SUPPLEMENTAL MATERIAL

A Pooled Safety Analysis of Evolocumab in Over 6000 Patients from Double-blind and Open-label Extension Studies

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Table 1. Reasons for Non-enrollment in Open-label Extension Studies

<table>
<thead>
<tr>
<th>Reason</th>
<th>Any Control (N=588)</th>
<th>Any Evolocumab (N=973)</th>
<th>Total (N=1561)</th>
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<tbody>
<tr>
<td>Ended study drug early</td>
<td>110 (18.7)</td>
<td>192 (19.7)</td>
<td>302 (19.3)</td>
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<tr>
<td>Administrative decision</td>
<td>1 (0.2)</td>
<td>7 (0.7)</td>
<td>8 (0.5)</td>
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<tr>
<td>Adverse event</td>
<td>35 (6.0)</td>
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<td>92 (5.9)</td>
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<td>Death</td>
<td>0</td>
<td>2 (0.2)</td>
<td>2 (0.1)</td>
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<tr>
<td>Full consent withdrawn</td>
<td>10 (1.7)</td>
<td>12 (1.2)</td>
<td>22 (1.4)</td>
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<tr>
<td>Lost to follow-up</td>
<td>8 (1.4)</td>
<td>17 (1.7)</td>
<td>25 (1.6)</td>
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<td>Other</td>
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<td>Physician decision</td>
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<td>Death</td>
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<td>Full consent withdrawn</td>
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<td>6 (0.6)</td>
<td>6 (0.4)</td>
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<tr>
<td>Did not end study early, and reported intention to roll-over but did not roll over</td>
<td>121 (20.6)</td>
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<td>348 (22.3)</td>
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<td>882 (56.5)</td>
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<td>Due to level of commitment</td>
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<td>169 (17.4)</td>
<td>264 (16.9)</td>
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<tr>
<td>Due to parent experience</td>
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<td>30 (3.1)</td>
<td>61 (3.9)</td>
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<tr>
<td>Due to personal reasons</td>
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<td>332 (34.1)</td>
<td>557 (35.7)</td>
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<td>Did not end study early, and unknown intention to roll over</td>
<td>4 (0.7)</td>
<td>16 (1.6)</td>
<td>20 (1.3)</td>
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Table 2. Baseline Characteristics According to Lowest LDL-C Level Achieved

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<tr>
<th>Characteristic</th>
<th>Lowest LDL-C Achieved and Treatment Group</th>
<th>&lt;25 mg/dL</th>
<th>≥25 mg/dL and &lt;40 mg/dL</th>
<th>All Patients With &lt;40 mg/dL</th>
<th>≥40 mg/dL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All Patients With &lt;40 mg/dL</td>
<td>Any Evolocumab N = 1609</td>
<td>Any Evolocumab N = 956</td>
<td>Any Evolocumab N = 2565</td>
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<tr>
<td>Initial Parent Trials*</td>
<td></td>
<td>≥40 mg/dL and &lt;40 mg/dL</td>
<td>N = 1609</td>
<td>N = 956</td>
<td>N = 2565</td>
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<tr>
<td>Age, yr, mean (SD)</td>
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<td>Initial parent trials</td>
<td>58.5 (10.3)</td>
<td>57.8 (11.6)</td>
<td>58.2 (10.8)</td>
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<td>58.9 (10.4)</td>
<td>58.5 (10.1)</td>
<td>58.7 (10.3)</td>
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<td>Male sex, n (%)</td>
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<td>Initial parent trials</td>
<td>953 (59.2)</td>
<td>455 (47.6)</td>
<td>1408 (54.9)</td>
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<td></td>
<td>OLE</td>
<td>500 (64.7)</td>
<td>394 (51.9)</td>
<td>894 (58.4)</td>
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<td>Race or ethnicity, n (%)</td>
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<td>White</td>
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<td>Initial parent trials</td>
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<td>1290 (84.2)</td>
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<tr>
<td>Black or African American</td>
<td>66 (4.1)</td>
<td>65 (6.8)</td>
<td>131 (5.1)</td>
<td>111 (8.3)</td>
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<td>24 (3.1)</td>
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<td>49 (3.2)</td>
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<td>Other race</td>
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<td>Hispanic</td>
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<td>36 (4.7)</td>
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<td>68 (4.4)</td>
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### Lipids, mean (SD)

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<th>OLE</th>
<th>OLE</th>
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<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>103.4 (27.0)</td>
<td>122.5 (29.1)</td>
<td>110.5 (29.3)</td>
<td>159.4 (50.1)</td>
<td>126.9 (42.5)</td>
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<td></td>
<td>108.1 (29.0)</td>
<td>118.2 (30.5)</td>
<td>113.1 (30.1)</td>
<td>143.6 (51.9)</td>
<td>129.1 (45.6)</td>
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<td>PCSK9 (ng/mL)</td>
<td>415.0 (150.3)</td>
<td>379.1 (139.4)</td>
<td>401.7 (147.3)</td>
<td>356.5 (134.6)</td>
<td>378.4 (141.6)</td>
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<td></td>
<td>397.8 (137.1)</td>
<td>399.2 (139.0)</td>
<td>398.5 (138.0)</td>
<td>379.3 (145.8)</td>
<td>381.8 (143.6)</td>
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### Cardiovascular risk factors, n (%)

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<th>OLE</th>
<th>OLE</th>
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</thead>
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<tr>
<td>NCEP risk category high</td>
<td>631 (39.2)</td>
<td>320 (33.5)</td>
<td>951 (37.1)</td>
<td>425 (31.7)</td>
<td>623 (30.6)</td>
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<td>328 (42.4)</td>
<td>292 (38.5)</td>
<td>620 (40.5)</td>
<td>410 (28.8)</td>
<td>526 (36.1)</td>
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<td>Coronary artery disease</td>
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<td>365 (22.7)</td>
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<td>182 (19.0)</td>
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<td>547 (21.3)</td>
<td>357 (23.3)</td>
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<td>237 (17.7)</td>
<td>231 (16.2)</td>
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<td>343 (16.8)</td>
<td>297 (20.4)</td>
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<table>
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<th>Cerebrovascular or peripheral arterial disease</th>
<th>Initial parent trials</th>
<th>OLE</th>
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<td>149 (9.3)</td>
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<td>82 (8.6)</td>
<td>74 (9.7)</td>
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<td>231 (9.0)</td>
<td>160 (10.4)</td>
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<td>122 (9.1)</td>
<td>103 (7.2)</td>
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<td>150 (7.4)</td>
<td>138 (9.5)</td>
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*Median study exposure: 3 months
†Control placebo and/or ezetimibe
‡Year 1 standard of care-controlled period of open-label extension studies; median study exposure: 11 months
OLE, open-label extension; SoC, standard of care
Table 3. Adverse Events According to Lowest LDL-C Level Achieved

<table>
<thead>
<tr>
<th>AE</th>
<th>Lowest LDL-C Achieved and Treatment Group</th>
<th>Initial Parent Trials*</th>
<th>OLE ‡</th>
<th>OLE</th>
<th>Initial parent trials</th>
<th>OLE</th>
<th>Initial parent trials</th>
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<th>Initial parent trials</th>
<th>OLE</th>
<th>Initial parent trials</th>
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<tbody>
<tr>
<td></td>
<td>&lt;25 mg/dL</td>
<td>≥25 mg/dL and &lt;40 mg/dL</td>
<td>All Patients With &lt;40 mg/dL</td>
<td>≥40 mg/dL</td>
<td>Any Evolocumab N = 1609</td>
<td>Any Evolocumab N = 956</td>
<td>Any Evolocumab N = 2565</td>
<td>Any Evolocumab N = 1339</td>
<td>Any Control† N = 2038</td>
<td>Evolocumab + SoC N = 773</td>
<td>Evolocumab + SoC N = 759</td>
<td>Evolocumab + SoC N = 1532</td>
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<td>Any AE, %</td>
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<td>Muscle-related AEs, %</td>
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</table>

*Median study exposure: 3 months
†Control placebo and/or ezetimibe
‡Year 1 standard of care-controlled period of open-label extension studies; median study exposure: 11 months
§Not applicable; standard of care group did not receive investigational drug

AE, adverse event; N/A, not applicable; OLE, open-label extension; SAE, serious AE; SoC, standard of care; IP, investigational product
Table 4. Laboratory Parameters According to Lowest LDL-C Level Achieved

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Lowest LDL-C Achieved and Treatment Group</th>
<th>Initial Parent Trials*</th>
<th>OLE †</th>
<th>Evolocumab + SoC</th>
<th>Evolocumab + SoC</th>
<th>Evolocumab + SoC</th>
<th>Evolocumab + SoC</th>
<th>SoC</th>
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<tbody>
<tr>
<td></td>
<td>&lt;25 mg/dL</td>
<td>≥25 mg/dL and &lt;40 mg/dL</td>
<td>All Patients With &lt;40 mg/dL</td>
<td>≥40 mg/dL</td>
<td>Any Evolocumab N = 1609</td>
<td>Any Evolocumab N = 956</td>
<td>Any Evolocumab N = 2565</td>
<td>Any Evolocumab N = 1339</td>
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<td>CK &gt;5 x ULN, %</td>
<td>Initial parent trials</td>
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<td>0.7</td>
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<td>0.3</td>
<td>0.2</td>
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<td>0.1</td>
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<td>ALT or AST &gt;3 x ULN, %</td>
<td>Initial parent trials</td>
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<td>0.3</td>
<td>0.4</td>
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<td>1.2</td>
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<td>Total bilirubin &gt;2 x ULN, %</td>
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<td>0.1</td>
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</tr>
<tr>
<td></td>
<td>OLE</td>
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<td>0.1</td>
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</tr>
</tbody>
</table>

*Median study exposure: 3 months
†Control placebo and/or ezetimibe
‡Year 1 standard of care-controlled period of open-label extension studies; median study exposure: 11 months

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; OLE, open-label extension; SoC, standard of care; ULN, upper limit of normal