The Medicines Company

8th Annual SVB Leerink Global Healthcare Conference

Mark Timney, Chief Executive Officer

New York City • 28th February 2019

Safe Harbor

Forward-looking statements

Statements contained in this presentation about The Medicines Company that are not purely historical, and all other statements 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,” “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 we will be successful in obtaining and maintaining the capital necessary to fund our operations; 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 Securities and Exchange Commission (SEC), including, without limitation, the risk factors detailed in the Company’s Annual Report on Form 10-K filed with the SEC on February 27, 2019, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

Introduction
Mark Timney, Chief Executive Officer

25 years experience leading US and global organizations most with Merck, including a focus on primary care

Broad and deep track record building leading cardiovascular brands

Commitment to all strategic options to maximize value of inclisiran

Focused on driving and unlocking shareholder value

2019 is a defining year for MDCO

The countdown to data has begun

Fully aligned and committed to maximizing the value of inclisiran

Full commercial rights to inclisiran in all markets and market exclusivity to 2034, with anticipated extensions through 2035

Secured cash to fund clinical and pre-commercial activities into 2020

Inclisiran is anticipated to address the world's leading cause of death

Topics for today
Setting the agenda for 2019

– The unsolved problem of cardiovascular disease for patients globally

– Inclisiran as a potential game changer

– Progress update

– Anticipated news flow

Globally, 34 people died of CVD as I walked to this podium

Another 49,000 will be dead by this time tomorrow

CVD is responsible for 1 in 3 deaths worldwide

America's #1 Killer

>17 million die from CVD annually[1]

6.3 million are <70 year olds[1]

854,000 die from CVD annually[2]

160,000 <65 year olds[2]

Majority of premature deaths are preventable

1. WHO, CVD Facts, 17 May 2017; 2. CDC Wonder Database 2018

LDL Cholesterol

America's #1 modifiable risk factor

LDL-C is the leading cause of cardiovascular disease

50% of premature CV deaths could be prevented with better LDL-C management

2018 AHA/ACC guidelines and PCSK9 trials support the principle that lowering LDL-C levels to very low levels reduces ASCVD events across a spectrum of CV risk

Unmet needs

Lack of adherence

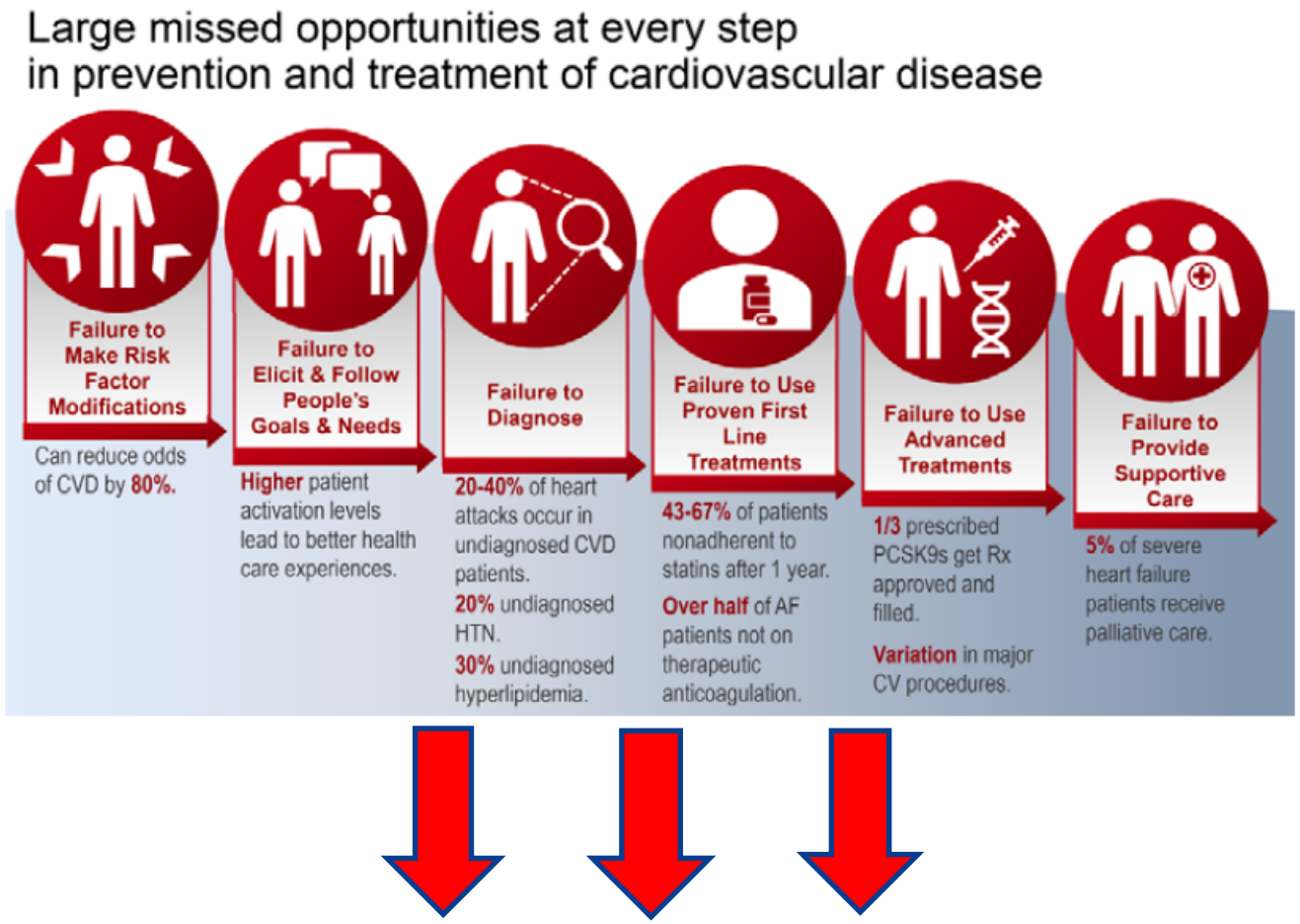
LDL-C not at goal despite statins

Prevention of second event

Under-treated cholesterol population

Unmet needs

AHA declares urgent challenges in CVD



Inclisiran could be the potential solution

1. McClellan et al, Circulation. 2019;139:00/e1-e11

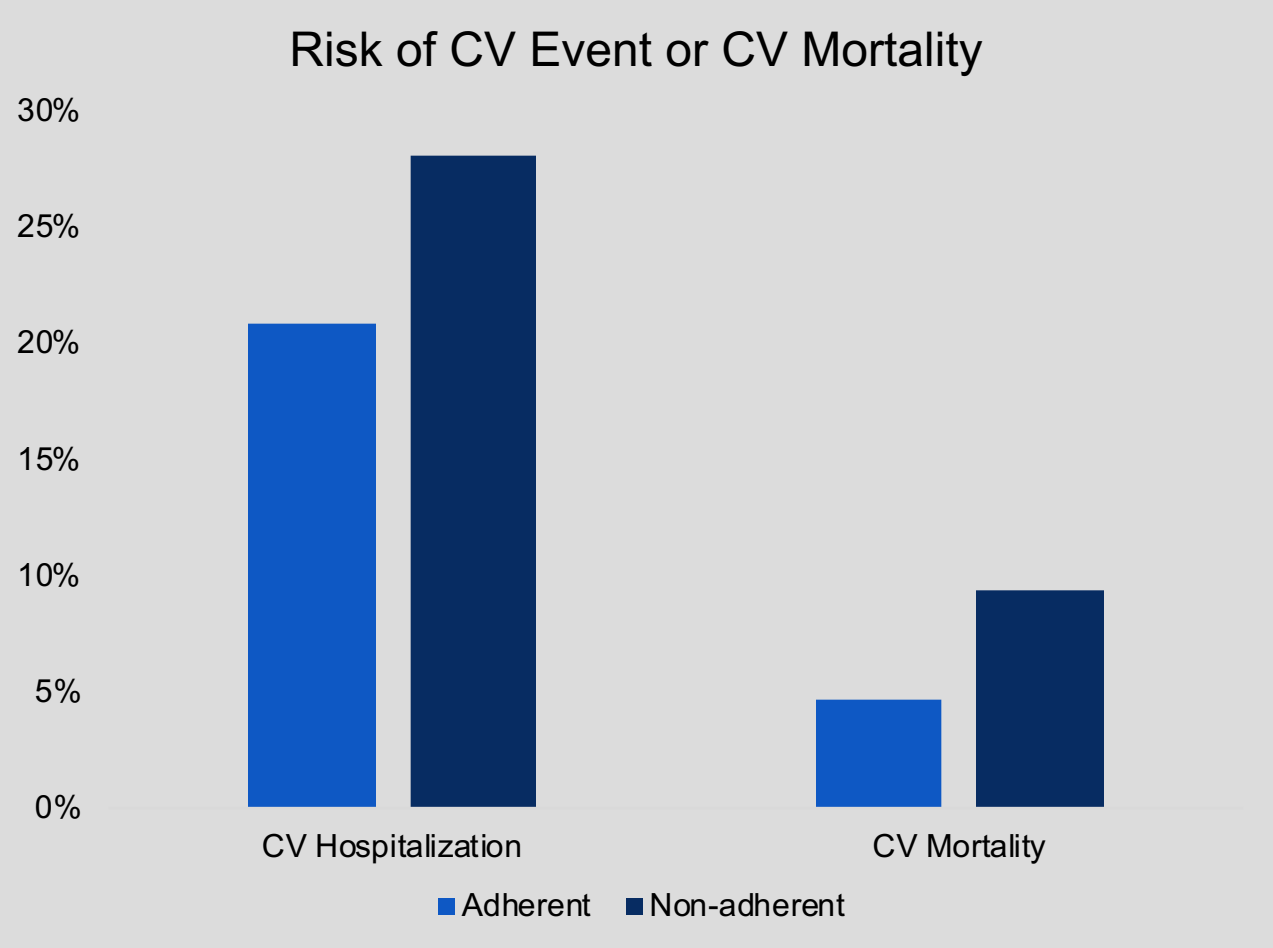
Unmet needs
Lack of adherence

43 to 67% of patients are non-adherent to statins after one year[1]

- **40%** of high risk patients discontinue by 6 months[2]
- Only **5%** maintain treatment for 5 years or longer[3]

Non-adherence is a major driver of CV death

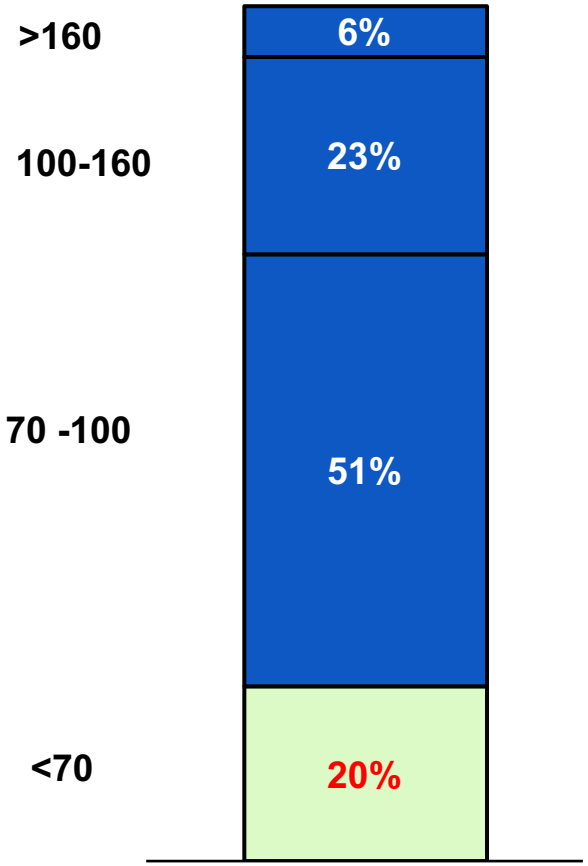
- **2X** increased risk of CV death[4]
- **4X** increased risk of CV events



1. 1. McClellan et al, Circulation. 2019;139:00/e1-e11; 2. Lin et al, J Manag Care Spec Pharm. 2016;22(6):685-98; 3. May et al, 2019; 4. De Vera et al, Br J Clin Pharmacol 2014 78:4 / 684–698;

Unmet needs

80% of patients with ASCVD are not at LDL-C goal



Available therapies are not optimized in many patients, but even when they are…

14% high-intensity statins with ezetimibe is not enough

10% don't tolerate high intensity statins

>50% are non-adherent

1. Ho et al, Am Heart J 2008;155:772-9

Unmet needs

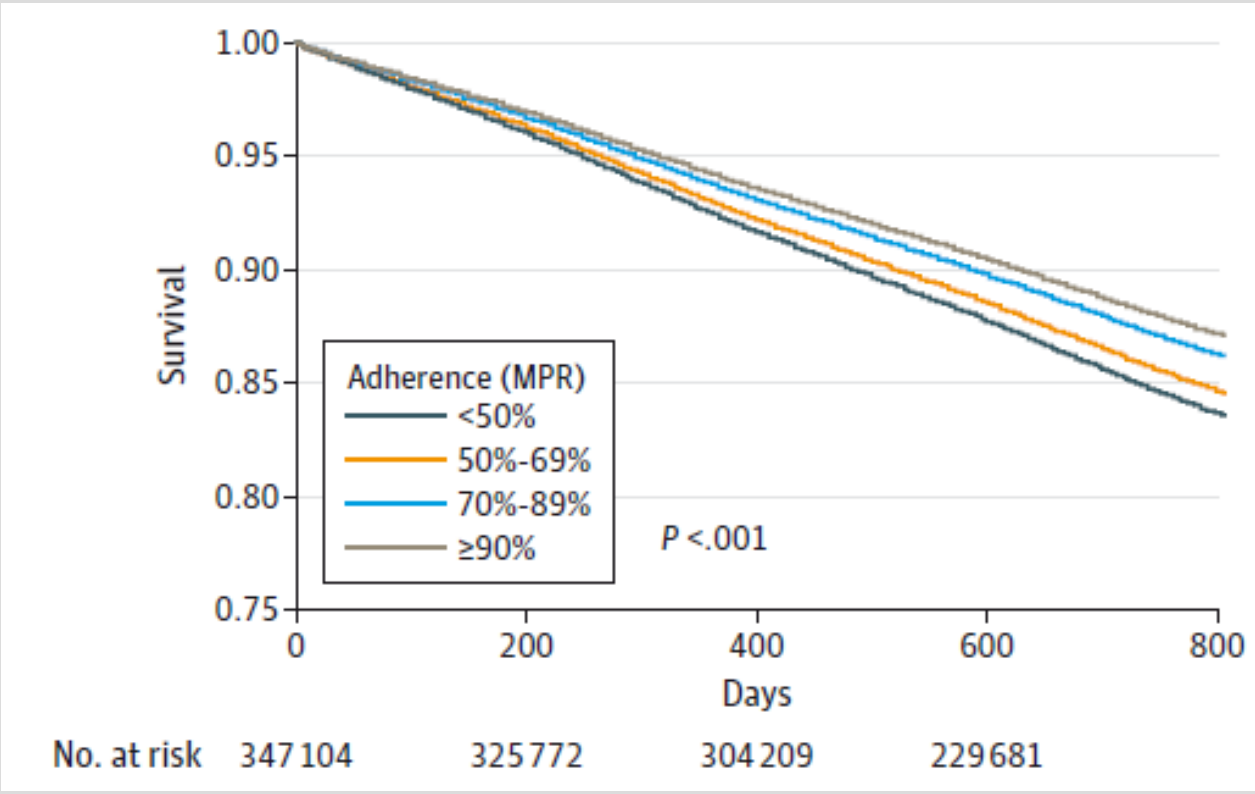
Statins are falling short of reducing second event and mortality

CV RRR accrues with time on therapy

14% with one year of treatment[1]

31% with 3 years of treatment[2]

Survival curves by statin adherence level[2]



Statin adherence is defined by the medication possession ratio (MPR)

1. Baigent et al 2005; 2. Rodriguez et al, JAMA Cardiology, 2019, e1-e9

Unmet needs

12.7 million Americans could potentially benefit from inclisiran

Highest risk hypercholesterolemia population
(Millions of patients)



	US[1]	EU5[2]	Japan[3]	Total
Diagnosed FH or ASCVD	27.5	19.7	10.3	57.4
Treated with oral LLTs	15.1	12.2	4.7	32.0
Failing to reach LDL-C goal	**12.7**	**9.5**	**2.4**	**24.7**

1. 1 US National Health and Nutrition Examination Survey (CDC); NHANES FH definition includes all patients with baseline LDL-C> 190 mg/dl
2. 2 ESC CVD statistics 2017; Steel et al. BMI 2017;7(2):e013255; Marz et al. atherosclerosis 2018;268:99-107; Geller et al. EHJ 2007;28:3051-58; Ferrieres et al. poster in ESC 2015; Khunti K, Danese MD, Kutikova L, et al. *JAMA Netw Open.* 2018;1(8):e185554; Sierra et al. Adv Ther 2015;32:944-961; Arca A et al. Atherosclerosis 2018;271:120-127. Teramoto T et al. Atherosclerosis 2016;24:8e254;
3. 3 Nagar, et al. 2017; Circ J doi:10.1253/circj.CJ-17-0811

Unmet needs

Inclisiran uniquely suited to be a preferred solution

Unmet needs	Inclisiran
Lack of adherence	Built in patient adherence
LDL-C not at goal despite LLT	Potent, durable, and consistent efficacy – mean LDL-C ↓ >50%
Prevention of second CV event	Potential for a 25% CV risk benefit
Under-treated population eligible for LLT	Potential for primary, and secondary prevention

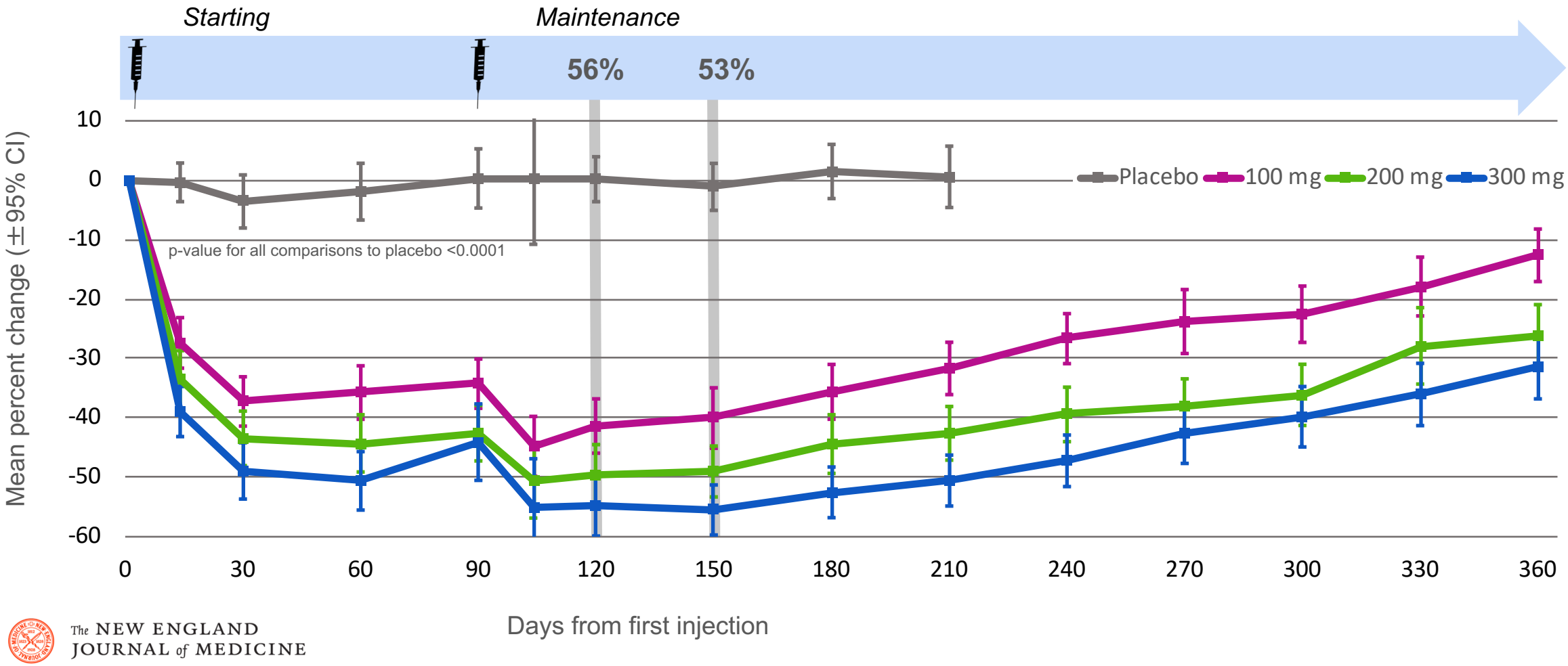
Inclisiran

A new class of lipid lowering therapy

Therapeutic profile	Inclisiran
Dosage	Twice a year
Mechanism of action	Inhibits the synthesis of PCSK9
Current lipid treatment paradigm	Aligns with current treatment pathways
Adherence	HCP administration provides adherence reassurance
Efficacy	Long and durable
Cold chain	Not required
LDL-C Variability	Minimal
Potential for better CV outcomes	High
Manufacturing	Synthetic and easily scalable

Inclisiran: Ph. II results

56% peak LDL-C reduction with 300mg dose

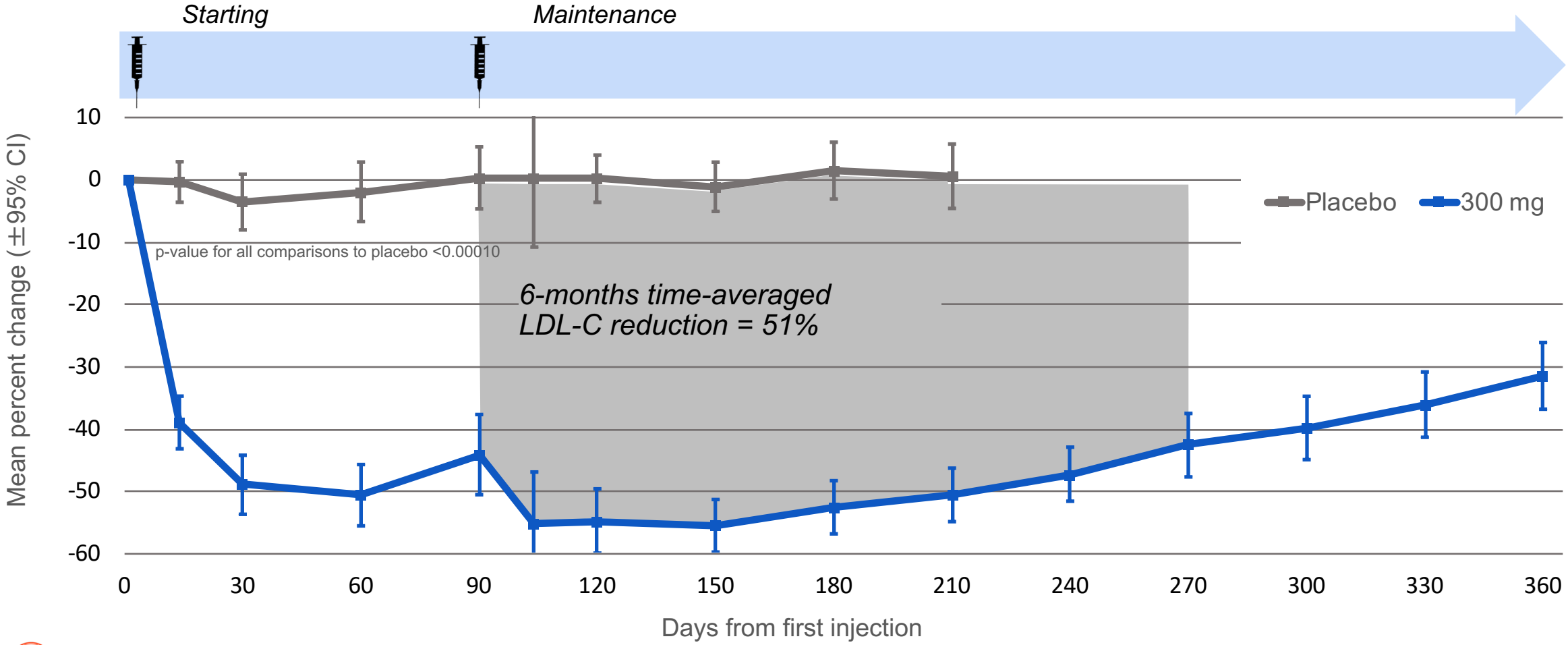


The NEW ENGLAND JOURNAL of MEDICINE

Ray KK et al. *NEJM* 2017; 376: 1430-40.

Inclisiran: Ph. II results

51% time-averaged LDL-C reduction over 6 months



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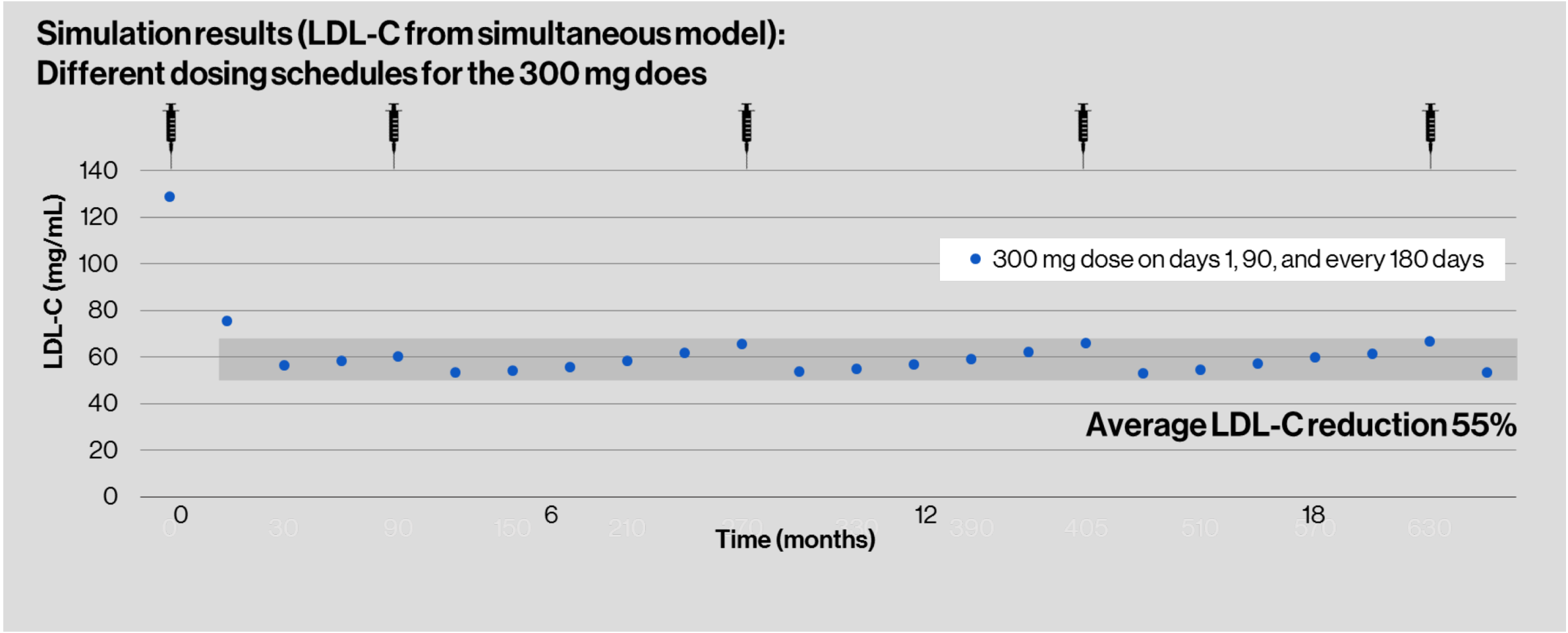
Ray KK et al. *NEJM* 2017; 376: 1430-40.

Inclisiran: Ph. III design

Twice-a-year dosing regimen targeting >50% average LDL-C reduction



Update on progress
Countdown to Phase III results

- Phase III trials continue to progress according to plan
- No material safety observations to date
- Cardiovascular outcomes trial (ORION-4) enrollment ongoing
- Manufacturing efficiency enables pricing flexibility
- Critical pre-commercialization activities underway

Phase III programs for NDA / MAA in LDL-lowering

18-months treatment trials have completed enrollment (March 2018)

Study	Countries	Main inclusion criteria	Baseline LDL-C	Patients
ORION-9	US, EU, SA	Heterozygous FH		482
ORION-10	US	ASCVD secondary prev.	>70 mg/dL	1,561
ORION-11	EU, SA	ASCVD secondary prev. High risk primary prev.	>70 mg/dL >100 mg/dL	1,617
			Total	3,660

Inclisiran: Safety profile

No material adverse events to date

Five positive DSMB reviews of 3,660 patients in Phase III trials to date

Substantially all patients who had received their third dose of study medication have completed a 60-day follow up visit

To date > 2,750 patient-years of inclisiran safety data have been collected in the ORION program, with no material safety observations as we enter the final months of these trials.

Ongoing review of blinded data

- Very low incidence of reported mild, transient injection site reactions
- No reports of study-medication-related LFT elevations
- Emerging data at least as favorable as published Phase II ORION-1 trial

ORION-4

A streamlined secondary prevention CVOT study

- 15,000 patients – enrollment underway
- Target baseline LDL-C ≥100 mg/dL
- Patients will be treated with 300 mg of inclisiran or matching placebo, given on Day-1, Day-90 and every six months thereafter.
- Median follow-up 4 or 5 years
- Primary endpoint CHD death, MI, fatal or non-fatal ischemic stroke, urgent revascularization
- Key secondary endpoints include 1) CHD death/MI and 2) CV death

ORION-4

Designed to demonstrate 25% or greater risk reduction

	LDL-C levels (mg/dL)		Potential CV outcomes
	Baseline	50%↓	annualized risk reduction[1]
	150	75	44%
Typical baseline in clinical trials	125	63	37%
	100	**50**	**29%**
	75	38	22%
	50	25	15%

1: Assumes 5 years median observation

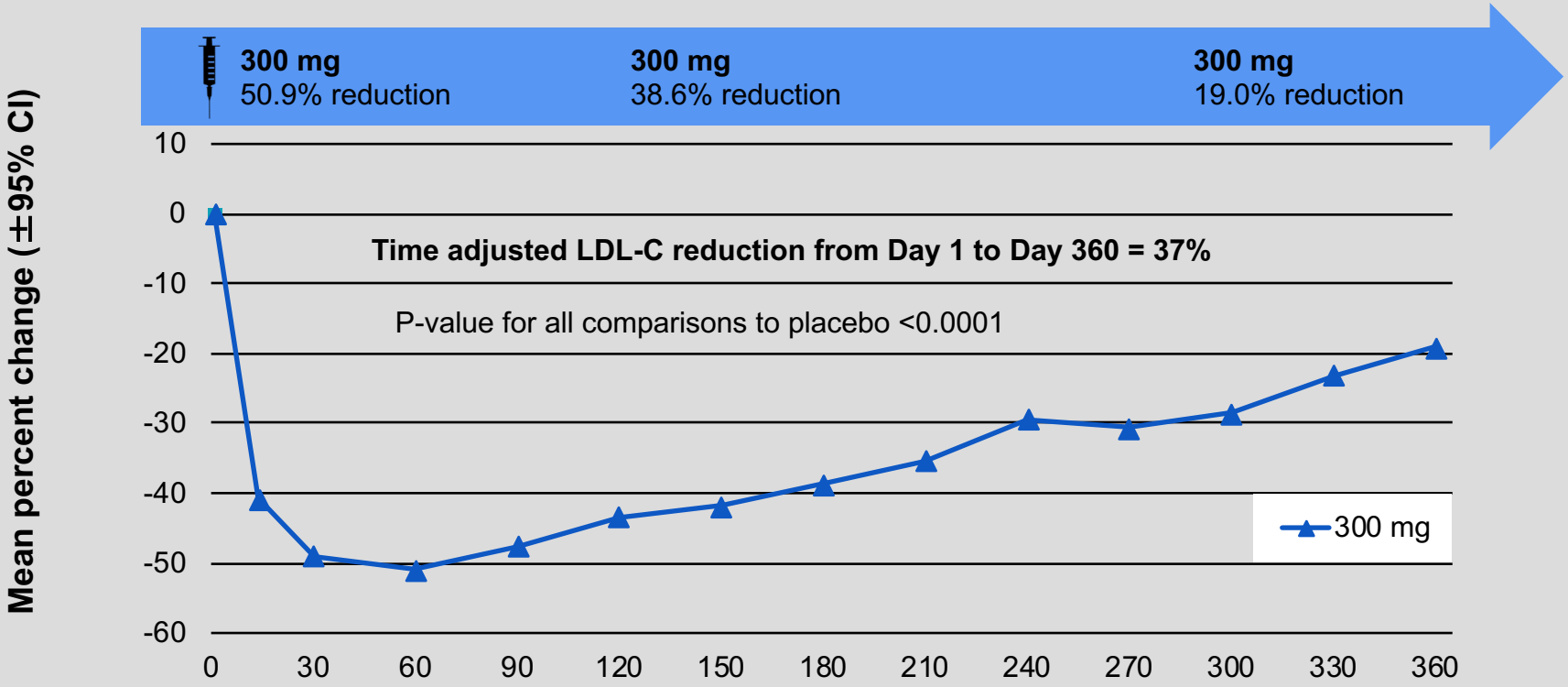
ORION-4

Statistically powered to show mortality benefit

Outcome	Assumed annual event rate for placebo	Power (2P<0.01)	Power (2P<0.05)
MACE	2.7%	>99%	>99%
CHD death or MI	1.7%	99%	>99%
CV death	0.9%	90%	97%

Inclisiran: unique effectiveness

Potent, durable, and consistent LDL-C reductions – 300 mg optimal



Development to NDA and MAA

Anticipated news flow over next 12 months

Potential event	Timing
Sixth DSMB review of phase III data	2Q 2019
Validation of manufacturing batches	3Q 2019
Phase III data from pivotal trials	3Q 2019
Potential NDA submission	4Q 2019
Potential MAA submission	1Q 2020

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Q&A