Atherosclerotic Cardiovascular Risk Assessment in a 24-Week, Randomized, Double-Blind, Placebo-Controlled Study of Aldafermin

- Aldafermin (NGM282) is an engineered FGF19 analogue that inhibits bile acid synthesis and regulates metabolic homeostasis ¹
- In a 24-week, randomized, double-blind, placebo-controlled study in NASH patients with serial liver biopsies, aldafermin treatment resulted in liver fat reduction, fibrosis improvement and NASH resolution ²
- Here we report results on cardiovascular risk assessment and key lipoproteins implicated in atherosclerosis from this study

Population:
NASH, F2 or F3, NAS ≥4, MRI-PDFF ≥8%

Lipid management:
As pre-specified in the protocol, subjects were to start with rosuvastatin if statin naïve or switch to rosuvastatin if already on statin therapy, to treat LDL-C elevations of >10 mg/dL from baseline ³

**Table**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>Placebo (n=25)</td>
</tr>
<tr>
<td>Aldafermin 1 mg (n=53)</td>
<td></td>
</tr>
</tbody>
</table>

Gunn et al., Abstract 1082 (EASL 2021)

¹DePaoli et al., Diabetes 2019;68:1315-1328; ²Harrison et al., Gastroenterology 2021;160:219-231; ³Gunn, AASLD 2020
10-Year ASCVD Risk Score Was Reduced in the Aldafermin Group Compared to Placebo at Week 24

### 10-Year ASCVD Risk Score

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>W24</th>
<th>Mean ASCVD Score (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>11.6</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>Aldafermin</td>
<td>15</td>
<td>11.8</td>
<td></td>
</tr>
</tbody>
</table>

P=0.72

### Change in 10-Year ASCVD Risk Score

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>W24</th>
<th>Mean Change in ASCVD Score from Baseline at Week 24 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td>-1.2</td>
</tr>
<tr>
<td>Aldafermin</td>
<td></td>
<td></td>
<td>-3.4</td>
</tr>
</tbody>
</table>

P=0.032

NGM Bio

Both Triglyceride Content and Cholesterol Content in the TRLs Were Lower in the Aldafermin Group versus Placebo at Week 24

**TRL Triglyceride Content**

- **Placebo** (n=25): Baseline TRLTG (mg/dL) 118.8 (115.5)
- **Aldafermin** (n=52): Baseline TRLTG (mg/dL) 127.4 (67.6)

Percent Change in TRLTG From Baseline at Week 24:

- Placebo: -15.5
- Aldafermin: -27.4

**TRL Cholesterol Content**

- **Placebo** (n=25): Baseline TRLC (mg/dL) 33.7 (22.6)
- **Aldafermin** (n=52): Baseline TRLC (mg/dL) 34.5 (14.0)

Percent Change in TRLC From Baseline at Week 24:

- Placebo: -7.5
- Aldafermin: -17.1

Source: Gunn et al., Abstract 1082 (EASL 2021)

TRL, triglyceride-rich lipoproteins; TRLTG, TRL triglyceride content; TRLC, TRL cholesterol content
Reduction of the Pro-Atherogenic Lipoprotein ApoB and Increase of the Anti-Atherogenic Lipoprotein ApoA1 in the Aldafermin Group

**Apo B**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=25)</th>
<th>Aldafermin (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ApoB (mg/dL)</td>
<td>86.0 (23.8)</td>
<td>88.1 (20.4)</td>
</tr>
</tbody>
</table>

Percent Change in ApoB From Baseline at Week 24:

- Placebo: -5.6% (P=0.13)
- Aldafermin: -11% (P=0.002)

**Apo A1**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=25)</th>
<th>Aldafermin (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline ApoA1 (mg/dL)</td>
<td>139.3 (25.0)</td>
<td>136.7 (23.0)</td>
</tr>
</tbody>
</table>

Percent Change in ApoA1 From Baseline at Week 24:

- Placebo: 1.1% (P=0.70)
- Aldafermin: 5.5% (P=0.037)

P vs baseline
Conclusion

• Aldafermin-associated cholesterol increase can be safely managed with a statin

• At the end of treatment, a greater reduction in the 10-year ASCVD risk score was achieved in the aldafermin group compared with placebo

• Patients in the aldafermin group had lower triglyceride and cholesterol content in TRL, lower levels of pro-atherogenic lipoprotein ApoB, and higher levels of the anti-atherogenic lipoprotein ApoA1 at week 24

• Patients in the aldafermin group, but not the placebo group, had reductions from baseline in lipoprotein insulin resistance index at week 24

• In this study in patients with NASH and fibrosis, an overall favorable cardiovascular risk profile was achieved in the aldafermin arm

Acknowledgment

• We thank all of the patients who participated in this study, and the investigators, study coordinators and staff for their support