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.
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
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

- Risk of CV Event or CV Mortality

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
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

31% with 3 years of treatment

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

## Unmet needs

12.7 million Americans could potentially benefit from inclisiran

### Highest risk hypercholesterolemia population

(Millions of patients)

<table>
<thead>
<tr>
<th></th>
<th>US¹</th>
<th>EU5²</th>
<th>Japan³</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed FH or ASCVD</td>
<td>27.5</td>
<td>19.7</td>
<td>10.3</td>
<td>57.4</td>
</tr>
<tr>
<td>Treated with oral LLTs</td>
<td>15.1</td>
<td>12.2</td>
<td>4.7</td>
<td>32.0</td>
</tr>
<tr>
<td>Failing to reach LDL-C goal</td>
<td>12.7</td>
<td>9.5</td>
<td>2.4</td>
<td>24.7</td>
</tr>
</tbody>
</table>

---

1. US National Health and Nutrition Examination Survey (CDC); NHANES FH definition includes all patients with baseline LDL-C > 190 mg/dl
## Unmet needs

**Inclisiran uniquely suited to be a preferred solution**

<table>
<thead>
<tr>
<th>Unmet needs</th>
<th>Inclisiran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of adherence</td>
<td>Built in patient adherence</td>
</tr>
<tr>
<td>LDL-C not at goal despite LLT</td>
<td>Potent, durable, and consistent efficacy – mean LDL-C &gt;50% ↓</td>
</tr>
<tr>
<td>Prevention of second CV event</td>
<td>Potential for a 25% CV risk benefit</td>
</tr>
<tr>
<td>Under-treated population eligible for LLT</td>
<td>Potential for primary, and secondary prevention</td>
</tr>
</tbody>
</table>
# Inclisiran

## A new class of lipid lowering therapy

<table>
<thead>
<tr>
<th>Therapeutic profile</th>
<th>Inclisiran</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage</td>
<td>Twice a year</td>
</tr>
<tr>
<td>Mechanism of action</td>
<td>Inhibits the synthesis of PCSK9</td>
</tr>
<tr>
<td>Current lipid treatment paradigm</td>
<td>Aligns with current treatment pathways</td>
</tr>
<tr>
<td>Adherence</td>
<td>HCP administration provides adherence reassurance</td>
</tr>
<tr>
<td>Efficacy</td>
<td>Long and durable</td>
</tr>
<tr>
<td>Cold chain</td>
<td>Not required</td>
</tr>
<tr>
<td>LDL-C Variability</td>
<td>Minimal</td>
</tr>
<tr>
<td>Potential for better CV outcomes</td>
<td>High</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Synthetic and easily scalable</td>
</tr>
</tbody>
</table>
Inclisiran: Ph. II results

56% peak LDL-C reduction with 300mg dose

Mean percent change (±95% CI) from baseline over time.

- Placebo
- 100 mg
- 200 mg
- 300 mg

*p-value for all comparisons to placebo <0.0001
Inclisiran: Ph. II results

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

Starting

Maintenance

Mean percent change (±95% CI)

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

p-value for all comparisons to placebo < 0.00010

The NEW ENGLAND JOURNAL OF MEDICINE

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)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Main inclusion criteria</th>
<th>Baseline LDL-C</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORION-9</td>
<td>US, EU, SA</td>
<td>Heterozygous FH</td>
<td></td>
<td>482</td>
</tr>
<tr>
<td>ORION-10</td>
<td>US</td>
<td>ASCVD secondary prev.</td>
<td>&gt;70 mg/dL</td>
<td>1,561</td>
</tr>
<tr>
<td>ORION-11</td>
<td>EU, SA</td>
<td>ASCVD secondary prev. High risk primary prev.</td>
<td>&gt;70 mg/dL</td>
<td>1,617</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;100 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3,660</td>
</tr>
</tbody>
</table>

Total
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**

<table>
<thead>
<tr>
<th>LDL-C levels (mg/dL)</th>
<th>Potential CV outcomes annualized risk reduction¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline 50%↓</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>44%</td>
</tr>
<tr>
<td>Typical baseline</td>
<td></td>
</tr>
<tr>
<td>in clinical trials</td>
<td></td>
</tr>
<tr>
<td>125</td>
<td>37%</td>
</tr>
<tr>
<td>100</td>
<td>29%</td>
</tr>
<tr>
<td>75</td>
<td>22%</td>
</tr>
<tr>
<td>50</td>
<td>15%</td>
</tr>
</tbody>
</table>

¹: Assumes 5 years median observation
## ORION-4
Statistically powered to show mortality benefit

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Assumed annual event rate for placebo</th>
<th>Power (2P&lt;0.01)</th>
<th>Power (2P&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>2.7%</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>CHD death or MI</td>
<td>1.7%</td>
<td>99%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>CV death</td>
<td>0.9%</td>
<td>90%</td>
<td>97%</td>
</tr>
</tbody>
</table>
Inclisiran: unique effectiveness
Potent, durable, and consistent LDL-C reductions – 300 mg optimal

Time adjusted LDL-C reduction from Day 1 to Day 360 = 37%

P-value for all comparisons to placebo <0.0001

Mean percent change (±95% CI)

Days from first injection

0 30 60 90 120 150 180 210 240 270 300 330 360

300 mg
50.9% reduction

300 mg
38.6% reduction

300 mg
19.0% reduction
## Development to NDA and MAA

### Anticipated news flow over next 12 months

<table>
<thead>
<tr>
<th>Potential event</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sixth DSMB review of phase III data</td>
<td>2Q 2019</td>
</tr>
<tr>
<td>Validation of manufacturing batches</td>
<td>3Q 2019</td>
</tr>
<tr>
<td>Phase III data from pivotal trials</td>
<td>3Q 2019</td>
</tr>
<tr>
<td>Potential NDA submission</td>
<td>4Q 2019</td>
</tr>
<tr>
<td>Potential MAA submission</td>
<td>1Q 2020</td>
</tr>
</tbody>
</table>
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 in to 2020

Inclisiran is anticipated to become a game-changer addressing world’s leading cause of death
Q&A