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Novartis leading cardiovascular portfolio and capabilities

2015

Entresto®
sacubitril/valsartan

Essential first choice for chronic heart failure

~15m patients

2020

LEQVIO®
inclisiran

Potential to tackle LDL-C related ASCVD at scale

~60m patients

~2025

pelacarsen (TQJ230)

Potential to lower CV risk for people with elevated Lp(a)

High unmet need: CV disease leading cause of mortality

Strong worldwide commercial and scientific presence

Deep understanding of customer needs across primary and specialty care

Note: Dates refer to first launch for Entresto® and Leqvio®, to submission for pelacarsen.
Population numbers refer to US & EUS (Germany, France, Spain, Italy, UK). Source: Decision Resources Group.
Entresto®

David Soergel MD
Global Head of Cardiovascular, Renal and Metabolism Development

Rod Wooten
Global Head of Marketing
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Novartis | Reimagining Medicine
Entresto® development program across heart failure

**CHF disease continuum**

**HFrEF**
- Approved 2015
- Increased penetration potential – approx. 70% of HFrEF patients can still benefit
- Geographic expansion ongoing (e.g. China)

**HFpEF (US)**
- Label expanded 2021
- Covers HFpEF patients with ejection fraction below normal
- 5/6 HF patients covered by expanded CHF label

**Post-MI**
- Study completed
  (see subsequent slides)
- 800,000 MI events per year in US
- 1/3 patients expected to subsequently develop CHF

**Pediatric HF**
- Study readout 2022
- Potential to be first approved treatment

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**All pivotal studies with active comparator against standard of care**

HFrEF – Heart Failure with reduced Ejection Fraction  
HFpEF – Heart Failure with preserved Ejection Fraction  
CHF – Chronic Heart Failure  
MI – Myocardial Infarction  
HF – Heart Failure

1. Eligible patients defined as prevalent HFrEF patients within each market's label. G7 = US, CA, JP, DE, FR, IT, UK.  
PARADISE-MI a landmark trial in post acute MI patients

PARADISE-MI study design

Screen
Randomize between 12hrs up to 7 days after an AMI

Entresto® (titrate to 200 mg bid; dose adjustment permitted)
Ramipril (titrate to 5 mg bid; dose adjustment permitted)

Week 1 Week 2 Month 1 Month 2 Month 4 Month 8 Month 12 Month 16 Month 20

Patients
5,669 patients without prior history of heart failure

Primary objective
Demonstrate superior efficacy, time to first composite event

Primary composite endpoint
CV death, HF hospitalizations, outpatient HF visits

Secondary endpoints
- CV Death or HF hospitalization
- HF hospitalization or outpatient HF
- CV death, non-fatal MI or non-fatal stroke
- CV death and total hospitalizations for HF, MI or stroke
- All-cause death

Trial profile
Head-to-head superiority to ramipril, a current standard of care

High risk patient population with recent MI
In-hospital/early initiation in fragile patients

This information is based on preliminary study data analysis and contain information that has not been approved by the regulatory authorities. MI – Myocardial Infarction AMI – Acute Myocardial Infarction CV – Cardiovascular HF – Heart Failure. Note: primary endpoint not met.
Positive trend against a high bar, though primary endpoint not met (1/2)

Entresto® vs. ramipril

Ramipril
373 events, 7.4 per 100 pt-years

Entresto®
338 events, 6.7 per 100 pt-years

HR 0.90 (95% CI, 0.78-1.04)
p = 0.17

This information is based on preliminary study data analysis and contain information that has not been approved by the regulatory authorities. HR – Hazard Ratio  Source: Pfeffer, Angiotensin-Nephrilysin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
Positive trend against a high bar, though primary endpoint not met (2/2)

Mortality (%)

- Placebo
- ACE Inhibitor
  - Valsartan
  - Captopril
- Ramipril (242 deaths)
- Entresto® (213 deaths)

HR 0.88 (95% CI, 0.73-1.05)  
**p = 0.16**

This information is based on preliminary study data analysis and contains information that has not been approved by the regulatory authorities.  
ACE – Angiotensin Converting Enzyme  
HR – Hazard Ratio  
MI – Myocardial Infarction

Source: Pfeffer, Angiotensin-Nephrilysin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
The positive trend was consistent across all secondary endpoints

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, HF hospitalization, outpatient HF</td>
<td>0.88 (0.73-1.05)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary endpoints</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death or HF hospitalization</td>
<td>0.91 (0.78-1.07)</td>
</tr>
<tr>
<td>HF hospitalization or outpatient HF</td>
<td>0.84 (0.70-1.02)</td>
</tr>
<tr>
<td>CV death, MI or stroke</td>
<td>0.90 (0.77-1.05)</td>
</tr>
<tr>
<td>CV death and hospitalizations for HF, MI, stroke</td>
<td>0.84 (0.70-1.00)</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.88 (0.73-1.05)</td>
</tr>
</tbody>
</table>

This information is based on preliminary study data analysis and contains information that has not been approved by the regulatory authorities. CV – Cardiovascular, HF – Heart Failure, MI – Myocardial Infarction, HR – Hazard Ratio. Source: Pfeffer, Angiotensin-Nephrilysin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
Nominal significance in total recurrent adjusted primary events and investigator reported events (pre-specified)

**Total (first and recurrent) CEC adjudicated primary events**

- **Ramipril**: 539 events, 10.1 per 100 pt-years
- **Entresto®**: 452 events, 8.4 per 100 pt-years

RR* 0.79 (95% CI, 0.65-0.97)  
*p = 0.02

**Investigator reported primary endpoint**

- **Ramipril**: 516 events, 10.8 per 100 pt-years
- **Entresto®**: 443 events, 9.1 per 100 pt-years

HR 0.85 (95% CI, 0.75-0.96)  
*p = 0.01

This information is based on preliminary study data analysis and contain information that has not been approved by the regulatory authorities.  
*Rate ratio derived from negative binomial regression with Weibull baseline intensity function

CEC – Clinical Events Committee  
RR – Relative Risk  
HR – Hazard Ratio  
Source: Pfeffer, Angiotensin-Nepri.lysin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
Safety profile reassuring in this setting where treatment initiated early, in-hospital ...

<table>
<thead>
<tr>
<th>Adverse Events (%)</th>
<th>Entresto® N=2830</th>
<th>Ramipril N=2831</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>213 (8%)</td>
<td>242 (9%)</td>
</tr>
<tr>
<td>Angioedema (adjudicated)</td>
<td>14 (0.5%)</td>
<td>15 (0.5%)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>1145 (40%)</td>
<td>1126 (40%)</td>
</tr>
<tr>
<td>Adverse events</td>
<td>2351 (83%)</td>
<td>2325 (82%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>802 (28%)*</td>
<td>620 (22%)</td>
</tr>
<tr>
<td>Cough</td>
<td>255 (9%)*</td>
<td>371 (13%)</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>329 (12%)</td>
<td>326 (12%)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>301 (11%)</td>
<td>285 (10%)</td>
</tr>
<tr>
<td>Liver abnormalities</td>
<td>132 (5%)</td>
<td>167 (6%)</td>
</tr>
</tbody>
</table>

This information is based on preliminary study data analysis and contain information that has not been approved by the regulatory authorities. Note: balanced if not noted by *p<0.005. Source: Pfeffer, Angiotensin-Neprilysin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
... with fewer adverse event related discontinuations on Entresto®

<table>
<thead>
<tr>
<th>Reasons for treatment discontinuation</th>
<th>Entresto® N=2830, n (%)</th>
<th>Ramipril N=2831, n (%)</th>
<th>Total N=5661, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed</td>
<td>2210 (78.09)</td>
<td>2172 (76.72)</td>
<td>4382 (77.41)</td>
</tr>
<tr>
<td>Discontinued study treatment</td>
<td>610 (21.55)</td>
<td>644 (22.75)</td>
<td>1254 (22.15)</td>
</tr>
</tbody>
</table>

**Primary reason for discontinuation of study treatment**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Entresto®</th>
<th>Ramipril</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse events</td>
<td>356 (12.58)</td>
<td>379 (13.38)</td>
<td>735 (12.98)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>37 (1.31)</td>
<td>16 (0.57)</td>
<td>53 (0.94)</td>
</tr>
<tr>
<td>Cough</td>
<td>34 (1.20)</td>
<td>65 (2.30)</td>
<td>99 (1.75)</td>
</tr>
<tr>
<td>Renal impairment1</td>
<td>19 (0.67)</td>
<td>18 (0.64)</td>
<td>37 (1.31)</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>12 (0.42)</td>
<td>14 (0.49)</td>
<td>26 (0.46)</td>
</tr>
<tr>
<td>Death</td>
<td>109 (3.85)</td>
<td>127 (4.49)</td>
<td>236 (4.17)</td>
</tr>
<tr>
<td>Physician decision</td>
<td>50 (1.77)</td>
<td>55 (1.94)</td>
<td>105 (1.85)</td>
</tr>
<tr>
<td>Subject/guardian decision</td>
<td>236 (8.34)</td>
<td>219 (7.74)</td>
<td>455 (8.04)</td>
</tr>
<tr>
<td>Never received study treatment</td>
<td>10 (0.35)</td>
<td>15 (0.53)</td>
<td>25 (0.44)</td>
</tr>
</tbody>
</table>

This information is based on preliminary study data analysis and contain information that has not been approved by the regulatory authorities. 1. Renal impairment includes renal impairment, renal failure, acute kidney injury.

Source: Pfeffer, Angiotensin-Nephrin Inhibition Following Acute Myocardial Infarction: Primary Results of the PARADISE-MI Trial, presented at ACC (2021).
Entresto® comprehensive data across indications and treatment settings support first line use in chronic heart failure

<table>
<thead>
<tr>
<th>HFrEF</th>
<th>HFpEF</th>
<th>In-hospital management</th>
<th>Post-MI</th>
<th>Real-world evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARADIGM-HF</td>
<td>PARAGON-HF</td>
<td>TRANSITION de novo HF, ACEi/ARB naïve, AF, T2D, CKD</td>
<td>PARADISE-MI</td>
<td>ARIADNE</td>
</tr>
<tr>
<td>PROVE-HF, EVALUATE-HF</td>
<td>PARALLAX</td>
<td></td>
<td></td>
<td>EU treatment patterns</td>
</tr>
<tr>
<td>OUTSTEP-HF/ACTIVITY-HF</td>
<td>PIONEER-HF</td>
<td>NT-proBNP, symptoms, functional capacity, QoL</td>
<td>NT-proBNP</td>
<td>CHAMP-HF</td>
</tr>
<tr>
<td></td>
<td>PARAGLIDE</td>
<td>In-hospital initiation, NT-proBNP</td>
<td></td>
<td>US treatment patterns</td>
</tr>
</tbody>
</table>

Most comprehensive evidence of all HF therapies

Data from: >50,000 patients in clinical trials
>320,000 patients real world evidence (RWE)

- Improved mortality in HFrEF vs. conventional RAAS inhibition
- Safe and effective in broad population including ACEi/ARB naïve patients
- Easy and safe initiation in-hospital or immediately after discharge
- Diverse study population based on global study footprint
- Well characterized reversal of cardiac remodelling based on MoA
- Effectiveness and safety confirmed by large body of RWE in clinical practice
- Guideline support as SoC in HFrEF

**Entresto® could address hypertension in Asia, a remaining unmet need**

**Strong remaining unmet need in Asian population**
- Higher sodium intake with 1.6m related CV deaths³,⁴
- In China, only 15% of patients have controlled HTN⁵ vs. 52% in the US⁶

**Comprehensive trial program**
- 13 studies including ~7k patients across a broad population
- Regulatory review ongoing in Japan/China

**Entresto® superior to most potent ARB at the time with comparable safety¹**

**Entresto® superior at reducing BP at week 8²**
BP Change from baseline, mmHg

<table>
<thead>
<tr>
<th>Treatment</th>
<th>msSBP</th>
<th>msDBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olmesartan 20mg</td>
<td>-5.9</td>
<td>-2.9</td>
</tr>
<tr>
<td>Entresto® 200mg</td>
<td>-13.2</td>
<td>-7.8*</td>
</tr>
<tr>
<td>Entresto® 400mg</td>
<td>-18.2*</td>
<td>-8.8*</td>
</tr>
</tbody>
</table>

Robust antihypertensive effects over 24 hours

- *p<0.001 vs. olmesartan

ARO - Angiotensin II Receptor Blocker  
HTN – Hypertension  
BP – Blood Pressure  
msSBP – mean seated Systolic Blood Pressure  
msDBP – mean seated Diastolic Blood Pressure  
SBP – Systolic Blood Pressure  
AM – Ante Meridiem  
PM – Post Meridiem  
¹. Study 1306 (one of two pivotal ph3 studies; results confirmed by A2315 study).  
². Results consistent across secondary endpoints (msDBP, msPP 24 hr BP and responder rates).  
1 in 3 post-MI patients likely to develop heart failure and enter labeled population for Entresto®

~8m CHF patients in US & EU5 can benefit from Entresto® today¹,⁵

~1.5m MI events in US and EU5 annually²,³,⁵

<table>
<thead>
<tr>
<th></th>
<th>US</th>
<th>EU5⁵</th>
<th>China</th>
<th>RoW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>800k</td>
<td>630k</td>
<td>1.5m</td>
<td>4.4m</td>
</tr>
</tbody>
</table>

¹. Based on label covering rEF in EU and CHF below normal in US; 60% of HFrEF and 80% of HFpEF patients have heart failure due to causes other than MI.
⁵. EU5: Germany, France, Spain, Italy, UK.
Entresto® trajectory continues; guideline support and label expansion drive above-market momentum

Strong momentum in CHF
- ACC ECDP is supporting first-line use in HFrEF
- Adoption in HFpEF is gaining momentum in US²
  - Unaided awareness +25% (HFpEF)
  - Intent to prescribe +30% (HFpEF)
  - Increase of use by cardiologist +50% (CHF)

Confident in future growth globally
- ~30% of eligible HFrEF patients, ~15% of eligible US CHF patients currently treated³
- Expanded US label strengthens essential role of Entresto® across HF continuum
- PARADISE-MI reinforces safety in fragile hospitalized patients

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1. IQVIA National Prescription Audit 2. Physician ATU February to April 2021 3. Eligible patients defined as prevalent HFrEF patients within each market's label. G7 = US, CA, JP, DE, FR, IT, UK.
The ACC consensus (updated Jan 2021) recommends ARNI ahead of ACEi / ARBs for HFrEF

**Symptomatic HFrEF**

**ARNI preferred**

ACEi/ARB only in patients with contraindications, intolerability, or inaccessibility

AND evidence-based beta-blocker\(^1\) with diuretic agent as needed

- Persistent volume overload, NYHA II-IV → Titrate → Diuretic agent\(^2\)
- eGFR ≥30 mL/min/1.73 m\(^2\), creatinine ≤2.5 mg/dL in males ≤2.0 mg/dL in females, K\(^+\) ≤5.0 mEq/L, NYHA II-IV → Add → Aldosterone antagonist\(^2\)
- eGFR criteria, NYHA II-IV → Add → SGLT2i\(^2\)
- Persistently symptomatic black patients despite ARNI/beta-blocker/aldosterone antagonist/SGLT2i, NYHA II-IV → Add → Hydralazine + isosorbide dinitrate\(^2\)
- Resting HR ≥70, maximally tolerated beta-blocker in sinus rhythm, NYHA II-III → Add → Ivabradine\(^3\)

ACC – American College of Cardiology  
HFrEF – Heart Failure with reduced Ejection Fraction  
ARNI – Angiotensin Receptor Neprilysin Inhibitor  
ACEi – Angiotensin Converting Enzyme inhibitor  
ARB - Angiotensin II Receptor Blocker  
eGFR - estimated Glomerular Filtration Rate  
GDMT – Guideline-Directed Medical Therapy  
HR – Heart Rate  
NYHA – New York Heart Association  
SGLT2i – Sodium-Glucose Cotransporter-2 inhibitor  
1. Carvedilol, metoprolol succinate, or bisoprolol.  
2. Class I therapy from clinical practice guidelines.  
3. Class II therapy.  
Entresto® summary

Entresto® use supported by data / evidence from comprehensive and broad development program

PARADISE showed positive trend vs. comparator and confirmed safety profile in fragile population; 1 in 3 post-MI patients may enter label population and benefit from Entresto® over time

Strong in-market performance continues based on updated ACC consensus recommendations to use before ACE/ARB, and uptake in broader CHF population in US

Potential hypertension indication could accelerate momentum in select Asian markets
Leqvio®

David Soergel MD
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Matthew Whitty
CEO, Accelerated Access Collaborative, NHS
Despite availability of effective treatments, the burden of cardiovascular disease on health systems is on the rise.

CVD accounts for more deaths than any other disease¹

% of deaths

Global CVD costs to surpass 1 trillion p.a. by 2025¹

USD billion

<table>
<thead>
<tr>
<th>Year</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>863</td>
</tr>
<tr>
<td>2015</td>
<td>906</td>
</tr>
<tr>
<td>2020</td>
<td>957</td>
</tr>
<tr>
<td>2025</td>
<td>1,002</td>
</tr>
<tr>
<td>2030</td>
<td>1,044</td>
</tr>
</tbody>
</table>

18m lives lost globally to CVD²

After years of decline, number of lives lost is rising again³

Disease burden is driven by healthcare costs (55%) and productivity loss (45%)¹

~60m patients with ASCVD in US and EU5⁴


Note: The effect of Leqvio® on cardiovascular morbidity and mortality is currently being studied in the ongoing Phase III ORION-4 trial.

50 years of evidence demonstrate that effective and sustained LDL-C reduction improves cardiovascular outcomes*1,2

Each mmol/L reduction in LDL-C reduces the relative risk of ASCVD events by 20% after 3 years and 1.5% in each subsequent year3

Relationship between LDL-C and MACE is supported by clinical trials involving ~500k patients3,4

Relation between LDL-C and outcomes is well established

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**Log-linear association per unit change in LDL-C and the risk of cardiovascular disease**5

Guidelines recognize link between LDL-C and outcomes; LDL-C reduction targets becoming more ambitious

<table>
<thead>
<tr>
<th>AHA/ACC (2018)¹</th>
<th>ESC/EAS (2019)²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical ASCVD</strong></td>
<td><strong>High CV risk</strong></td>
</tr>
<tr>
<td><strong>Very high CVD risk</strong></td>
<td>LDL-C reduction to &lt;70 mg/dL (1.8 mmol/L)</td>
</tr>
<tr>
<td>LDL-C reduction by ≥50%</td>
<td>and</td>
</tr>
<tr>
<td>LDL-C reduction to &lt;70 mg/dL (1.8 mmol/L)</td>
<td>LDL-C reduction by ≥50%</td>
</tr>
</tbody>
</table>

In the real world, consistent and sustained LDL-C lowering is in many cases not achieved due to adherence, access, and affordability challenges.

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AHA – American Heart Association  
ACC – American College of Cardiology  
ESC – European Society of Cardiology  
EAS – European Atherosclerosis Society  
ASCVD – Atherosclerotic Cardiovascular Disease  
CVD – Cardiovascular Disease  
CV – Cardiovascular

3. The effect of Leqvo® on cardiovascular morbidity and mortality is currently being studied in the ongoing Phase III ORION-4 trial.
Leqvio® delivers an effective and sustained LDL-C reduction of up to 52%1,2

Leqvio® effected significant reductions in LDL-C vs. placebo at Day 510, on top of SoC. Range, -47.9% - 52.3%

1. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol
Kausik K. Ray, M.D., M.Phil., R. Scott Wright, M.D., David Kallend, M.D., Wolfgang Koenig, M.D., Lawrence A. Leiter, M.D., Frederick J. Raal, Ph.D., Jenna A. Bisch, B.A., Tara Richardson, B.A., Mark Jaros, Ph.D., Peter L.J. Wijngaard, Ph.D., and John J.P. Kastelein, M.D., Ph.D., for the ORION-10 and ORION-11 Investigators*; March 18, 2020, at NEJM.org.DOI: 10.1056/NEJMoa1912387. 2. Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia
Frederick J. Raal, M.D., Ph.D., David Kallend, M.B., B.S., Kausik K. Ray, M.D., M.Phil., Traci Turner, M.D., Wolfgang Koenig, M.D., R. Scott Wright, M.D., Peter L.J. Wijngaard, Ph.D., Danielle Curcio, M.B.A., Mark J. Jaros, Ph.D., Lawrence A. Leiter, M.D., and John J.P. Kastelein, M.D., Ph.D., for the ORION-9 Investigators*; March 18, 2020, at NEJM.org.DOI: 10.1056/NEJMoa1913805. 3. Across the 6-month dosing interval. Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Leqvio® well tolerated safety profile

- No significant safety or tolerability concerns identified with the long-term administration of Leqvio®
- Most common adverse events occurred with similar frequency in Leqvio® and placebo groups
- Adverse events associated with Leqvio® include injection site reactions, all mild or moderate in severity, transient and resolved without sequelae

<table>
<thead>
<tr>
<th>Safety population</th>
<th>Leqvio® (n=241)</th>
<th>Placebo (n=240)</th>
<th>Leqvio® (n=781)</th>
<th>Placebo (n=778)</th>
<th>Leqvio® (n=811)</th>
<th>Placebo (n=804)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with at least one serious TEAE</td>
<td>18</td>
<td>7.5%</td>
<td>33</td>
<td>13.8%</td>
<td>175</td>
<td>22.4%</td>
</tr>
<tr>
<td>Pre-specified exploratory CV endpoint (MedDRA basket)</td>
<td>10</td>
<td>4.1%</td>
<td>10</td>
<td>4.2%</td>
<td>58</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
In the US, Leqvio® positioned to meet the needs of 80% of statin-treated ASCVD patients who are not at LDL-C goal

US ASCVD patient population

- Diagnosed
- Statin treated
- At LDL-C goal
- Non-statin therapy

Factors driving unmet need

- A1: Adherence
- A2: Access
- A3: Affordability

Leqvio® has the potential to offer:

- Effective and sustained LDL-C reduction with two doses a year
- Medical benefit reimbursement
- Reduced affordability challenges

ASCVD – Atherosclerotic Cardiovascular Disease
LDL-C – Low Density Lipoprotein Cholesterol
2. <70mg/dL
3. Non-statin lipid lowering therapies include ezetimibe and PCSK9 mAbs.
4. After an initial dose, again at 3 months, and again every six months thereafter.
5. Across the 6-month dosing interval. Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Adherence – real-world challenges compromise outcomes

Statin adherence in secondary prevention

- Not adherent: 25%
- Adherent: 75%

Non-adherent PCSK9i patient share

- 12 months: 54%
- 24 months: 76%

Sustained lipid lowering reduces CV risk

MACE according to adherence categories in secondary prevention

- PDC <40%
- PDC 40%-79%
- PDC ≥80%

Log-Rank P-value=.0002

CV – Cardiovascular  MACE – Major Adverse Cardiovascular Event  PCSK9i – Proprotein convertase subtilisin/kexin type 9 inhibitor  PDC – Percent Days Covered  Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Adherence – Leqvio® has the potential to address adherence challenges

Effective and sustained\(^4\) LDL-C reduction\(^{1,3}\)

<table>
<thead>
<tr>
<th>Days</th>
<th>No. of patients</th>
<th>Percentage change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Placebo 780</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>Inclisiran 781</td>
<td>20</td>
</tr>
<tr>
<td>90</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>150</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>270</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>330</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>4505</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>540</td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>

**ORION-10**

Percentage change in LDL cholesterol

- Placebo
- Inclisiran

Twice-yearly dosing\(^{1,2}\)

Dosing scheme\(^3\)

May integrate seamlessly into a patient’s health care routine

HCP administered

No patient education on administration required

L’LDL-C – Low Density Lipoprotein Cholesterol  
HCP – Healthcare Professional

2. After an initial dose, again at 3 months, and again every six months thereafter. As a strong complement to a maximally tolerated statin.  
3. LDL-C reduction was maintained during each 6-month dosing interval.  
4. Across the 6-month dosing interval.  

Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
# Access – majority of Leqvio® patients will be covered by medical benefit, reducing access hurdles

<table>
<thead>
<tr>
<th>Patient benefit</th>
<th>Part B FFS (39%)</th>
<th>Medicare Advantage (19%)</th>
<th>Commercial (34%)</th>
<th>PCSK9i mAbs Pharmacy benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration</td>
<td>HCP-administered</td>
<td></td>
<td></td>
<td>Self-administered</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Buy-and-bill</td>
<td>Buy-and-bill, specialty pharmacy</td>
<td>Buy-and-bill, specialty pharmacy</td>
<td>Specialty or retail pharmacy</td>
</tr>
<tr>
<td>Access restrictions (step edits, prior authorizations)</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Reimbursement of administrative effort</td>
<td>Efforts reimbursed (medical benefit)</td>
<td>Efforts not reimbursed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CV outcomes evidence as driver of access decisions</td>
<td>Access mirrors FDA label</td>
<td>Focus on efficacy, safety, cost</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>More favorable</th>
<th>Less favorable</th>
</tr>
</thead>
</table>

CV – Cardiovascular  FFS – Fee For Service  HCP – Healthcare Professional  PCSK9i – Proprotein convertase subtilisin/kexin type 9 inhibitor  mAbs – monoclonal Antibodies  FDA – Food and Drug Administration  Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Affordability – medical benefit coverage for Leqvio® creates opportunity for 0 USD co-pay for 2/3 patients at launch

**PCSK9i abandonment rate by OOP cost**

<table>
<thead>
<tr>
<th>Co-pay (USD)</th>
<th>% of Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9%</td>
</tr>
<tr>
<td>40-50</td>
<td>22%</td>
</tr>
<tr>
<td>75-125</td>
<td>41%</td>
</tr>
<tr>
<td>250-500</td>
<td>66%</td>
</tr>
</tbody>
</table>

**Anticipated payer mix and co-pay for Leqvio® at launch**

- **Medicare Part B**
  - % of eligible population: 39%
  - Anticipated co-pay: 80% pay as little as 0 USD
- **Medicare Advantage**
  - % of eligible population: 19%
  - Anticipated co-pay: Varies; 0-20% co-insurance
- **Commercial**
  - % of eligible population: 34%
  - Anticipated co-pay: Eligible patients pay as little as 0 USD
- **Other (Medicaid, federal)**
  - % of eligible population: 8%
  - Anticipated co-pay: <10 USD

PCSK9i – Proprotein convertase subtilisin/kexin type 9 inhibitor  
OOP – Out Of Pocket  
Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
To comprehensively manage non-clinical barriers, our US launch focuses on partnering with health systems

**Health systems as primary customer**
- Buy-and-bill infrastructure implemented
- Centralized prescribing influence
- Centralized EHR enables patient identification
- Established processes for product adoption

45% of target customers currently prioritize ASCVD

**Majority of US cardiologists employed by health systems**

- Health system
- Independent

<table>
<thead>
<tr>
<th>Year</th>
<th>Health system</th>
<th>Independent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>2010</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>2012</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>2014</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>2016</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>2018</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

84% of cardiologists employed by health systems

**~200 systems represent 2/3 of prescription volume**

- Health systems: 200
- ASCVD diagnosis and prescription volume: 35%

EHR – Electronic Health Record  
ASCVD – Atherosclerotic Cardiovascular Disease  
2. Xponent Plan Trak (October 2019).  
3. IQVIA Rx Claims (August 2019).  
Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Account teams focused on identifying unmet needs within systems and enhancing the customer experience

System of care account example

**ASCVD population**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ASCVD</td>
<td>128,147</td>
</tr>
<tr>
<td>LDL-C &gt;130</td>
<td>24,348</td>
</tr>
<tr>
<td>LDL-C 100-130</td>
<td>14,096</td>
</tr>
<tr>
<td>LDL-C 70-100</td>
<td>49,977</td>
</tr>
<tr>
<td>LDL-C &lt;70</td>
<td>39,726</td>
</tr>
</tbody>
</table>

**Payer mix**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial</td>
<td>53%</td>
</tr>
<tr>
<td>Medicare Part B FFS</td>
<td>30%</td>
</tr>
<tr>
<td>Medicare Advantage</td>
<td>10%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>7%</td>
</tr>
</tbody>
</table>

**Prescriber concentration**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of facilities</td>
<td>286</td>
<td>80%</td>
</tr>
<tr>
<td>% ASCVD prescriptions</td>
<td>113</td>
<td>20%</td>
</tr>
</tbody>
</table>

**Account overview**

- Highly integrated IDN
- 23 hospitals, 1 dedicated lipid center, 7 advanced cardiac hospitals
- 40 owned cardiology groups
- >10,000 affiliated HCPs
- 800 outpatient sites
- 10 outpatient infusion centers
- Own specialty pharmacy

IDN – Integrated Delivery Network LDL-C – Low Density Lipoprotein Cholesterol HCP – Healthcare Professional FFS – Fee For Service ASCVD – Atherosclerotic Cardiovascular Disease Source: Data on file. Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
Leqvio® has the potential to become the leading choice for ASCVD patients\(^3\) by providing effective and sustained\(^4\) LDL-C reduction

Leqvio® is uniquely positioned to address unmet needs in ASCVD

**A1** Adherence

Effective and sustained\(^4\) LDL-C reduction with **two doses per year,**\(^*\) generally well-tolerated\(^1,2\)

**A2** Access

**Medical benefit coverage** for majority of patients at launch

**A3** Affordability

**0 USD co-pay** for 2/3 patients at launch

Novartis is pursuing a customer-centric go-to-market model to address non-clinical barriers to adoption

Focused on ~200 prioritized health systems at launch

Developing a robust alternate injection center network to provide acquisition & administration flexibility

Deploying a best-in-class field team to help systems and HCPs navigate early reimbursement complexity

45% of field access & reimbursement team with 5+ years of buy-and-bill experience

ASCVD – Atherosclerotic Cardiovascular Disease  
LDL-C – Low Density Lipoprotein Cholesterol  
HCP – Healthcare Professional  
*After an initial dose, again at 3 months, and again every six months thereafter.  
3. On maximally tolerated statins.  
4. Across the 6-month dosing interval.  
Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.
The Accelerated Access Collaborative

Objectives

• The Accelerated Access Collaborative brings together industry, government, regulators, patients and the NHS to remove barriers and accelerate the introduction of ground-breaking innovations which can transform care

• Innovations include medicines, diagnostics, devices and digital products

• Our work supports the NHS to more quickly adopt clinically and cost-effective innovations, to ensure patients get access to the best new treatments and technologies

Partners

This slide has been created by the Accelerated Access Collaborative of NHS England. AMRC – Association of Medical Research Charities BIA – UK Biolndustry Association BIVDA – British In Vitro Diagnostic Association NHS – National Health Service ABHI – Association of British HealthTech Industries ABPI – Association of the British Pharmaceutical Industry AHSN – Academic Health and Science Network
In the UK, the NHS and Novartis are partnering on a population health approach to impact CVD at scale

The population-level agreement aims lower LDL-C by ~50% in a high-risk population of people with cardiovascular disease, supporting the Long Term Plan (LTP) ambition of preventing 150,000 heart attacks, strokes and dementia cases over the next 10 years.

To achieve this the implementation is focused in three areas:

<table>
<thead>
<tr>
<th>Primary Care Mobilisation</th>
<th>Patient Identification</th>
<th>Stakeholder Engagement &amp; Consultation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A co-created integrated care system-based strategy led by the AAC. A combination of specialist knowledge in lipid management with an oversight of the local population needs forming the basis of a PHM service pathway focused on achieving an at-scale, primary care-based, secondary prevention programme in CVD; including access to Inclisiran for ~300,000 patients by 2024</td>
<td>Collaboration with NHS Digital, working with GP software &amp; systems provides, that enables the use of data to easily identify and manage the ‘at risk’ populations within primary care networks of 30,000-50,000 people</td>
<td>Transferring responsibility to a primary care-based population approach requires full system support. A co-created comprehensive stakeholder engagement and consultation strategy, spanning across all parts of the health care system, to support with development and implementation of the integrated care system-based strategy primary care by the AHSNs</td>
</tr>
</tbody>
</table>

This slide has been created by the Accelerated Access Collaborative of NHS England. ASCVD – Atherosclerotic Cardiovascular Disease  LDL-C – Low Density Lipoprotein Cholesterol  AAC – Accelerated Access Collaborative  NHS – National Health Service  GP – General Practitioner  AHSN – Academic Health and Science Network
Focus by the NHS and Novartis collaboration will have a major impact on CV deaths and health inequalities in the UK

- The programme breaks from a traditional approach and aims to ‘level up’ cholesterol services ensuring access to the full eligible population
- Co creation with the AAC and AHSN of shared patient uptake targets with a consideration for improving health inequalities in CVD
- Mutually agreed KPIs for each of the AHSN’s for the adoption and uptake of Inclisiran, monitored throughout implementation

This slide has been created by the Accelerated Access Collaborative of NHS England.  
KPI – Key Performance Indicator  DOAC/ NDAC – Direct/ Novel Oral Anticoagulants  
NHS – National Health Service  CV – Cardiovascular  AAC – Accelerated Access Collaborative  
AHSN – Academic Health and Science Network  CHD – Cardiovascular Heart Disease
### Implementation of NHS-Novartis collaboration is geared to impact CV outcomes at scale

<table>
<thead>
<tr>
<th>Objective setting</th>
<th>HCP education</th>
<th>Patient identification</th>
<th>Adherence support</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NHS and Novartis mutually agreed draft commercial agreement fully aligned to national CVD &amp; PHM goals</td>
<td>• Novartis &amp; NHSE joint education programme aimed at primary care HCPs: ‘Cholesterol Now’</td>
<td>• Collaboration with NHS Digital to create a national ASCVD patient identification and stratification tool directly integrated into primary care GP systems</td>
<td>• NHS Digital collaboration includes system prompts for patient recall for all patients that have been initiated on inclisiran</td>
</tr>
<tr>
<td>• Implementation of ASCVD secondary prevention programme by the NHS through the AHSNs</td>
<td>• Comprehensive NHS driven communications programme; including internal NHS ‘Townhall’ meetings and external events</td>
<td>• Approach allows for proactive and reactive patient identification and inclisiran initiation</td>
<td>• The approach builds on the strengths that the NHS have used for patient recall in other national programmes, e.g. Breast screening, Flu vaccine, etc.</td>
</tr>
<tr>
<td>• Patient uptake trajectories and tracking KPIs to be agreed with all AHSNs</td>
<td>• Full repository of materials available via NHS channels to support inclisiran initiation &amp; management</td>
<td>• Implementation toolkits per geography; including targeted roll-out approach</td>
<td></td>
</tr>
</tbody>
</table>

---

This slide has been created by the Accelerated Access Collaborative of NHS England. NHS – National Health Service AHSN – Academic Health and Science Network  
CV – Cardiovascular  
ASCVD – Atherosclerotic Cardiovascular Disease  
GP – General Practitioner
Robust clinical trial program to support Leqvio®

- **Current submissions** supported by completed ORION-9/10/11 trials
  - US planned Q2-Q3 2021
- **CV outcomes** expected 2026
- **Phase 3b/4** studies to support access and drive demand
  - Bridging implementation gaps
  - Expanding on benefit/risk profile and selected patient populations
- **Primary prevention** program to be announced H2/2021

*Expected timelines  LDL-C – Low Density Lipoprotein Cholesterol*
Burden of Atherosclerotic Cardiovascular Disease (ASCVD) rising, despite effective treatments

Link between LDL-C reduction and outcomes firmly established\(^1\); **suboptimal outcomes in real world** setting mainly due **adherence, access and affordability** challenges (non-clinical barriers)

US launch focuses on **partnering with health systems** to manage non-clinical barriers

In UK, **NHS and Novartis are partnering on a population health** approach to impact CVD at scale
Pelacarsen (TQJ230)

David Soergel MD
Global Head of Cardiovascular, Renal and Metabolism Development

Rod Wooten
Global Head of Marketing
Novartis Pharmaceuticals
**Lp(a) is an independent risk factor for ASCVD** that cannot currently be treated

Lp(a) is an **independent, inherited and causal risk factor** for CVD, with elevated Lp(a) mediating MI, stroke, and PAD.

Lp(a) consists of an **LDL-like particle** which is covalently bound to apo(a).

Lp(a) levels are primarily **genetically determined** and not influenced by diet or exercise.

There are currently **no approved therapies** to treat elevated Lp(a).

---

**ASCVD** — Atherosclerotic Cardiovascular Disease  
Lp(a) — Lipoprotein a  
CVD — Cardiovascular Disease  
LDL — Low Density Lipoprotein  
MI — Myocardial Infarction  
PAD — Peripheral Artery Disease  
Apo(a) — Apolipoprotein (a)  
ApoB-100 — Apolipoprotein B-100  
KIV — Kringle IV  
Lp(a) figure adapted from Tsimikas S. J Am Coll Cardiol 2017;69:692–711.  
1. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials.  
Note: pelacarsen is an investigational product.
Elevated Lp(a) increases cardiovascular risk\(^5\) ~2-fold, a level similar to LDL-C

Lp(a) is an independent, genetic and causal risk factor for MI, stroke and PAD\(^1,2,3\)

Emerging Risk Factors Collaboration
Individual records of 126,634 participants in 36 long-term, prospective epidemiological studies

Elevated Lp(a) increases risk for CV-events ~2-fold\(^1,3,4\)

Emerging Risk Factors Collaboration
Individual records of 126,634 participants in 36 long-term, prospective epidemiological studies

---

CI – Confidence Interval   CV – Cardiovascular   KIV – Kringle IV   Lp(a) – Lipoprotein(a)

The correlation between Lp(a) and LDL-C is weak, thus separate treatment approaches are required

In the US, Lp(a) is elevated in more than 25% of patients with ASCVD

However, Lp(a) is rarely measured (0.4%) in routine clinical practice

The weak association of Lp(a) and LDL-C suggests it is not possible to impute Lp(a) levels by measuring LDL-C

Reinforces need for separate Lp(a) testing in ASCVD patients as part of the CV risk profile assessment

Pearson correlation coefficient between Lp(a) and LDL-C: 0.065 (p<0.0001)

LP(a) – Lipoprotein a  LDL-C – Low Density Lipoprotein Cholesterol  ASCVD – Atherosclerotic Cardiovascular Disease  CV – Cardiovascular  Source: Lahoz  Lp(a) distribution and correlation with LDL-C in patients with atherosclerotic cardiovascular disease (ASCVD) in the US.  1. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials.  Note: pelacarsen is an investigational product.
In Phase 2b, pelacarsen significantly reduced Lp(a) in CVD patients

Ph2b results – pelacarsen vs. placebo
NEJM Tsimikas, et al. 2020

Ph2b data showed:

- Lp(a) levels were reduced to ≤50mg/dL in 98% of CVD patients following treatment with pelacarsen 20mg once a week
- Dose-dependent Lp(a) reductions up to 80%
- Good tolerability and safety profile

80mg monthly is being evaluated in Ph3

P-values represent comparison to pooled placebo

Prevalence study and Ph3 outcome study ongoing with expected readouts in 2021 and 2024

**Prevalence study**

- Study to evaluate prevalence of elevated Lp(a) levels in patients with established CVD
- ~45,000 patients, > 900 sites in 48 countries
- Study initiated April 2019
- Study results expected 2021

**Phase 3 outcome study**

- CV outcome trial to assess effect of pelacarsen on MACE in patients with established CV disease and elevated Lp(a) on optimal therapy for other risk factors\(^1\)
- Pioneering trial to evaluate impact of Lp(a) lowering on CV outcomes
- Study initiated December 2019
- Primary outcome: 2024

---

Elevated Lp(a) is highly prevalent and one of the strongest genetic CVD risk factors\textsuperscript{1-6}

1 in 5 people worldwide have elevated Lp(a)*\textsuperscript{1,2}

- 1.4 billion people have elevated Lp(a)*, increasing their ASCVD risk\textsuperscript{1,2}
- Lp(a) is both the most common monogenic CVD risk factor and one of the strongest genetic CVD risk factors\textsuperscript{2-5}

The prevalence of elevated Lp(a)* varies by geography

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>20%</td>
<td>73m</td>
</tr>
<tr>
<td>Latin America</td>
<td>15%</td>
<td>97m</td>
</tr>
<tr>
<td>Europe</td>
<td>20%</td>
<td>148m</td>
</tr>
<tr>
<td>Asia</td>
<td>10%</td>
<td>261m</td>
</tr>
<tr>
<td>S. Asia</td>
<td>25%</td>
<td>469m</td>
</tr>
<tr>
<td>Oceania</td>
<td>20%</td>
<td>8m</td>
</tr>
<tr>
<td>Africa</td>
<td>30%</td>
<td>376m</td>
</tr>
</tbody>
</table>

*Lp(a) >50 mg/dL or >125 nmol/L

6. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials. Note: pelacarsen is an investigational product.
Awareness of Lp(a) and testing are low among ASCVD patients

Unaided awareness of Lp(a) as CV risk factor (%)

- Specialists: 12%
- GPs: 2%

Perceived relative importance of CV risk factors (%)

- LDL-C: 61%
- Diabetes: 61%
- Smoking: 54%
- HTN: 35%
- Obesity: 20%
- Lp(a): 17%
- Age: 17%

Share of ASCVD patients tested for Lp(a) in US

- Not tested: >99%
- Tested: <1%

Source: Physician ATU report (2020)
Need to test for Lp(a) is growing in clinical guidelines

NLA

- **Lp(a) screening**: All adults with personal or family history of premature ASCVD, severe hypercholesterolemia, suspected FH
- **Lp(a) threshold**: >50 mg/dL (>100 nmol/L) for ASCVD
- **Treatment**: Consider intensification of treatment of LDL and other risk factors

ESC/ EAS

- **Lp(a) screening**: All adults once in a lifetime
- **Lp(a) threshold**: None for ASCVD. Primary prevention patients with >180 mg/dL (>430 nmol/L) CV risk equivalent to HeFH
- **Treatment**: Consider intensification of treatment of LDL and other risk factors

Note. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials.
Pelacarsen is an investigational product.

Synergies with Leqvio® and Entresto® commercially

Synergy at the customer level, building on existing strong presence

Cardiologists, endocrinologists, lipid specialists and PCPs who manage LDL-C also expected to treat Lp(a)

Leqvio® medical teams can provide education on Lp(a) early on

Leqvio® commercial teams can generate health system insights on comprehensive ASCVD management

Ongoing close dialogue with medical societies issuing CV guidelines

There is overlap in patients as well as a unique pool for pelacarsen

Like the overall ASCVD population, ~50% of Lp(a) patients have LDL>100 mg/dL

Note: pelacarsen is an investigational product. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials.
Pelacarsen summary

Lp(a) is a causal, **independent risk factor** for ASCVD

Currently, **no specific pharmacologic treatments**, but access to Lp(a) levels can guide HCPs to optimize the management of other risk factors

Awareness of Lp(a) is low and the **rate of testing is low** among ASCVD patients

In Phase 2b, **pelacarsen significantly reduced Lp(a) in CVD patients**

Potentially **commercial synergies** with Leqvio® and Entresto®
## Novartis leading cardiovascular portfolio and capabilities

<table>
<thead>
<tr>
<th>2015</th>
<th>2020</th>
<th>~2025</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Entresto" /> sacubitril/valsartan</td>
<td><img src="image" alt="LEQVIO" /> inclisiran</td>
<td>Pelacarsen (TQJ230)</td>
</tr>
</tbody>
</table>

- **Essential first choice for chronic heart failure**
- **Potential to tackle LDL-C related ASCVD at scale**
- **Potential to lower CV risk for people with elevated Lp(a)**

- ~15m patients
- ~60m patients

- **High unmet need: CV disease leading cause of mortality**
- **Strong worldwide commercial and scientific presence**
- **Deep understanding of customer needs across primary and specialty care**

LDL-C – Low Density Lipoprotein Cholesterol
ASCVD – Atherosclerotic Cardiovascular Disease
CV – Cardiovascular
Lp(a) – Lipoprotein(a)

Note: Dates refer to first launch for Entresto® and Leqvio®, to submission for pelacarsen.
Population numbers refer to US & EUS (Germany, France, Spain, Italy, UK). Source: Decision Resources Group.
Q&A session

David Soergel MD
Global Head of Cardiovascular, Renal and Metabolism Development

Rod Wooten
Global Head of Marketing
Novartis Pharmaceuticals

Victor Bulto
Head of Novartis
Pharmaceuticals US

Matthew Whitty
CEO, NHS Accelerated Access Collaborative

Samir Shah MD
Global Head of Investor Relations
Appendix
# Cardio, Renal, Metabolism pipeline

## Phase 1

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Mechanism</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBL949</td>
<td>MBL949</td>
<td>-</td>
<td>Obesity related diseases</td>
</tr>
</tbody>
</table>

## Phase 2

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Mechanism</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFZ533</td>
<td>iscalimab</td>
<td>CD40 inhibitor</td>
<td>Lupus nephritis, T1DM</td>
</tr>
<tr>
<td>HSY244</td>
<td>HSY244</td>
<td>-</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>LMB763</td>
<td>nidufexor</td>
<td>FXR agonist</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>LNP023</td>
<td>iptacopan</td>
<td>CFB inhibitor</td>
<td>C3G, iMN, aHUS</td>
</tr>
</tbody>
</table>

## Phase 3

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Mechanism</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KJX839</td>
<td>Leqvio®</td>
<td>siRNA (regulation of LDL-C)</td>
<td>CVRR-LDLC, Ped Hyperlipidemia</td>
</tr>
<tr>
<td>LCZ696</td>
<td>Entresto®</td>
<td>Angiotensin receptor/neprilysin inhibitor</td>
<td>Post-AMI, Pediatric CHF³)</td>
</tr>
<tr>
<td>LNP023</td>
<td>Iptacopan</td>
<td>CFB inhibitor</td>
<td>PNH, IgAN</td>
</tr>
<tr>
<td>TQJ230</td>
<td>Pelacarsen</td>
<td>ASO targeting Lp(a)</td>
<td>CVRR-Lp(a)</td>
</tr>
</tbody>
</table>

## In registration

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Mechanism</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KJX839</td>
<td>Leqvio®</td>
<td>siRNA (regulation of LDL-C)</td>
<td>Hyperlipidemia</td>
</tr>
</tbody>
</table>