are refractory or intolerant to current approaches for management of their LDL-C levels. PCSK9 therapies have now emerged as a new class of drugs for treatment of hypercholesterolemia, and I believe that these agents have the potential to make a meaningful difference for patients. ORION-1 strengthens prior data with inclisiran, especially the degree and durability of LDL-C lowering effects. If the safety and efficacy of this novel investigational PCSK9 synthesis inhibitor can be confirmed in Phase 3 studies to support approval, it may offer an important treatment option for patients, physicians, and payers."

John Maraganore, Ph.D., Chief Executive Officer of Alnylam, added, "We are delighted with these data from the ORION development program for inclisiran and thankful for the progress made by investigators and our partner, The Medicines Company. We are very excited to see the rapid progression of the program worldwide and are confident that our RNAi platform provides the opportunity to create new medicines for important diseases such as hypercholesterolemia, which have major unmet medical needs."

Conference Call and Webcast Details

The Medicines Company will host a conference call and webcast today at 3:00 p.m., Eastern Time.

The dial-in information to access the call is:

U.S./Canada: (877) 359-9508
International: (224) 357-2393
Conference ID: 1645474

An audio replay will be available commencing approximately two hours following the conclusion of the call and will be available for one week. The replay may be accessed as follows:

U.S./Canada: (855) 859-2056
International: (404) 537-3406
Conference ID: 1645474

A live audio webcast and accompanying slide presentation will be available in the "Investors" section of The Medicines Company website. A replay of the webcast will also be available.

About ORION-1

ORION-1 is a placebo-controlled, double-blind, randomized Phase 2 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 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.

In a previous, single-ascending dose study, inclisiran was associated with maximal PCSK9 knockdown of 88.7% with mean

maximum knockdown of up to 82.3 ± 2.0% and maximal LDL-C reduction of 78.1% with mean maximum lowering of up to 59.3 ± 5.0%. At Day 180, a single dose of inclisiran was associated with an up to 53% reduction in LDL-C, with a least squares mean percent lowering of 47.0% in the 300 mg dose cohort.

In a previous multiple ascending dose study, inclisiran was associated with maximal PCSK9 knockdown of 94.4% with mean maximum knockdown of up to 88.5 ± 1.6% and maximal LDL-C reduction of 83.0% with mean maximum lowering of up to 64.4 ± 5.4%.

Inclisiran was generally well tolerated following single and multiple subcutaneous dose administration, with no serious adverse events or discontinuations due to adverse events.

The Medicines Company and Alnylam Pharmaceuticals, Inc. are collaborating in the advancement of inclisiran per the companies' agreement formed in early 2013. Under the terms of the agreement, Alnylam completed certain pre-clinical studies and the Phase 1 clinical study, with The Medicines Company leading and funding the development of inclisiran from Phase 2 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.

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 quarterly report on Form 10-Q filed with the Securities and Exchange Commission on October 27, 2016, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

About Alnylam Pharmaceuticals, Inc.

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.

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 inclisiran, including the potential dosing regimen, the timing of clinical studies and the presentation of clinical data, 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 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 discussed 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 the safety or effectiveness of this therapeutic.

View source version on businesswire.com: http://www.businesswire.com/news/home/20161115005596/en/

The Medicines Company
Media
Meg Langan, 973-290-6319
Vice President
margaret.langan@themedco.com
or
Investors
Krishna Gorti, M.D., 973-290-6122
Vice President, Investor Relations
krishna.gorti@themedco.com
or
Alnylam Pharmaceuticals
Investors and Media
Christine Regan Lindenboom, 617-682-4340
Vice President
clindenboom@alnylam.com
or
Investors
Josh Brodsky, 617-551-8276
Associate Director
jbrodsky@alnylam.com

Source: The Medicines Company and Alnylam Pharmaceuticals, Inc.