Presenters

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Agenda

Strategic Overview | Dean Li

Verquvo (Heart Failure) | Joerg Koglin & Arpa Garay

MK-7962/sotatercept & MK-5475 (Pulmonary Arterial Hypertension) | Eliav Barr & Arpa Garay

MK-2060 (Thrombosis) | Joerg Koglin & Arpa Garay

MK-0616 (Atherosclerosis) | Fiona Marshall & Arpa Garay

Discovery | Fiona Marshall

Closing Remarks | Dean Li

Q&A
Forward-looking statement of Merck & Co., Inc., Kenilworth, N.J., USA

This presentation of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline candidates that the candidates will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company’s 2021 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).
Merck has a 60-year legacy of cardiovascular disease innovation

<table>
<thead>
<tr>
<th>Category</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics</td>
<td>multi-ion channel blockers</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>statins, ezetimibe</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>hydrochlorothiazide, ACE inhibitors, ARBs, sGC stimulators</td>
</tr>
<tr>
<td>Hypertension</td>
<td>hydrochlorothiazide, calcium channel blockers, ACE inhibitors, and ARBs</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>platelet aggregation inhibitors (Glycoprotein IIb/IIIa and PAR-1)</td>
</tr>
</tbody>
</table>

Zontivity and Brinavess are out-licensed products.
Focus on areas of greatest remaining unmet need for patients

**Merck focus areas**

<table>
<thead>
<tr>
<th>Heart Failure</th>
<th>PAH</th>
<th>Thrombosis</th>
<th>Atherosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>~50%</td>
<td>~43%</td>
<td>~20x</td>
<td>~85%</td>
</tr>
</tbody>
</table>

**Cardiovascular disease is the #1 cause of global mortality**

- Chronic heart failure patients continue to progress over time on current therapies
- Existing therapies only treat PAH symptoms, not the underlying cause of disease
- Existing forms of administration have systemic side effects

- Higher risk of CV death in patients with ESRD
- Patients with ESRD have high risk of thrombotic disease AND bleeding
- Patients with ESRD often excluded from clinical trials
- Large proportion of patients do not reach goals for LDL-C despite existing lipid-lowering therapies

Late-stage pipeline has tripled in size through internal advancements and business development over the past year

<table>
<thead>
<tr>
<th>Candidates</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Approved</th>
<th>LCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verquvo (vericiguat) tablets</td>
<td></td>
<td></td>
<td></td>
<td>HFrEF</td>
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<tr>
<td>Adempas riociguat</td>
<td></td>
<td></td>
<td></td>
<td>PAH, CTEPH</td>
</tr>
<tr>
<td>Activin receptor type IIA fusion protein (MK-7962, sotatercept)</td>
<td></td>
<td></td>
<td></td>
<td>PAH, PH-LHD</td>
</tr>
<tr>
<td>Inhaled sGC (MK-5475)</td>
<td></td>
<td></td>
<td></td>
<td>PAH, PH-COPD</td>
</tr>
<tr>
<td>Factor XI (MK-2060)</td>
<td></td>
<td>Thrombosis (ESRD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral PCSK9 (MK-0616)</td>
<td>Atherosclerosis</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Verquvo and Adempas are part of a collaboration with Bayer

Represents advancement since January 1, 2021
Cardiovascular portfolio well positioned for growth into the next decade

Eight potential new approvals across cardiovascular pipeline expected by 2030

CV Pipeline Potential

> $10 billion in peak revenue approaching mid-2030s

1. Includes the expanded indication for Verquvo plus all indications where studies are underway or being planned for clinical assets MK-7962, MK-5475, MK-2060, MK-0616
Verquvo & oral sGC
Heart Failure
Worsening chronic heart failure is an unmet clinical need

- **Initial diagnosis and treatment**: Presentation with symptoms either in outpatient setting or hospital.
- **Daily life**: May have 30-day follow-up. HCP office visits follow.
- **HF management**: E.g., 1-2 weeks post event. Medication adjustment continues throughout journey.
- **Decompensation event**: Step-wise SoC.
- **Stabilization: HCP/clinics**: Adjust therapy *
- **Stabilization: hospital**: Adjust therapy

Cardiac function over time:
- **Death**
- **Decompensation events**

HF Management (Verquvo)
Worsening chronic heart failure is associated with high mortality and morbidity even after acute treatment

**Hospitalization**

~900,000

Annual hospitalizations in the U.S.\(^1\)

(~1/3 of patients with HFrEF experience worsening HF)

**Readmission**

~27%

Patients readmitted to the hospital within 30 days\(^2,3\)

~50%

Patients readmitted to the hospital within 60 days\(^2,3\)

**Mortality**

~18%

Patients will die within 1 year following a HFH\(^4\)

~50%

Patients will die within 5 years of diagnosis\(^5\)

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Verquvo is part of a collaboration with Bayer; worsening heart failure is defined as hospitalization in the preceding 6 months or treatment with IV diuretic.

Novel oral sGC stimulators have shown efficacy

- sGC stimulators reduce oxidative stress by increasing levels of nitric oxide in the heart and blood vessels.
- This mechanism has been approved for the treatment of pulmonary hypertension and heart failure.
- Merck is currently marketing two sGC stimulators: Verquvo and Adempas and is studying a third in its pipeline: MK-5475, an inhaled formulation.

Verquvo and Adempas are part of a collaboration with Bayer.
Verquvo showed statistically significant and clinically meaningful reduction in risk of CV death or heart failure hospitalization in VICTORIA study.

- Verquvo is indicated to reduce the risk of cardiovascular death and HFH following a worsening HF event as an add-on to standard of care.
  - 24 patients needed to treat for 1 year to prevent 1 CV death or HFH.
- In the Phase 3 VICTORIA outcomes study, Verquvo showed an annualized ARR of 4.2% compared to placebo for CV death or HFH.

Potential to broaden Verquvo’s patient benefit in the Phase 3 VICTOR trial
VICTOR: Targeting reduction in CV death and hospitalization

**Purpose**

- To evaluate the efficacy of vericiguat compared with placebo on reducing the risk of cardiovascular death or HFH
- Complementary to VICTORIA trial

**Trial Design**

- Global, randomized, event-driven outcomes study
- Patients with stable heart failure
  - Chronic HFrEF with no recent decompensation
- Target enrollment: 6,000 participants

**Endpoints**

- Primary: Time from randomization to the first event of cardiovascular death or HFH
- Secondary: Time from randomization to:
  - CV death
  - First event of HFH
  - All HFH events
  - First event of all-cause mortality or HFH
  - All-cause mortality

**Timing**

- Event-driven trial; final duration will be a result of actual trial recruitment and observed accrual rate for confirmed study endpoint events
- Anticipated primary completion date of March 2025

Verquvo is part of a collaboration with Bayer
https://clinicaltrials.gov/ct2/show/NCT05093933?term=vericiguat&draw=2&rank=1
Unmet need and potential of VICTOR trial in stable HFrEF patients represent expanded Verquvo commercial opportunities

Target population
- The estimated prevalence of patients impacted by worsening heart failure globally is \textbf{4.2M}.
- Successful completion of VICTOR trial in patients with stable HFrEF will increase labeled population by \textbf{3-fold} to \textbf{12.5M}.

Commercial outlook
- Although 10+ therapies are indicated to treat heart failure, Verquvo is the first and only HF therapy specifically approved for chronic symptomatic HFrEF patients following a worsening HF event.
- Unmet medical need remains in the chronic, generally stable HFrEF patient population.
- Verquvo targets a molecular pathway not addressed by other HF therapies and data demonstrates benefit on top of guideline directed SOC.
- VICTOR study expected to broaden label and strengthen evidence on top of current therapies.

Market size

- \textbf{3.1} (2020) USD Billions
- \textbf{8.2} (2026) USD Billions
- \textbf{CAGR +18%}

Verquvo is part of a collaboration with Bayer; Merck has the commercial rights to Verquvo in the United States and Bayer has the exclusive commercial rights in the rest of the world.

Worsening heart failure is defined as hospitalization in the preceding 6 months or treatment with IV diuretic.

1. Evaluate Pharma Chronic Heart Failure Feb 2022
MK-7962 (sotatercept) & MK-5475
Pulmonary Arterial Hypertension
Significant unmet need remains in PAH

PAH is a rare, rapidly progressive and fatal disease

- Mortality is high despite advances in treatment and use of combination therapy
- Devastating disease with adverse impacts on all aspects of life: physical, social and emotional
- Current therapy goals include delaying disease progression, managing symptoms and reducing hospitalization
- Payors and health care professionals recognize the need for additional treatment options
- Current standard of care through vasodilators with potential systemic effects that treat the symptoms of PAH, as opposed to underlying disease

Benza et al, Chest 2012; 142(2):448-456
MK-7962
sotatercept
Sotatercept (MK-7962): A potential first-in-class soluble activin receptor type IIA fusion protein

Sotatercept is a novel, first-in-class fusion protein comprising the extracellular domain of human activin receptor type IIA linked to the Fc domain of human immunoglobulin G1.

Source: Data presentation at PVRI 2021 of Phase 2 PULSAR Biomarker Analysis for Treatment of PAH
Sotatercept resolved vascular remodeling in a rat model of PAH

Normal blood vessels in a healthy rat

Week 1–5: SU/Hx/Nx – PAH

Rats exposed to sugen/hypoxia and then normoxia for 5 weeks to induce PAH

Week 5–9: Placebo

Rats given placebo the following 4 weeks showed continued PAH disease progression; blood vessels appear more cellular and even thicker

Week 5–9: Sotatercept

Rats given RAP-011 (murine analogue of sotatercept) the following 4 weeks showed reversal of cell proliferation (blood vessels appear close to normal image)

Sotatercept clinical efficacy in the Phase 2 PULSAR study

**Pulmonary vascular resistance**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Change in Pulmonary Vascular Resistance (dyn.s/cm²)</th>
<th>Placebo-corrected LS mean difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo + SOC n=32</td>
<td>-16 ± 35.3 (-2.1%)</td>
<td>0</td>
<td>p=0.0027</td>
</tr>
<tr>
<td>Sotatercept 0.3 mg/kg+SOC n=32</td>
<td>-162 ± 33.3 (-20.5%)</td>
<td>0</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Sotatercept 0.7 mg/kg+SOC n=42</td>
<td>-256 ± 29.6 (-33.9%)</td>
<td>-25 ± 11.1 (SE=11.1)</td>
<td>P=0.03*</td>
</tr>
</tbody>
</table>

**Change in 6-minute walking distance (m)**

- Placebo + SOC (n=32): 29 ± 9.3 m
- Sotatercept + SOC all doses (n=74): 54 ± 6.1 m

*Statistically significant effect on primary endpoint pulmonary vascular resistance

*Nearly 2x improvement observed in key secondary endpoint of 6-minute walking distance

* Nominal

Efficacy that was enhanced or maintained for up to 48 weeks in the PULSAR study

**PULSAR open label extension 48-week interim results** *(May 2021)*

**6MWD (m)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuing 0.3 mg/kg + SOC</strong></td>
<td>57.4 ± 6.7</td>
<td>67.7 ± 17.7</td>
<td></td>
</tr>
<tr>
<td><strong>Continuing 0.7 mg/kg + SOC</strong></td>
<td>53.9 ± 8.7</td>
<td>66.5 ± 12.5</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.3 mg/kg + SOC</strong></td>
<td>43.0 ± 22.1</td>
<td>82.4 ± 24.7</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.7 mg/kg + SOC</strong></td>
<td>24.3 ± 11.8</td>
<td>53.6 ± 22.8</td>
<td></td>
</tr>
</tbody>
</table>

**NT-proBNP (pg/mL)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuing 0.3 mg/kg + SOC</strong></td>
<td>-689.2 ± 169.9</td>
<td>-655.5 ± 198.7</td>
<td></td>
</tr>
<tr>
<td><strong>Continuing 0.7 mg/kg + SOC</strong></td>
<td>-433.3 ± 124.7</td>
<td>-246.2 ± 163.9</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.3 mg/kg + SOC</strong></td>
<td>365.8 ± 211.4</td>
<td>-248.2 ± 115.0</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.7 mg/kg + SOC</strong></td>
<td>-782.1 ± 417.3</td>
<td>13.9 ± 157.1</td>
<td></td>
</tr>
</tbody>
</table>

**WHO FC improvement (%)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Week 24 (receiving sotatercept during placebo-controlled period)</th>
<th>Week 24 (receiving placebo during placebo-controlled period)</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuing 0.3 mg/kg + SOC</strong></td>
<td>31 ± 8.2</td>
<td>38 ± 8.6</td>
<td></td>
</tr>
<tr>
<td><strong>Continuing 0.7 mg/kg + SOC</strong></td>
<td>17 ± 5.8</td>
<td>33 ± 7.4</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.3 mg/kg + SOC</strong></td>
<td>13 ± 8.8</td>
<td>29 ± 12.1</td>
<td></td>
</tr>
<tr>
<td><strong>Placebo + SOC / 0.7 mg/kg + SOC</strong></td>
<td>13 ± 8.8</td>
<td>53 ± 12.9</td>
<td></td>
</tr>
</tbody>
</table>

*Interim extension analysis data cut-off date: 14 September 2020.*


Clinical efficacy was enhanced or maintained through extension period. Clinically meaningful improvements observed across all key secondary endpoints.
Robust development program for sotatercept with opportunities to improve patient mortality

<table>
<thead>
<tr>
<th>Development stage</th>
<th>STELLAR</th>
<th>HYPERION</th>
<th>ZENITH</th>
<th>SOTERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed Phase 3 Enrollment</td>
<td>Initiated Phase 3</td>
<td>Initiated Phase 3</td>
<td>Initiated Phase 3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intent¹</th>
<th>Registration</th>
<th>Label extension</th>
<th>Label extension</th>
<th>OLE long-term follow-up</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Focus area</th>
<th>PAH Class II or III (newly diagnosed intermediate/high risk)</th>
<th>PAH Class II or III (at high risk of mortality)</th>
<th>Ongoing/previous sotatercept PAH study patients</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>6MWD</th>
<th>TTCW</th>
<th>Time to death or PAH related hospitalization</th>
<th>Safety &amp; tolerability</th>
</tr>
</thead>
</table>

¹. Intent based on U.S. filing strategy, ex-US timing may vary
Also evaluating sotatercept in Phase 2 in patients with Cpc-PH due to HFpEF
STELLAR: Enrollment completed ahead of plan

**Purpose**
- To evaluate the efficacy and safety of sotatercept treatment versus placebo (on top of background PAH therapy) at 24 weeks in adults with PAH
- Initial registrational trial

**Trial Design**
- Randomized, double-blind, placebo-controlled, multicenter, parallel-group study
- Patients who are PAH WHO FC II or III
- Target enrollment: 284 participants

**Endpoints**
- Primary: Change from baseline in 6MWD
- Secondary: Various

**Timing**
- Anticipated primary completion date of December 2022

MK-5475
Inhaled sGC
PAH disease is localized, yet primary therapies are systemic

- Current vasodilators are **oral** and therefore create **systemic and pulmonary vasodilation in equal measure**

- Oral sGC is a **well-received** therapy, but its use is limited because of the inability to tolerate **maximal pulmonary vasodilatory dose due to systemic hypotension**

Limitations of current therapeutic approach:

- Systemic AEs (e.g., hypotension)
- Dose limiting side effects
- Careful monitoring
- Complex titrations
- Drug-drug interactions
Developing a pulmonary selective vasodilator by combining a proven MoA with an established inhaled delivery device

- **Small molecule** stimulator of sGC that is formulated as a dry powder for inhaled delivery
- **Selective pulmonary arterial vasodilation** with limited systemic exposure
- **No dose titration** and **once a day dosing**
- Versatile, **add-on therapy** including with a PDE5i

**sGC stimulator**

- ADEMPAS (Riociguat) - an oral sGC stimulator approved for use in PAH & CTEPH

**Dry Powder Inhaler**

- TWISTHALER based on ASMANEX design for inhaled delivery
MK-5475: Pre-clinical proof of concept shows targeted reduction in vascular resistance and pressure

- MK-5475 is an investigational, inhaled sGC stimulator being studied for the treatment of PAH
- MK-5475 is a long-acting, once daily inhaled drug, with potential to provide more targeted exposure compared to oral sGCs
- Potential to improve risk/benefit profile given targeted dosing and less toxicity versus oral sGCs

Data from Sugen hypoxia PAH rat model
MK-5475: Operationally seamless phase 2/3 study in PAH

Phase 2
Intent: Dose selection cohort
primary endpoint: PVR at 12 wks

Phase 3
Intent: Confirmatory cohort
primary endpoint 6MWD at 12 wks

- Ph3 cohort includes a blinded long-term extension period to evaluate long term MK-5475 effects
- A second Ph3 study (with similar population & design) will also be performed to further evaluate MK-5475 effects on 6MWD & be pooled with first Ph3 study to evaluate TTCW

Anticipated primary completion date of December 2024
Leading PAH portfolio and significant unmet need translates to exciting growth opportunity

**Market size**

<table>
<thead>
<tr>
<th>Year</th>
<th>Annual Worldwide Revenue (USD Billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>6.1</td>
</tr>
<tr>
<td>2026</td>
<td>7.8</td>
</tr>
</tbody>
</table>

**CAGR** +4%

**Target population**

- **~90K** The estimated prevalence of patients impacted by PAH globally²,³,⁴
  - ~45–60K (US)
  - ~19–30K (EU)
  - ~3–4K (Japan)

**Commercial outlook**

- PAH recognized as an orphan disease which supports health authorities’ priorities for development of new treatments
- **Sotatercept**: First non-vasodilator with the potential to address underlying disease
- **MK-5475**:
  - Selective pulmonary arterial vasodilation with limited systemic exposure
  - Once-daily administration with no titration requirement

**Merck’s leading PAH portfolio will support patients across their treatment journey with novel targeted therapies**

Opportunities exist to expand further into pulmonary hypertension

### Initial focus

| Group 1 PAH | Sotatercept & MK-5475 | PAH |

### Additional potential opportunities

<table>
<thead>
<tr>
<th>Group 2</th>
<th>Group 3 PH Lung Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH Left Heart Disease</td>
<td>Sotatercept</td>
</tr>
<tr>
<td>cpc-PH HFpEF</td>
<td>MK-5475</td>
</tr>
<tr>
<td>PH-COPD</td>
<td></td>
</tr>
</tbody>
</table>

- **Key considerations**
  - No currently marketed therapies indicated for cpc-PH HFpEF and PH-COPD
  - Cpc-PH due to HFpEF prevalence not well established due to low diagnosis rate and lack of treatment algorithms
  - Patients with COPD that develop PH have a poor prognosis with a 37% 5-year survival rate
  - Uptitration of systemic PH therapies is limited by systemic side effects
  - Up to 30% of all COPD patients have elevated PH pressures

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MK-2060
Thrombosis
Anticoagulation without increased bleeding risk as an unmet need
High thrombosis and bleed risk in patients with ESRD

- Patients with ESRD are more likely to clot and to bleed than the general population.
- Anticoagulants may increase bleeding risk in patients with ESRD.
- There remains a high burden of cardiovascular disease in patients with ESRD compared to the general population.
- Patients with ESRD have a significant unmet need for an effective anticoagulant with minimal bleeding risk (currently no standard of care).

Significant unmet need:

- Higher risk of stroke: 6x
- Higher risk of venous thromboembolism: >2x
- Higher risk of myocardial infarction: 5x
- Higher prevalence of atrial fibrillation: 10x

Potential for FXI inhibition to be an effective anticoagulant with minimal bleeding risk

FXI is an integral component of the intrinsic pathway of the coagulation cascade

Human genetics and epidemiological studies

• FXI deficiency (Hemophilia C) confers reduced risk of ischemic stroke, VTE and MACE
• FXI deficiency has reduced bleeding risk
• Conversely, increased levels of FXI are associated with higher risk of VTE and ischemic stroke

Preclinical validation

• FXI knockout mice exhibit thromboprotection in multiple models, without bleeding diathesis
• In contrast, fatal bleeding observed in FX and prothrombin KO mice

FXI inhibition may serve as a safer anticoagulant

• Ability to uncouple thrombosis from hemostasis and provide opportunities for treatment of a wider range of patients, including those at high risk for bleeding

Source: Preis M et al., Blood 2017; Gailani D et al., Thromb Haemost 2015; Hsu et al., JACC 2021; Sano, K et al., SICOT J 2017; Salomon O et al. Thromb Haemost 2019
MK-2060: Dual inhibition of FXI/FXIIa

**Mechanism of action**

- IV dosing evaluated in healthy volunteers, IV dosing evaluated in ESRD

- Blocks FXI activation and FXIIa activity (dual mode of blockade)

- Results in anticoagulant effect:
  - Prolongation of activated partial thromboplastin time
  - Inhibition of FXI activity
  - No effect on prothrombin time

**Key attributes**

- IV dosing evaluated in healthy volunteers, IV dosing evaluated in ESRD

- Blocks FXI activation and FXIIa activity (dual mode of blockade)

- Results in anticoagulant effect:
  - Prolongation of activated partial thromboplastin time
  - Inhibition of FXI activity
  - No effect on prothrombin time
MK-2060: Strategically targeting select ESRD patient population to show proof of concept

**Purpose**
- To evaluate the efficacy and safety of two different doses of MK-2060 in ESRD participants receiving hemodialysis via an AVG
- Data from this study will be used to aid dose selection of MK-2060 in future studies

**Trial Design**
- Phase 2 multi-site, randomized, double-blind, placebo-controlled, clinical outcome trial of prevention of AVG thrombosis and safety of MK-2060 in patients with ESRD receiving hemodialysis
- Target enrollment: 489 participants

**Endpoints**
- **Primary:** Time to first AVG thrombosis event
- **Secondary:**
  - Number of AVG thrombosis events
  - Number of participants who experience one or more AEs
  - Number of major bleeding events or clinically relevant non-major bleeding events
  - Number of participants who discontinue study intervention due to an AE

**Timing**
- Event-driven trial; final duration will be a result of actual trial recruitment and observed accrual rate for confirmed study endpoint events
- Anticipated primary completion date of March 2023

Phase 2 study will inform the evaluation of a broader set of ASCVD endpoints in patients with ESRD

### Phase 2 strategy
- Enrolls patients with ESRD on hemodialysis via AVG only
- High rate of AVG thrombosis enables rapid accrual of endpoints

### Phase 3 considerations
- AVG thrombosis to act as a surrogate for MTCVEs
  - Fatal and non-fatal myocardial infarction
  - Ischemic stroke
  - Pulmonary embolism
  - Deep vein thrombosis
  - Acute limb ischemia

#### Potential Phase 3 Endpoints

- **Vascular access failure**
  - (# of events per 100 patient years)

  ![Vascular access failure chart](chart)

  - AVG: 69 events
  - AVF: 13 events

#### Plan to enroll
- All patients with ESRD on hemodialysis regardless of dialysis access type (i.e., AVG, AVF or catheter)

Patients with ESRD represent a compelling initial opportunity for MK-2060 as a next-generation anticoagulant.

### Target population

- Currently no standard of care in anti-coagulation treatment for patients with ESRD.
- MK-2060 is the sole dual FXI/FXIa inhibitor in development for ESRD.
- Factor XI inhibition uncouples thrombosis from hemostasis, providing opportunity to treat a wide range of patients including those at high risk of bleeding.
- MK-2060’s IV dosing during hemodialysis is the preferred route of administration.
- Beyond ESRD, LCM opportunities in areas of high unmet need provide future growth potential.

### Antithrombotic market size

- **CAGR +1%**
  - **2020**: 31.9 USD billions
  - **2026**: 34.6 USD billions

### Commercial outlook

- The estimated worldwide prevalence of diagnosed and treated patients with ESRD on hemodialysis:
  - ~1.5M
  - ~800K (China)
  - ~512K (US)
  - ~200K (EU5)

1. Evaluate Pharma Antithrombotic Agents Feb 2022; 2. Bayer/JNJ partnership – ELQUIS (LOE 2026) and Pfizer/BMS partnership – Xarelto (LOE 2024); 3. USRDS, CNRDS, Merck country research.
MK-0616
Atherosclerosis
Significant unmet need for patients not meeting LDL-C lowering goals creates opportunity for differentiated approach to lipid reduction.

**Residual cardiovascular risk**

LDL-C is causative in development of atherosclerotic CV disease so the residual CV risk remains high if LDL-C is elevated.

**Da Vinci study of patients at LDL-C goal**

Despite available lipid lowering therapies, most patients still do not reach their LDL-C goal.

Source: Vrablik et al., Lipid-lowering therapy use in primary and secondary care in Central and Eastern Europe: Da Vinci Observational Study 2021.
PCSK9 as a validated therapeutic target in hypercholesterolemia

- **Genetic evidence** supports targeting PCSK9
  - PCSK9 loss-of-function mutants: decrease LDL-C, decrease CV risk
  - PCSK9 gain-of-function mutants: increase LDL-C, increase CV risk

- Three **injectable** PCSK9 inhibitors on the market show ~50–60% LDL-C reduction, but use remains limited by current payor access and adherence challenges

- Currently no marketed oral PCSK9 inhibitors

Cyclic peptide platform enables targeting “difficult-to-drug” proteins

Cyclic peptide platform offers “mAb-like” potency/selectivity at a lower molecular weight

- Identifies macrocyclic peptides as inhibitors of protein-protein interactions

Structure-based drug discovery

- Cyclic peptides bind to the flat PCSK9-LDL-R interface with mAb-like affinity

Cyclic peptide modality

- MW =~1500 g/mol
- Ki = 2-5 pM

MK-0616: Potential to be a highly effective, differentiated oral cholesterol-lowering medicine

- **MK-0616** is a *cyclic peptide* that binds to PCSK9 enzyme with a similar mechanism of action as the marketed mAbs but delivered orally once daily
- **Well-tolerated** in single and multiple dose studies
- Potential to be differentiated from other oral lipid lowering therapies on the market based on its *favorable efficacy and safety profile*
- Potential to *overcome barriers* to the use of the PCSK9i class, helping more patients with hypercholesterolemia reach goal LDL-C and reduce risk CV events

**Selected findings from early clinical studies**

- **>90% reduction in free PCSK9**
- **>60% LDL-C reduction** by day 14 in statin-treated participants

Presented at American Heart Association Scientific Session in November 2021
MK-0616: Phase 2b trial to inform further development plan

**Purpose**

- Phase 2b dose finding study of MK-0616 in participants with hypercholesterolemia, including those with established ASCVD or ASCVD-risk equivalents

**Trial Design**

- The study will evaluate efficacy and safety of MK-0616 versus placebo in patients who have elevated LDL-C on or off background statin therapy
- Target enrollment: 375 participants

**Endpoints**

- **Primary:**
  - % reduction of LDL-C at 8 weeks
  - % of participants who experience one or more AEs
  - % of participants who discontinue study intervention due to AEs
- **Secondary:**
  - % change from baseline in apolipoprotein B at week 8
  - % change from baseline in non-high-density lipoprotein cholesterol at week 8
  - % of participants with LDL-C value at goal at week 8

**Timing**

- Anticipated primary completion date of February 2023

[Link to clinicaltrials.gov]
MK-0616 has the potential to impact cholesterol management at global scale

Target population

- **41M** The estimated prevalence of patients impacted by hypercholesterolemia globally
  - **18M (US)**
  - **23M (EU5 & Japan)**

- **7 out of 10** Patients are not at guideline recommended LDL-C levels, despite a multitude of approved therapies

Commercial outlook

- MK-0616 is expected to be a potent cholesterol lowering agent with the simplicity of oral dosing
- MK-0616 has the potential to be the first oral PCSK9i to market
- Early customer insights have indicated strong interest in an oral PCSK9i that can deliver the same efficacy and safety as the injectables

Sources:
1. Evaluate Pharma
2. Optum claims data 2019
3. ESC Congress 2016. Abstract P4990
4. DRG Clarivate 2021

Lipid market size

- **CAGR +8%**
- **2020: 7.1**
- **2026: 11.2**

Annual Worldwide Revenue (USD Billions)
MRL Discovery
Building depth in disease biology expertise by focusing on key cell pathways

Continue to explore human biology through...

- Genetics and genomics
- Clinical samples and data
- Human tissues and cell models

Focus on key pathways and cell types

- Inflammation
- Vascular dysfunction
- Tissue dysfunction
- Fibrosis
Unprecedented capabilities to understand disease-relevant biology and translate to therapeutics and vaccines

**Increased Automation/Data Science**

- **Robotics**
- **Data science**
- **Machine learning**

**New Modalities**

- **Biologics**
- **Macrocyclic Peptides**
- **ADC/mRNA**

**New Capabilities**

- **Screening Genomics Profiling Bioanalytical**

**Human Disease Models**

- **Organoids**
- **iPSCs**
- **Humanized mice**

**Translational PKPD**

- **Enhanced models**
- **Dose prediction**

**Improving Translation**
Functional respiratory imaging was used to visualize the increase in blood flow following administration of MK-5475.
Recently established South San Francisco site is focused on cardiometabolic disease

- >300 Merck employees
- Biologists are working alongside chemists
- Scientists co-located with business development colleagues
- Located in vibrant scientific research geography with local biotechnology companies and leading universities
- One of three discovery research hubs, in addition to Cambridge and London
Closing Remarks
Cardiovascular portfolio well positioned for growth into the next decade

Eight potential new approvals across cardiovascular pipeline expected by 2030

CV Pipeline Potential

> $10 billion in peak revenue approaching mid-2030s

1. Includes the expanded indication for Verquvo plus all indications where studies are underway or being planned for clinical assets MK-7962, MK-5475, MK-2060, MK-0616
Poised to impact cardiovascular disease

- **Rich cardiovascular legacy** of improving patient care and changing treatment paradigms

- Cardiovascular disease remains the **largest cause of mortality** worldwide despite significant innovation

- **Uniquely positioned** to impact cardiovascular mortality and morbidity with differentiated science and capabilities

- Robust cardiovascular portfolio could have a **significant impact on patient outcomes** across all major cardiovascular disease areas
Q&A

Dean Li
President, Merck Research Laboratories

Eliav Barr
SVP, Head of Global Clinical Development & Chief Medical Officer

Fiona Marshall
SVP, Discovery, Preclinical & Translational Medicine

Joerg Koglin
VP, Global Clinical Development, CV & Respiratory

Arpa Garay
Chief Marketing Officer, Human Health

Peter Dannenbaum
VP, Investor Relations
Thank you
Appendix
Dean Li, MD, PhD
President Merck Research Laboratories

Dean Li is executive vice president and president, Merck Research Laboratories. He leads the company’s worldwide human vaccines and therapeutics research and development organization.

Since joining Merck in 2017, Dean has held leadership roles in the Translational Medicine and Discovery functions and was appointed to President, Merck Research Laboratories in January 2021.

Prior to joining Merck, Dean held positions of increasing responsibility in translational medical research at the University of Utah. Most recently he served as the H.A. & Edna Benning Professor of Medicine and Cardiology, Chief Scientific Officer, Associate Vice President and Vice Dean at the University of Utah Health System. In addition, from 2015 to 2016, he served as interim CEO of Associated Regional University Pathologists, the nation’s third largest clinical reference laboratory. During his tenure at the University of Utah, he co-founded multiple biotech companies based upon research conducted in his laboratory, including Recursion Pharmaceuticals, Hydra Biosciences and Navigen Pharmaceuticals.

Dean received his BA from the University of Chicago and an MD, PhD and clinical medicine and cardiology training at Washington University School of Medicine in St. Louis. He is a member of the American Society for Clinical Investigation and the Association of American Physicians.
Arpa Garay is Chief Marketing Officer of Human Health. Arpa leads Human Health Global Marketing and is responsible for long-term portfolio strategy and global marketing for the company’s in-line and pipeline human health medicines and vaccines. This includes global market access & pricing strategy; data & analytics; digital marketing; and commercial business development.

Prior to this role, Arpa led Global Marketing and Digital for Oncology, and previously led Global Marketing for Pharmaceuticals, Commercial Analytics and Digital Marketing from 2019 to 2021. Arpa joined Merck in 2006 and has served in a wide range of commercial and marketing roles with increasing responsibility across the organization. Before joining Merck, Arpa was a consultant with Monitor Deloitte, gaining diverse experience across industries and business challenges.

Arpa holds a BS in Economics from the Massachusetts Institute of Technology, where she focused on medicine, public health and public policy.
Joerg Koglin, MD, PhD
Vice President
Global Clinical Development – Cardiovascular & Respiratory

Joerg Koglin is vice president and the Global Therapeutic Area Head of Cardiovascular & Respiratory, Global Clinical Development. In this role, Joerg provides clinical and medical oversight for all cardiovascular development programs at Merck Research Laboratories (MRL). He and his team are responsible for cardiovascular strategy and business development. Joerg also oversees the Global Scientific and Medical Publications team.

Since joining Merck 2007, Joerg has held positions of increasing importance in Global Clinical Development. He has worked on various early and late-stage development programs in heart failure, pulmonary hypertension, atherosclerosis, hypertension, ischemia/reperfusion, thrombosis and atrial fibrillation compounds.

Joerg is a board-certified cardiologist. He received his MD from the University of Heidelberg, Germany. He earned his PhD from the University of Munich, Germany following a postdoctoral fellowship at the Cardiovascular Biology Laboratory of the Harvard School of Public Health.
Eliav Barr, MD  
Senior Vice President  
Head of Global Clinical Development, Chief Medical Officer

Eliav Barr is senior vice president and head of Global Clinical Development and Chief Medical Officer at Merck Research Laboratories (MRL). He leads all late-stage clinical development for Merck’s human health portfolio and pipeline.

Prior to his current role, Eliav led MRL’s Global Medical Affairs organization expanding Merck’s scientific engagement and implementation efforts in oncology, vaccines and infectious diseases. Since joining Merck in 1995, Eliav has held positions of increasing responsibility including leadership roles in oncology and infectious diseases clinical development. He was also previously Therapeutic Area Head for Infectious Diseases and managed product development teams in Oncology and Infectious Disease.

Eliav is a cardiologist by training. He received his undergraduate degree from Penn State University and his medical degree from Thomas Jefferson University. He completed his Internal Medicine residency and Cardiology Fellowship at Johns Hopkins University, and subsequently pursued post-doctoral training at the University of Michigan. Prior to joining Merck, he held a faculty position at the University of Chicago.
Fiona Marshall, PhD
Senior Vice President
Discovery, Preclinical & Translational Medicine

Fiona Marshall is senior vice president of Discovery, Preclinical and Translational Medicine at Merck Research Laboratories.

Fiona joined Merck in 2018 as head of the new Discovery Research Centre in London, where she focused on diseases of aging. In 2019, she was appointed head of neuroscience discovery and in 2021 she was promoted to her current role. Previously, Fiona was Chief Scientific Officer at Sosei Heptares. Fiona is most well known for her work in the field of G protein-coupled receptors. Prior to founding Heptares, Fiona served as Head of Discovery Biology Europe for Millennium Pharmaceuticals and previously Head of Molecular Pharmacology and Head of the Receptor Systems Unit, at GlaxoSmithKline.

Fiona won the 2012 WISE Women of Outstanding Achievement for Innovation and Entrepreneurship and the 2015 Royal Society of Chemistry (RSC) Malcolm Campbell Award for chemistry. She is a Fellow of the Academy of Medical Sciences, Honorary Fellow of the British Pharmacological Society and Honorary Fellow of the RSC. In 2021, she was elected a fellow of the Royal Society, a distinguished U.K. organization made up of eminent scientists, engineers and technologists.

Fiona received her PhD in Neuroscience from University of Cambridge and a BS in Biochemistry from University of Bath.
Acronyms

6MWD = 6 Minute Walking Distance
ACE = Angiotensin Converting Enzyme
ActRIIA = Activin Receptor Type IIA
ADC = Antibody Drug Conjugate
ARB = Angiotensin Receptor Blocker
ASCVD = Atherosclerotic Cardiovascular Disease
AVF = Arteriovenous Fistula
AVG = Arteriovenous Graft
BMPR-II = Bone Morphogenetic Protein Receptor-II
cpc-PH = Combined Post-capillary and Pre-capillary Pulmonary Hypertension
CTEPh = Chronic Thromboembolic Pulmonary Hypertension
ESRD = End Stage Renal Disease
FC = Functional Class
HFH = Heart Failure Hospitalization
HFrEF = Heart Failure with Reduced Ejection Fraction
iPSC = Induced Pluripotent Stem Cell
OLE = Open Label Extension
LDL-C = Low-Density Lipoprotein Cholesterol
LHD = Left Heart Disease
NT-proBNP = N-Terminal-pro hormone B-type Natriuretic Peptide
MTCVE = Major Thrombotic Cardiovascular Event
PAH = Pulmonary Arterial Hypertension
PAR-1 = Protease Activated Receptor
PDE5i = Phosphodiesterase 5 Inhibitor
PVR = Pulmonary Vascular Resistance
sGC = Soluble Guanylate Cyclase
sSBP = Systolic Systemic Blood Pressure
sPAP = Systolic Pulmonary Arterial Pressure
SU/Hx/Nx = Sugen/Hypoxia/Normoxia
SVR = Systemic Vascular Resistance
TGFβ = Transforming Growth Factor Beta
TTCW = Time to Clinical Worsening