Press Release

The Medicines Company Announces that the ORION-10 Study of Inclisiran in ASCVD Patients Showed Durable and Potent Lowering of LDL-C with Twice-Yearly Dosing

- Inclisiran achieved 58% LDL-C lowering with time-adjusted reductions of 56% sustained over 18 months of treatment in patients with atherosclerotic cardiovascular disease (ASCVD)

- ORION-10 study affirmed inclisiran's excellent safety profile, including no treatment-related liver or renal abnormalities

- Results presented today during late-breaking science session at American Heart Association annual meeting in Philadelphia

- The Medicines Company to host investor conference call and webcast on Monday, November 18, 12:00 pm EST

PHILADELPHIA--(BUSINESS WIRE)--The Medicines Company (NASDAQ: MDCO) today announced detailed results from ORION-10, the second of three pivotal 18-month low-density lipoprotein cholesterol (LDL-C) lowering Phase 3 clinical studies of inclisiran, an investigational twice-yearly therapy to reduce LDL-C and the first and only cholesterol-lowering treatment in the siRNA (small-interfering RNA) class. In ORION-10, twice-yearly dosing with inclisiran sodium 300 mg met all primary and secondary efficacy endpoints, was well-tolerated and again demonstrated an excellent safety profile. Full study results were presented during a late-breaking science session at the American Heart Association (AHA) Scientific Sessions in Philadelphia.

"Cumulative exposure to high LDL-C levels presents a significant risk of future heart attacks and strokes for millions of people, particularly those with ASCVD," said study principal investigator R. Scott Wright, M.D., Professor of Medicine, Consultant in Cardiology, Mayo Clinic in Rochester, Minnesota. "The data from ORION-10 show that inclisiran lowers LDL-C significantly and sustains reductions over a six-month period with a safety profile similar to placebo."

For the primary endpoints of ORION-10, inclisiran delivered placebo-adjusted LDL-C reductions of 58% ($p<0.0001$) at day 510 and demonstrated time-averaged placebo-adjusted LDL-C reductions of 56% ($p<0.0001$) from days 90 through 540.

The overall adverse event profiles of the placebo- and inclisiran-treated groups in ORION-10 were similar. A similar proportion of patients in the placebo and inclisiran groups experienced at least one serious treatment emergent adverse event (26.3% vs. 22.4%). The incidences of deaths (1.4% vs. 1.5%) and malignancies (3.3% vs. 3.3%) were also comparable between the placebo and inclisiran groups, respectively.

Clinically significant elevations in liver function tests (ALT 0.3% vs. 0.3%, AST 0.6% vs. 0.5%) and serum creatinine increases (3.9% vs. 3.9%) were similar between the placebo and inclisiran groups, respectively. Clinically relevant adverse events at the injection site, predominantly mild and always transient, were reported in 0.9% of placebo-treated patients vs. 2.6% of inclisiran-treated patients.

“The results from ORION-10 are outstanding and provide yet another confirmation of the highly differentiated clinical profile of inclisiran,” said Mark Timney, Chief Executive Officer of The Medicines Company. “We believe that inclisiran is ideally suited to address the effects of cumulative exposure to LDL-C and has the potential to change the course of how healthcare professionals manage ASCVD risk for the millions of patients who struggle to reach their LDL-C goals.”

ORION-10 data will be submitted to a peer-reviewed medical journal. The company expects to file regulatory submissions in the U.S. in the fourth quarter of 2019 and in Europe in the first quarter of 2020.

Data from ORION-9, a Phase 3 clinical study of inclisiran in patients with heterozygous familial hypercholesterolemia (HeFH), will be presented at AHA on Monday, November 18, 9:24am EST, during Late Breaking Science VI: New Frontiers in Lipid Therapy. The company previously announced topline results of ORION-9.

ORION-10 Study Design

The ORION program is studying the efficacy and safety of inclisiran in patients with ASCVD and FH, with ORION-9, ORION-10 and ORION-11 comprising the pivotal Phase 3 LDL-C lowering studies.

ORION-10 is a pivotal Phase 3, placebo-controlled, double-blind, randomized study to evaluate the efficacy and safety of inclisiran sodium 300 mg administered subcutaneously in 1,561 participants with ASCVD and elevated LDL-C, despite maximum tolerated dose of LDL-C-lowering therapies (e.g., a statin or ezetimibe). The primary endpoints are percentage change in LDL-C from baseline to day 510 (17 months) and time-adjusted percentage change in LDL-C from baseline after day 90 (three months) and up to day 540 (18 months). Key secondary endpoints include the mean absolute change at Day 510 (17 months), the average absolute reduction from Day 90 (three months) up to Day 540 (18 months), and changes in other lipids and lipoproteins. The study was conducted at 145 sites in the United States. Each study participant received inclisiran sodium 300 mg administered as a subcutaneous injection initially, again at three months and then every six months thereafter. The majority of study participants were taking inclisiran or placebo in addition to existing lipid-lowering therapy with a maximally tolerated statin (with or without ezetimibe).

Patients who have completed their respective Phase 3 studies are now enrolling into ORION-8, an open-label, long-term extension study where patients completing ORION-9, ORION-10 and ORION-11 will receive inclisiran for three years to evaluate the efficacy and safety of long-term dosing of inclisiran.

About Inclisiran

Inclisiran, the first and only cholesterol-lowering therapy in the siRNA (small-interfering RNA) class, is The Medicines Company's investigational twice-yearly therapy in Phase 3 clinical development to evaluate its ability to reduce low-density lipoprotein cholesterol (also known as LDL-C). As a siRNA, inclisiran harnesses the body's natural process of RNA interference to specifically prevent production of the PCSK9 protein in the liver, which enhances the liver's ability to remove LDL-C from the bloodstream, thereby lowering LDL-C levels. In Phase 3 studies, inclisiran reduced LDL-C up to 58% and sustained durable time-adjusted LDL-C reductions of up to 56% throughout a twice-yearly dosing schedule when administered along with statins and/or ezetimibe. Inclisiran is not yet approved by the FDA or any other regulatory authority. The Medicines Company obtained global rights to develop, manufacture and commercialize inclisiran under a license and collaboration agreement with Alnylam Pharmaceuticals.

Commercial Opportunity

Nearly 60 million people with ASCVD or FH across the U.S., the largest European countries, China and Japan are currently treated with lipid-lowering therapies to manage cardiovascular risk. More than 70% of these patients are not achieving LDL-C treatment goals with current therapies, and approximately two-thirds of patients do not adhere to available first-line cholesterol-lowering treatments after one year. This implies a population of more than 40 million people who could potentially benefit from the investigational candidate inclisiran in the aforementioned countries alone. Inclisiran is the first cholesterol-lowering siRNA with the potential to deliver potent and durable lowering of LDL-C levels via twice-yearly dosing that can help address two critical unmet needs – additional LDL-C lowering and poor adherence to therapy.

About The Medicines Company

The Medicines Company (NASDAQ: MDCO) is a biopharmaceutical company with a singular, relentless focus on addressing the greatest global healthcare challenge and burden today – cardiovascular disease. Our purpose is to halt the deadly progression of atherosclerosis and the cardiovascular risk created by high levels of LDL-C, or bad cholesterol. The Company is headquartered in Parsippany, New Jersey. For more information, please visit www.themedicinescompany.com and follow us on Twitter @MDCONews and LinkedIn.

Forward Looking Statements

Statements contained in this press release that are not purely historical, including, but not limited to, statements about the Company, the proposed offering described herein and the use of proceeds therefrom, are 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," "plans," "expects," "should," and "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 ability of the Company to effectively develop inclisiran; whether inclisiran will advance in the clinical trials process on a timely basis or at all, or succeed in achieving its specified endpoints; whether the Company will make regulatory submissions for inclisiran on a timely basis; whether its regulatory submissions will receive approvals from regulatory agencies on a timely basis or at all; the extent of the commercial success of inclisiran, if approved; the strength, durability and life of the Company’s patent protection for inclisiran and whether the Company will be successful in extending exclusivity; 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 SEC, including, without limitation, the risk factors detailed in the Company's Quarterly Report on Form 10-Q filed with the SEC on October 30, 2019. The Company specifically disclaims any obligation to update these forward-looking statements.