Online Appendix Figure 1 – Patient Disposition

| Day 1 | PBO n=50 | 5 mg n=51 | 15 mg n=51 | 50 mg n=46 | 100 mg n=53 | 200 mg n=51 |
|-------|----------|-----------|------------|------------|-------------|------------|
| Day 85 | PBO n=42 | 5 mg n=39 | 15 mg n=37 | 50 mg n=29 | 100 mg n=42 | 200 mg n=39 |

D/C, discontinued; F-U, follow-up; W/D, withdrawn; Rx, therapy; Non-compl, non-compliance.

Online Appendix Table 1 – Clinical Characteristics at Baseline

| Placebo | 5 mg | 15 mg | 50 mg | 100 mg | 200 mg |
|---------|------|-------|-------|--------|--------|
| N       | 50   | 51    | 51    | 46     | 53     | 51    |
| Age, yrs| 52 ± 11 | 55 ± 9 | 52 ± 10 | 54 ± 9 | 54 ± 9 | 52 ± 10 |
| Male, n (%)| 25 (50) | 30 (59) | 24 (47) | 22 (48) | 28 (53) | 21 (41) |
| Female, n (%)| 25 (50) | 21 (41) | 27 (53) | 24 (52) | 25 (47) | 30 (59) |
| Duration T2D, yrs| 6.7 ± 6 | 5.3 ± 5 | 6.4 ± 5 | 5.8 ± 5 | 6.9 ± 6 | 6.0 ± 5 |
| Metformin Dose, g/d| 1.5 ± 0.5 | 1.4 ± 0.6 | 1.5 ± 0.6 | 1.4 ± 0.5 | 1.6 ± 0.5 | 1.6 ± 0.6 |
| A1c, %| 8.3 ± 1 | 8.2 ± 1 | 8.3 ± 1 | 8.3 ± 1 | 8.2 ± 1 | 8.2 ± 1 |
| FPG, mg/dL| 179 ± 51 | 172 ± 41 | 175 ± 44 | 178 ± 53 | 170 ± 64 | 165 ± 41 |
| Weight, kg| 91 ± 16 | 91 ± 19 | 96 ± 22 | 84 ± 14 | 89 ± 20 | 86 ± 17 |
| BMI, kg/m²| 33 ± 5 | 33 ± 6 | 34 ± 5 | 31 ± 4 | 32 ± 5 | 32 ± 5 |
| Cholesterol, mg/dL| 198 ± 52 | 190 ± 40 | 177 ± 37 | 193 ± 54 | 205 ± 45 | 194 ± 36 |
| LDL-C, mg/dL| 112 ± 33 | 107 ± 34 | 99 ± 345 | 111 ± 44 | 121 ± 37 | 110 ± 27 |
| HDL-C, mg/dL| 49 ± 16 | 47 ± 13 | 44 ± 9 | 46 ± 12 | 48 ± 10 | 47 ± 11 |
| Triglyceride, mg/dL| 188 ± 105 | 189 ± 125 | 196 ± 153 | 188 ± 121 | 187 ± 92 | 195 ± 127 |
| sBP, mm Hg| 127 ± 12 | 125 ± 15 | 127 ± 15 | 123 ± 11 | 127 ± 15 | 125 ± 13 |
| dBP, mm Hg| 78 ± 8 | 75 ± 8 | 78 ± 8 | 76 ± 8 | 80 ± 8 | 78± 7 |

Data are mean ± STD unless otherwise noted.

Online Appendix Table 2 – Endpoint Electrolyte Assessments

| Electrolyte | Placebo | 5 mg | 15 mg | 50 mg | 100 mg | 200 mg |
|-------------|---------|------|-------|-------|--------|--------|
| Potassium   | 3.4-5.4 mmol/L | 4.4 ± 0.4 | 4.5 ± 0.4 | 4.3 ± 0.4 | 4.3 ± 0.3 | 4.4 ± 0.4 | 4.3 ± 0.4 |
| Sodium      | 132-147 mmol/L | 140 ± 3 | 142 ± 5 | 141 ± 3 | 141 ± 4 | 142 ± 4 | 141 ± 3 |
| Chloride    | 94-112 mmol/L | 102 ± 3 | 103 ± 2 | 102 ± 3 | 103 ± 3 | 102 ± 3 |
| Bicarbonate | 17.0-30.6 mmol/L | 24.3 ± 2.8 | 23.9 ± 3.1 | 24.5 ± 3.2 | 24.4 ± 3.2 | 24.4 ± 2.7 | 24.2 ± 3.4 |

Electrolyte data are Week 12 mean ± STD. Central lab normal reference ranges are provided.
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