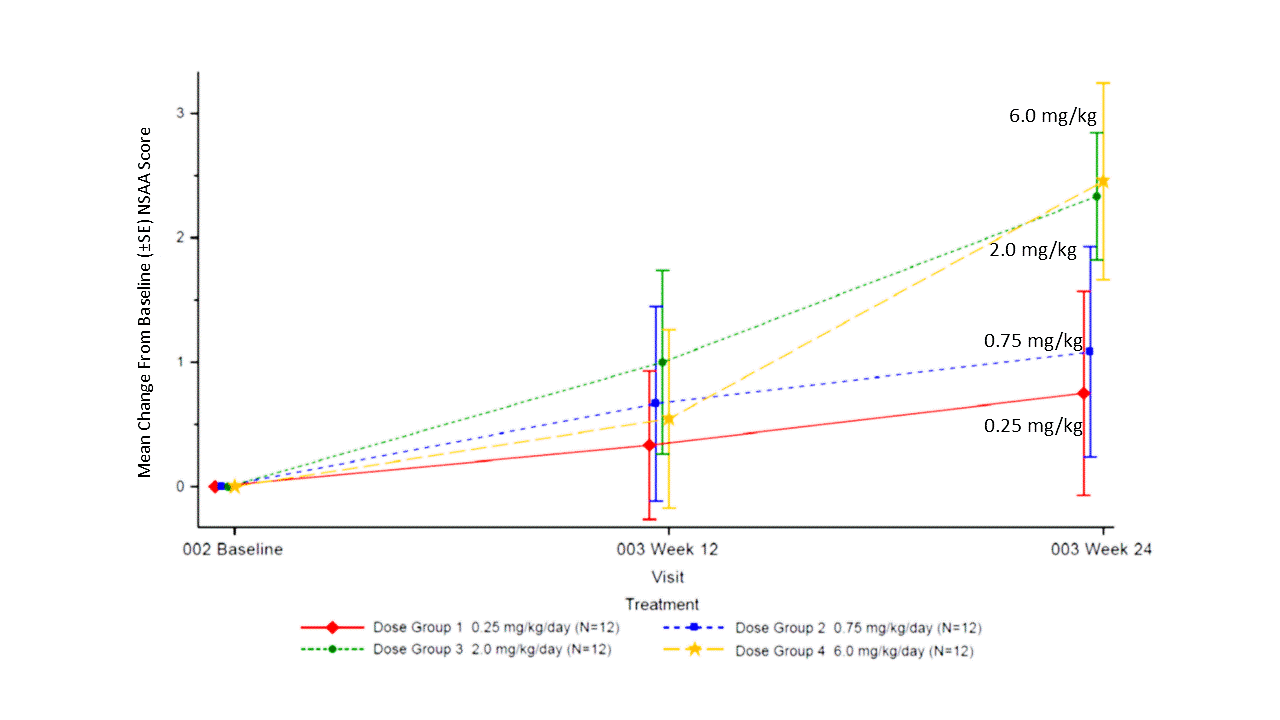
**Supplemental Figure 1. NSAA Mean (±SE) Score Change from Baseline.**

****

**Supplemental Table 1. 6-month and 12-month changes in outcomes in 4-<8 year-old DMD boys treated with prednisone (0.75 mg/kg/day) vs. steroid-naïve comparators.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome | Time months | CINRG DNHS (steroid naïve) | | CINRG prednisone trial | | N needed per group to detect a significant difference- Using observed changes | N needed per group to detect a significant difference – Using conservative change estimates\* | N needed per group to detect a significant difference – Using conservative change estimates\*\* |
| n | Mean ± SD | N | Mean ± SD |
| BMI z score | 6 | 40 | -0.14 ± 0.78 | 13 | 0.54 ± 0.66 | 12 | 15 |  |
| 12 | 26 | -0.2 5± 0.83 | 13 | 0.63 ± 0.45 | 7 | 6 |  |
| Time to run/walk 10 m velocity (m/s) | 6 | 39 | 0.02 ± 0.31 | 13 | 0.35 ± 0.32 | 12 | 19 | 28 |
| 12 | 26 | 0.01 ± 0.25 | 12 | 0.42 ± 0.23 | 5 | 7 | 11 |
| Time to climb 4 stairs velocity (climb/s) | 6 | 40 | 0.01 ± 0.07 | 13 | 0.11 ± 0.08 | 7 | 11 | 17 |
| 12 | 26 | 0.01 ± 0.06 | 12 | 0.16 ± 0.10 | 5 | 7 | 10 |
| Time to stand from supine velocity (rise/s) | 6 | 38 | 0.004 ± 0.07 | 12 | 0.10 ± 0.10 | 10 | 16 | 23 |
| 12 | 26 | -0.01 ± 0.06 | 11 | 0.11 ± 0.09 | 5 | 8 | 9 |

|  |
| --- |
| Notes: a) All patients are 4-<8 years of age at study start.  b) Data from untreated subjects in the CINRG DMD Natural history study; data from treated subjects in the CINRG Prednisone trial.  c) Compares all only daily dose prednisone-treated patients to untreated patients.  d) All calculations assume a repeated measures ANOVA model with one pre- and one post-measurement. Correlation between repeated measures used as follows: 0.70 for 6 month BMI changes, and 0.65 for 12 month BMI changes, and 0.575 for 6 and 12 month velocity changes. Power = 0.80 and alpha = 0.025 for all calculations to account for multiple group comparisons (i.e. two vamorolone doses, each compared to prednisone for safety and placebo for efficacy).  \* Conservative change estimates were defined as follows: For BMI, the expected change in vamorolone was set to 0.0 rather than the observed decrease. For timed tests, the expected change in vamorolone was set to 80% of the observed change in the prednisone group.  \*\* Conservative change estimates were defined as follows: For timed tests, the expected change in vamorolone was set to 60% of the observed change in the prednisone group (with SD at 80%). |

**Table 2. Reliability of Clinical Outcome Measures in VBP15-002**

|  |  |
| --- | --- |
| **Study Measurement** | **%CV Mean**  **Intra-patient variance (precision)** |
| **Time to Stand** | 62.0 |
| **Time 10 m Run/Walk** | 23.8 |
| **Time to Climb 4 Stairs** | 71.0 |
| **6 Minute Walk Test** | 19.5 |
| **North Star Ambulatory Assessment** | 28.1 |
| **QMT Elbow Flexion** | 42.5 |
| **QMT Elbow Extension** | 45.0 |
| **QMT Knee Flexion** | 58.4 |

**Supplemental Table 3: Time to Stand (TTSTAND) Velocity in Rises/Second (FAS).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Group 1**  **0.25 mg/kg/d**  **(N = 12)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)** | **Group 3 2.0 mg/kg/d (N = 12)** | **Group 4 6.0 mg/kg/d**  **(N = 12)** | **DNHSa**  **(N = 31)** |
| **VBP15-002 Baseline** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 31)** |
| Mean | 0.18 | 0.24 | 0.22 | 0.19 | 0.20 |
| SD | 0.065 | 0.090 | 0.082 | 0.056 | 0.065 |
| Median | 0.17 | 0.26 | 0.19 | 0.20 | 0.21 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.3 | 0.1, 0.4 | 0.1, 0.3 | 0.1, 0.3 |
| **VBP15-003 Week 12** | **(n = 11)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 30)** |
| Mean | 0.18 | 0.23 | 0.24 | 0.22 | 0.21 |
| SD | 0.072 | 0.102 | 0.089 | 0.075 | 0.071 |
| Median | 0.18 | 0.22 | 0.22 | 0.21 | 0.21 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.4 | 0.1, 0.4 | 0.1, 0.4 | 0.1, 0.3 |
| **Week 12 Change from BL** | **(n = 11)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 30)** |
| Mean | -0.01 | 0.00 | 0.02 | 0.02 | 0.01 |
| SD | 0.061 | 0.054 | 0.066 | 0.034 | 0.053 |
| Median | -0.03 | -0.01 | 0.02 | 0.02 | 0.00 |
| Minimum, Maximum | -0.1, 0.1 | -0.1, 0.1 | -0.1, 0.1 | 0.0, 0.1 | -0.1, 0.2 |
| MMRM p-value vs. DNHS | 0.3488 | 0.7587 | 0.3792 | 0.4953 |  |
| MMRM p-valuevs. Group 1 |  | 0.5849 | 0.1323 | 0.1764 |  |
| **VBP15-003 Week 24** | **(n = 10)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 29)** |
| Mean | 0.18 | 0.24 | 0.26 | 0.24 | 0.21 |
| SD | 0.081 | 0.114 | 0.108 | 0.086 | 0.077 |
| Median | 0.20 | 0.22 | 0.23 | 0.24 | 0.21 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.4 | 0.2, 0.6 | 0.0, 0.4 | 0.1, 0.4 |
| **Week 24 Change from BL** | **(n = 10)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 29)** |
| Mean | -0.01 | 0.00 | 0.05 | 0.04 | 0.01 |
| SD | 0.066 | 0.062 | 0.061 | 0.045 | 0.068 |
| Median | -0.04 | 0.01 | 0.05 | 0.04 | 0.00 |
| Minimum, Maximum | -0.1, 0.1 | -0.1, 0.1 | -0.1, 0.2 | 0.0, 0.1 | -0.1, 0.2 |
| MMRM p-value vs. DNHS | 0.4062 | 0.9554 | 0.0397 | 0.1048 |  |
| MMRM p-valuevs. Group 1 |  | 0.5067 | 0.0192 | 0.0442 |  |
| Abbreviations: BL = Baseline; MMRM = mixed model for repeated measures  aBaseline DNHS, Week 12 DNHS, Week 24 DNHS, and Change from Baseline DNHS are presented. | | | | | |

**Supplemental Table 4. Time to Run/Walk 10 Meters (TTRW) Velocity in Meters/Second (FAS).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Group 1**  **0.25 mg/kg/d**  **(N = 12)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)** | **Group 3 2.0 mg/kg/d (N = 12)** | **Group 4 6.0 mg/kg/d**  **(N = 12)** | **DNHSa**  **(N = 31)** |
| **VBP15-002 Baseline** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 31)** |
| Mean | 1.60 | 1.77 | 1.84 | 1.64 | 1.64 |
| SD | 0.312 | 0.367 | 0.347 | 0.279 | 0.441 |
| Median | 1.61 | 1.75 | 1.92 | 1.73 | 1.66 |
| Minimum, Maximum | 1.1, 2.2 | 1.3, 2.5 | 1.3, 2.4 | 1.1, 2.0 | 0.9, 2.3 |
| **VBP15-003 Week 12** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | 1.54 | 1.77 | 1.97 | 1.88 | 1.65 |
| SD | 0.306 | 0.550 | 0.503 | 0.341 | 0.439 |
| Median | 1.63 | 1.81 | 2.04 | 1.85 | 1.70 |
| Minimum, Maximum | 1.0, 2.1 | 0.8, 2.7 | 0.7, 2.7 | 1.3, 2.4 | 0.6, 2.4 |
| **Week 12 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | -0.06 | 0.00 | 0.13 | 0.26 | 0.01 |
| SD | 0.261 | 0.307 | 0.316 | 0.297 | 0.255 |
| Median | -0.03 | -0.04 | 0.17 | 0.16 | 0.00 |
| Minimum, Maximum | -0.6, 0.4 | -0.5, 0.7 | -0.7, 0.5 | 0.0, 1.0 | -0.5, 0.8 |
| MMRM p-value vs. DNHS | 0.6352 | 0.8971 | 0.1193 | 0.0108 |  |
| MMRM p-value vs. Group 1 |  | 0.6130 | 0.0950 | 0.0114 |  |
| **VBP15-003 Week 24** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 30)** |
| Mean | 1.55 | 1.84 | 1.90 | 1.89 | 1.65 |
| SD | 0.384 | 0.486 | 0.321 | 0.378 | 0.441 |
| Median | 1.52 | 1.93 | 1.96 | 1.88 | 1.63 |
| Minimum, Maximum | 1.0, 2.3 | 1.0, 2.8 | 1.3, 2.5 | 1.2, 2.6 | 0.9, 2.4 |
| **Week 24 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 30)** |
| Mean | -0.05 | 0.06 | 0.06 | 0.27 | -0.01 |
| SD | 0.311 | 0.210 | 0.210 | 0.254 | 0.256 |
| Median | -0.16 | 0.02 | 0.10 | 0.26 | -0.02 |
| Minimum, Maximum | -0.4, 0.6 | -0.3, 0.3 | -0.3, 0.4 | 0.0, 0.8 | -0.6, 0.8 |
| MMRM p-value vs. DNHS | 0.7248 | 0.3768 | 0.3500 | 0.0035 |  |
| MMRM p-value vs. Group 1 |  | 0.3082 | 0.2895 | 0.0059 |  |
| Abbreviations: BL = Baseline; MMRM = mixed model for repeated measures  aBaseline DNHS, Week 12 DNHS, Week 24 DNHS, and Change from Baseline DNHS are presented. | | | | | |

**Supplemental Table 5. Six-Minute Walk Test (6MWT) in Meters (FAS).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Group 1**  **0.25 mg/kg/d**  **(N = 12)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)** | **Group 3 2.0 mg/kg/d**  **(N = 12)** | **Group 4 6.0 mg/kg/d**  **(N = 12)** |
| **VBP15-002 Baseline** | **(n = 11)** | **(n = 12)** | **(n = 10)** | **(n = 11)** |
| Mean | 316.2 | 331.5 | 353.9 | 336.8 |
| SD | 59.47 | 52.76 | 65.40 | 63.18 |
| Median | 311.0 | 336.5 | 362.5 | 337.0 |
| Minimum, Maximum | 200, 406 | 223, 402 | 262, 440 | 243, 452 |
| **VBP15-003 Week 12** | **(n = 11)** | **(n = 11)** | **(n = 10)** | **(n = 9)** |
| Mean | 312.9 | 358.7 | 393.7 | 369.9 |
| SD | 60.93 | 71.47 | 59.72 | 69.47 |
| Median | 307.0 | 351.0 | 392.5 | 371.0 |
| Minimum, Maximum | 243, 427 | 225, 491 | 297, 471 | 272, 500 |
| **Week 12 Change from BL** | **(n = 10)** | **(n = 11)** | **(n = 10)** | **(n = 9)** |
| Mean | 6.0 | 20.8 | 39.8 | 27.6 |
| SD | 28.81 | 38.09 | 35.61 | 42.00 |
| Median | 3.5 | 7.0 | 37.5 | 19.0 |
| Minimum, Maximum | -38, 46 | -32, 89 | -22, 93 | -33, 87 |
| MMRM p-value vs. Group 1 |  | 0.3547 | 0.0532 | 0.2134 |
| **VBP15-003 Week 24** | **(n = 10)** | **(n = 12)** | **(n = 10)** | **(n = 10)** |
| Mean | 306.2 | 350.4 | 383.1 | 372.6 |
| SD | 68.08 | 64.23 | 63.38 | 69.12 |
| Median | 319.0 | 348.0 | 375.5 | 368.0 |
| Minimum, Maximum | 205, 396 | 210, 450 | 276, 458 | 250, 499 |
| **Week 24 Change from BL** | **(n = 10)** | **(n = 12)** | **(n = 10)** | **(n = 9)** |
| Mean | -11.6 | 18.9 | 29.2 | 43.9 |
| SD | 29.45 | 41.08 | 35.91 | 43.72 |
| Median | -3.0 | 39.0 | 16.5 | 51.0 |
| Minimum | -66, 21 | -65, 61 | -14, 92 | -54, 94 |
| MMRM p-value vs. Group 1 |  | 0.0644 | 0.0153 | 0.0019 |
| Abbreviations: BL = Baseline; MMRM = mixed model for repeated measures | | | | |

**Supplemental Table 6. Time to Climb (TTCLIMB) Velocity in Tasks/Second (FAS).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Group 1**  **0.25 mg/kg/d**  **(N = 12)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)** | **Group 3 2.0 mg/kg/d (N = 12)** | **Group 4 6.0 mg/kg/d**  **(N = 12)** | **DNHSa**  **(N = 31)** |
| **VBP15-002 Baseline** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 31)** |
| Mean | 0.20 | 0.29 | 0.29 | 0.24 | 0.21 |
| SD | 0.054 | 0.147 | 0.164 | 0.086 | 0.094 |
| Median | 0.19 | 0.27 | 0.28 | 0.23 | 0.22 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.5 | 0.1, 0.7 | 0.1, 0.4 | 0.1, 0.4 |
| **VBP15-003 Week 12** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | 0.21 | 0.34 | 0.31 | 0.26 | 0.21 |
| SD | 0.064 | 0.238 | 0.157 | 0.095 | 0.092 |
| Median | 0.21 | 0.29 | 0.27 | 0.28 | 0.23 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.8 | 0.1, 0.6 | 0.1, 0.4 | 0.1, 0.5 |
| **Week 12 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | 0.01 | 0.05 | 0.02 | 0.02 | 0.00 |
| SD | 0.044 | 0.115 | 0.107 | 0.051 | 0.061 |
| Median | 0.00 | 0.00 | 0.06 | 0.02 | 0.01 |
| Minimum, Maximum | 0.0, 0.1 | -0.1, 0.3 | -0.2, 0.2 | -0.1, 0.1 | -0.1, 0.2 |
| MMRM p-value vs. DNHS | 0.5850 | 0.0336 | 0.3107 | 0.3951 |  |
| MMRM p-value vs. Group 1 |  | 0.1952 | 0.7068 | 0.7986 |  |
| **VBP15-003 Week 24** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | 0.20 | 0.30 | 0.34 | 0.29 | 0.22 |
| SD | 0.071 | 0.166 | 0.148 | 0.097 | 0.090 |
| Median | 0.20 | 0.29 | 0.28 | 0.32 | 0.23 |
| Minimum, Maximum | 0.1, 0.3 | 0.1, 0.6 | 0.2, 0.6 | 0.1, 0.4 | 0.1, 0.4 |
| **Week 24 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 31)** |
| Mean | 0.00 | 0.01 | 0.04 | 0.05 | 0.01 |
| SD | 0.076 | 0.066 | 0.090 | 0.061 | 0.062 |
| Median | -0.02 | 0.00 | 0.06 | 0.04 | 0.01 |
| Minimum, Maximum | -0.1, 0.1 | -0.1, 0.1 | -0.1, 0.2 | -0.1, 0.2 | -0.1, 0.2 |
| MMRM p-value vs. DNHS | 0.8532 | 0.6581 | 0.0811 | 0.0507 |  |
| MMRM p-value vs. Group 1 |  | 0.6107 | 0.1180 | 0.0747 |  |
| Abbreviations: BL = Baseline; MMRM = mixed model for repeated measures  aBaseline DNHS, Week 12 DNHS, Week 24 DNHS, and Change from Baseline DNHS are presented. | | | | | |

Supplemental Table 7. Treatment-Emergent Adverse Events with ≥5 % Incidence Overall by SOC and PT (Safety Population).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **System Organ Class**  **Preferred Term** | **Group 1**  **0.25 mg/kg/d**  **(N = 12)**  **N (%)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)**  **N (%)** | **Group 3 2.0 mg/kg/d (N = 12)**  **N (%)** | **Group 4 6.0 mg/kg/d**  **(N = 12)**  **N (%)** | **Total**  **(N = 48)**  **N (%)** |
| **Subjects with any TEAE** | 10 (83.3) | 10 (83.3) | 11 (91.7) | 11 (91.7) | 42 (87.5) |
|  |  | | | | |
| **Gastrointestinal disorders** | | | | | |
| Abdominal pain upper | 0 | 0 | 1 (8.3) | 2 (16.7) | 3 (6.3) |
| Constipation | 1 (8.3) | 0 | 1 (8.3) | 2 (16.7) | 4 (8.3) |
| Diarrhoea | 2 (16.7) | 0 | 2 (16.7) | 1 (8.3) | 5 (10.4) |
| Vomiting | 1 (8.3) | 1 (8.3) | 3 (25.0) | 2 (16.7) | 7 (14.6) |
| **General disorders and administration site conditions** | | | | | |
| Pyrexia | 2 (16.7) | 7 (58.3) | 5 (41.7) | 3 (25.0) | 17 (35.4) |
| **Infections and infestations** | | | | | |
| Conjunctivitis | 1 (8.3) | 0 | 2 (16.7) | 1 (8.3) | 4 (8.3) |
| Ear infection | 1 (8.3) | 1 (8.3) | 1 (8.3) | 1 (8.3) | 4 (8.3) |
| Influenza | 1 (8.3) | 0 | 0 | 3 (25.0) | 4 (8.3) |
| Upper respiratory tract infection | 1 (8.3) | 1 (8.3) | 1 (8.3) | 0 | 3 (6.3) |
| Viral upper respiratory tract infection | 4 (33.3) | 4 (33.3) | 7 (58.3) | 5 (41.7) | 20 (41.7) |
| **Injury, poisoning, and procedural complications** | | | | | |
| Muscle strain | 1 (8.3) | 2 (16.7) | 0 | 1 (8.3) | 4 (8.3) |
| **Nervous System Disorders** | | | | | |
| Headache | 0 | 1 (8.3) | 2 (16.7) | 1 (8.3) | 4 (8.3) |
| **Respiratory, thoracic and mediastinal disorders** | | | | | |
| Cough | 1 (8.3) | 4 (33.3) | 1 (8.3) | 3 (25.0) | 9 (18.8) |
| Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing condition after initiation of the investigational product and through the subject’s last study visit (study completion or early termination). Serious adverse events were recorded for up to 30 days after the final administration of study drug. Within each category, subjects were counted only once if they had more than one event reported during the treatment period. AEs were coded using MedDRA version 19.0. | | | | | |

Supplemental Table 8. Treatment-Emergent Adverse Events with ≥5% Incidence Overall by Most Frequently Preferred Term (Safety Population).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Preferred Term** | **Group 1**  **0.25 mg/kg/d**  **(N = 12)**  **N (%)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)**  **N (%)** | **Group 3 2.0 mg/kg/d**  **(N = 12)**  **N (%)** | **Group 4 6.0 mg/kg/d**  **(N = 12)**  **N (%)** | **Total**  **(N = 48)**  **N (%)** |
| **Subjects with any TEAE** | 10 (83.3) | 10 (83.3) | 11 (91.7) | 11 (91.7) | 42 (87.5) |
|  |  |  |  |  |  |
| Viral upper respiratory tract infection | 4 (33.3) | 4 (33.3) | 7 (58.3) | 5 (41.7) | 20 (41.7) |
| Pyrexia | 2 (16.7) | 7 (58.3) | 5 (41.7) | 3 (25.0) | 17 (35.4) |
| Cough | 1 (8.3) | 4 (33.3) | 1 (8.3) | 3 (25.0) | 9 (18.8) |
| Vomiting | 1 (8.3) | 1 (8.3) | 3 (25.0) | 2 (16.7) | 7 (14.6) |
| Diarrhoea | 2 (16.7) | 0 | 2 (16.7) | 1 (8.3) | 5 (10.4) |
| Conjunctivitis | 1 (8.3) | 0 | 2 (16.7) | 1 (8.3) | 4 (8.3) |
| Constipation | 1 (8.3) | 0 | 1 (8.3) | 2 (16.7) | 4 (8.3) |
| Ear infection | 1 (8.3) | 1 (8.3) | 1 (8.3) | 1 (8.3) | 4 (8.3) |
| Headache | 0 | 1 (8.3) | 2 (16.7) | 1 (8.3) | 4 (8.3) |
| Influenza | 1 (8.3) | 0 | 0 | 3 (25.0) | 4 (8.3) |
| Muscle strain | 1 (8.3) | 2 (16.7) | 0 | 1 (8.3) | 4 (8.3) |
| Abdominal pain upper | 0 | 0 | 1 (8.3) | 2 (16.7) | 3 (6.3) |
| Upper respiratory tract infection | 1 (8.3) | 1 (8.3) | 1 (8.3) | 0 | 3 (6.3) |
| Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing condition after initiation of the investigational product and through the subject’s last study visit (study completion or early termination). Serious adverse events were recorded for up to 30 days after the final administration of study drug. Within each category, subjects were counted only once if they had more than one event reported during the treatment period. AEs were coded using MedDRA version 19.0. | | | | | |

**Supplemental Table 9. Summary of Body Mass Index (BMI) Z-score (Safety Population).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Group 1**  **0.25 mg/kg/d**  **(N = 12)** | **Group 2**  **0.75 mg/kg/d**  **(N = 12)** | **Group 3 2.0 mg/kg/d (N = 12)** | **Group 4 6.0 mg/kg/d**  **(N = 12)** | **Prednisonea**  **(N = 14)** |
| **BMI Z-score** |  |  |  |  |  |
| **VBP15-002 Baseline** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 14)** |
| Mean | 1.165 | 0.703 | 1.200 | 0.695 | 0.440 |
| SD | 0.6219 | 1.0738 | 0.5325 | 0.7189 | 1.1607 |
| Median | 1.278 | 0.891 | 1.135 | 0.870 | 0.685 |
| Minimum, Maximum | -0.38, 1.94 | -1.21, 2.09 | 0.35, 2.09 | -0.86, 1.68 | -1.79, 1.95 |
| **VBP15-003 Week 12** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 13)** |
| Mean | 1.103 | 0.494 | 1.261 | 1.011 | 1.014 |
| SD | 0.6457 | 1.0680 | 0.3981 | 0.7034 | 1.0091 |
| Median | 1.108 | 0.728 | 1.235 | 1.137 | 1.165 |
| Minimum, Maximum | -0.57, 1.92 | -1.93, 1.80 | 0.70, 1.81 | -0.68, 1.93 | -0.92, 2.34 |
| **Week 12 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 13)** |
| Mean | -0.062 | -0.209 | 0.062 | 0.174 | 0.527 |
| SD | 0.2438 | 0.4078 | 0.3886 | 0.5826 | 0.4652 |
| Median | -0.076 | -0.205 | 0.006 | 0.246 | 0.596 |
| Minimum, Maximum | -0.49, 0.32 | -1.03, 0.32 | -0.49, 0.85 | -1.10, 0.71 | -0.29, 1.47 |
| MMRM p-value vs. prednisone | 0.0085 | <0.0001 | 0.0570 | 0.0943 |  |
| MMRM p-value vs. Group 1 |  | 0.1645 | 0.4338 | 0.3159 |  |
| **VBP15-003 Week 24** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 13)** |
| Mean | 1.004 | 0.493 | 1.242 | 1.330 | 1.030 |
| SD | 0.6381 | 1.1696 | 0.4596 | 0.5857 | 0.9142 |
| Median | 1.188 | 0.836 | 1.293 | 1.433 | 1.074 |
| Minimum, Maximum | -0.52, 1.72 | -1.79, 1.97 | 0.61, 1.95 | 0.23, 2.28 | -0.84, 2.45 |
| **Week 24 Change from BL** | **(n = 12)** | **(n = 12)** | **(n = 12)** | **(n = 11)** | **(n = 13)** |
| Mean | -0.161 | -0.210 | 0.043 | 0.493 | 0.543 |
| SD | 0.3234 | 0.3629 | 0.3849 | 0.6363 | 0.6646 |
| Median | -0.130 | -0.167 | -0.085 | 0.407 | 0.271 |
| Minimum, Maximum | -0.73, 0.36 | -0.62, 0.53 | -0.37, 0.97 | -0.50, 1.58 | -0.20, 1.86 |
| MMRM p-value vs. prednisone | 0.0037 | 0.0003 | 0.0612 | 0.9261 |  |
| MMRM p-value vs. Group 1 |  | 0.4697 | 0.2680 | 0.0035 |  |
| Abbreviations: BL = Baseline; MMRM = mixed model for repeated measures  aBaseline CINRG prednisone cohort, Week 12 CINRG prednisone cohort, Week 24 CINRG prednisone cohort, and Change from Baseline CINRG prednisone cohort are presented.  Baseline is defined as VBP15- 002 Study Day -1. If Day -1 assessment was missing, then Screening assessment was used. BMI was calculated from height and weight measured at the same study visit where available, or from height measured at nearest previous visit if not measured at same visit. | | | | | |

**Supplemental Table 10. Summary of Bone Turnover Biomarkers (Safety Population) – Bone formation (Osteocalcin; P1NP).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Group 1  0.25 mg/kg/d  (N = 12) | Group 2  0.75 mg/kg/d  (N = 12) | Group 3 2.0 mg/kg/d (N = 12) | Group 4 6.0 mg/kg/d  (N = 12) | Total  (N = 48) |
| **Osteocalcin (ng/mL)** |  |  |  |  |  |
| VBP15-002 Baseline | (n = 12) | (n = 12) | (n = 12) | (n = 12) | (n = 48) |
| Mean | 37.94 | 35.66 | 41.17 | 44.36 | 39.78 |
| SD | 11.622 | 6.800 | 5.617 | 5.979 | 8.320 |
| Median | 32.15 | 34.80 | 41.95 | 42.80 | 39.55 |
| Minimum, Maximum | 25.4, 59.1 | 25.6, 47.6 | 33.5, 53.5 | 37.0, 55.2 | 25.4, 59.1 |
| VBP15-003 Week 24 | (n = 7) | (n = 12) | (n = 12) | (n = 10) | (n = 41) |
| Mean | 38.80 | 51.41 | 51.98 | 49.08 | 48.85 |
| SD | 6.292 | 11.265 | 9.372 | 7.771 | 10.058 |
| Median | 38.60 | 52.55 | 49.75 | 49.40 | 48.40 |
| Minimum, Maximum | 30.0, 46.4 | 27.7, 70.1 | 39.2, 69.1 | 34.2, 58.9 | 27.7, 70.1 |
| Week 24 Change from BL | (n = 7) | (n = 12) | (n = 12) | (n = 10) | (n = 41) |
| Mean | ‑1.34 | 15.75 | 10.81 | 5.29 | 8.83 |
| SD | 11.289 | 10.211 | 7.542 | 7.858 | 10.682 |
| Median | 3.00 | 16.95 | 7.85 | 4.45 | 7.70 |
| Minimum, Maximum | -20.4, 10.8 | -2.4, 33.1 | 0.9, 25.6 | -7.2, 17.4 | -20.4, 33.1 |
| p value change from 002 BL | 0.7636 | 0.0002 | 0.0004 | 0.0621 | <0.0001 |
| MMRM p value vs. Group 1 |  | 0.0010 | 0.0048 | 0.0669 |  |
| **P1NP (ng/mL)** |  |  |  |  |  |
| VBP15-002 Baseline | (n = 12) | (n = 11) | (n = 12) | (n = 12) | (n = 47) |
| Mean | 555.8 | 480.7 | 508.2 | 511.5 | 514.7 |
| SD | 184.72 | 118.20 | 94.36 | 106.50 | 129.49 |
| Median | 493.5 | 519.0 | 534.5 | 516.0 | 510.0 |
| Minimum, Maximum | 351, 1024 | 344, 663 | 336, 652 | 350, 696 | 336, 1024 |
| VBP15-003 Week 24 | (n = 8) | (n = 12) | (n = 12) | (n = 10) | (n = 42) |
| Mean | 457.1 | 471.1 | 565.5 | 526.2 | 508.5 |
| SD | 129.21 | 121.10 | 158.89 | 130.18 | 138.68 |
| Median | 461.5 | 461.5 | 498.5 | 559.0 | 494.5 |
| Minimum, Maximum | 256, 628 | 316, 697 | 383, 823 | 307, 721 | 256, 823 |
| Week 24 Change from BL | (n = 8) | (n = 11) | (n = 12) | (n = 10) | (n = 41) |
| Mean | -30.8 | 2.1 | 57.3 | 8.7 | 13.5 |
| SD | 113.64 | 165.16 | 150.36 | 88.95 | 134.49 |
| Median | -15.5 | -20.0 | -1.5 | 17.0 | -5.0 |
| Minimum, Maximum | -260, 133 | -209, 273 | -121, 265 | -114, 170 | -260, 273 |
| p value change from 002 BL | 0.4691 | 0.9673 | 0.2134 | 0.7641 | 0.5252 |
| MMRM p value vs. Group 1 |  | 0.4727 | 0.0677 | 0.2529 |  |

**Supplemental Table 11. Summary of Bone Turnover Biomarkers (Safety Population), bone resorption (CTX).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Group 1  0.25 mg/kg/d  (N = 12) | Group 2  0.75 mg/kg/d  (N = 12) | Group 3 2.0 mg/kg/d (N = 12) | Group 4 6.0 mg/kg/d  (N = 12) | Total  (N = 48) |
| CTX (pg/mL) |  |  |  |  |  |
| VBP15-002 Baseline | (n = 11) | (n = 10) | (n = 12) | (n = 12) | (n = 45) |
| Mean | 871.0 | 935.8 | 936.8 | 889.3 | 907.8 |
| SD | 160.85 | 286.50 | 256.25 | 186.68 | 220.54 |
| Median | 891.0 | 857.0 | 988.5 | 834.0 | 891.0 |
| Minimum, Maximum | 571, 1143 | 611, 1383 | 641, 1477 | 581, 1223 | 571, 1477 |
| VBP15-003 Week 24 | (n = 8) | (n = 12) | (n = 10) | (n = 10) | (n = 40) |
| Mean | 1109.3 | 1235.6 | 1248.7 | 1237.0 | 1214.0 |
| SD | 287.92 | 295.79 | 308.90 | 277.20 | 286.61 |
| Median | 1036.5 | 1188.5 | 1174.5 | 1309.5 | 1179.5 |
| Minimum, Maximum | 863, 1781 | 841, 1827 | 786, 1792 | 774, 1574 | 774, 1827 |
| Week 24 Change from BL | (n = 8) | (n = 10) | (n = 10) | (n = 10) | (n = 38) |
| Mean | 212.3 | 295.6 | 346.5 | 321.4 | 298.2 |
| SD | 318.86 | 357.93 | 327.16 | 264.65 | 309.59 |
| Median | 149.0 | 382.0 | 382.0 | 317.5 | 331.5 |
| Minimum, Maximum | -200, 890 | -362, 747 | -158, 776 | -235, 703, - | -362, 890 |
| p value change from 002 BL | 0.1018 | 0.0282 | 0.0085 | 0.0040 | <0.0001 |
| MMRM p value vs. Group 1 |  | 0.2900 | 0.1831 | 0.2094 |  |
| Abbreviations: 002 = VBP15-002; BL = Baseline; MMRM = mixed model for repeated measures | | | | | |

**Supplemental Table 12. Summary of Morning Cortisol and ACTH (Safety Population).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Group 1  0.25 mg/kg/d  (N = 12) | Group 2  0.75 mg/kg/d  (N = 12) | Group 3 2.0 mg/kg/d (N = 12) | Group 4 6.0 mg/kg/d  (N = 12) | Total  (N = 48) |
| Morning Cortisol (µg/dL) |  |  |  |  |  |
| VBP15-003 Week 24 | (n = 8)\* | (n = 12) | (n = 12) | (n = 9) | (n = 41) |
| Subjects with <100nmol/L (3.6 µg/dL) (%) | 0 | 1 (8.3) | 5 (41.7) | 8 (88.9) | 14 (34.1) |
|  |  |  |  |  |  |
| ACTH (pg/mL) |  |  |  |  |  |
| VBP15-002 Baseline | (n = 12) | (n = 11) | (n = 12) | (n = 12) | (n = 47) |
| Mean | 18.3 | 18.0 | 21.1 | 19.3 | 19.2 |
| SD | 2.96 | 6.88 | 6.13 | 8.67 | 6.39 |
| Median | 19.0 | 15.0 | 21.0 | 17.0 | 18.0 |
| Minimum, Maximum | 13, 23 | 12, 35 | 14, 35 | 11, 45 | 11, 45 |
| VBP15-003 Week 8 | (n = 12) | (n = 12) | (n = 12) | (n = 11) | (n = 47) |
| Mean | 13.0 | 7.1 | 7.8 | 6.5 | 8.6 |
| SD | 6.25 | 5.84 | 4.42 | 5.23 | 5.91 |
| Median | 13.0 | 4.3 | 8.5 | 2.5 | 8.0 |
| Minimum, Maximum | 7, 28 | 3, 21 | 3, 13 | 3, 17 | 3, 28 |
| Week 8 Change from BL | (n = 12) | (n = 11) | (n = 12) | (n = 11) | (n = 46) |
| Mean | -5.3 | -10.5 | -13.3 | -13.5 | -10.6 |
| SD | 6.92 | 9.32 | 7.33 | 7.84 | 8.32 |
| Median | -6.0 | -12.5 | -11.3 | -12.5 | -11.0 |
| Minimum, Maximum | -13, 13 | -33, 1 | -33, -4 | -33, -4 | -33, 13 |
| p value change from 002 BL | 0.0218 | 0.0039 | <0.0001 | 0.0002 | <0.0001 |
| MMRM p value vs. Group 1 |  | 0.0177 | 0.0131 | 0.0048 |  |
| VBP15-003 Week 16 | (n = 12) | (n = 11) | (n = 12) | (n = 9) | (n = 44) |
| Mean | 12.2 | 9.0 | 9.0 | 9.0 | 9.9 |
| SD | 4.93 | 5.86 | 14.18 | 4.49 | 8.45 |
| Median | 12.0 | 6.0 | 5.0 | 10.0 | 7.5 |
| Minimum, Maximum | 6, 22 | 3, 18 | 3, 53 | 3, 14 | 3, 53 |
| Week 16 Change from BL | (n = 12) | (n = 10) | (n = 12) | (n = 9) | (n = 43) |
| Mean | -6.2 | -9.1 | -12.0 | -12.2 | -9.7 |
| SD | 6.34 | 9.89 | 15.42 | 8.16 | 10.63 |
| Median | -7.0 | -9.3 | -13.8 | -9.0 | -9.5 |
| Minimum, Maximum | -13, 7 | -29, 5 | -33, 31 | -31, -4 | -33, 31 |
| p value change from 002 BL | 0.0062 | 0.0177 | 0.0205 | 0.0020 | <0.0001 |
| MMRM p value vs. Group 1 |  | 0.3622 | 0.2865 | 0.3224 |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Group 1  0.25 mg/kg/d  (N = 12) | Group 2  0.75 mg/kg/d  (N = 12) | Group 3 2.0 mg/kg/d (N = 12) | Group 4 6.0 mg/kg/d  (N = 12) | Total  (N = 48) |
| ACTH (pg/mL) |  |  |  |  |  |
| VBP15-003 Week 24 | (n =8) | (n = 12) | (n = 12) | (n = 10) | (n = 42) |
| Mean | 19.8 | 14.0 | 15.7 | 11.3 | 14.9 |
| SD | 6.32 | 3.88 | 9.63 | 7.52 | 7.51 |
| Median | 20.0 | 13.0 | 15.5 | 11.0 | 14.0 |
| Minimum, Maximum | 9, 27 | 9, 22 | 3, 38 | 3, 26 | 3, 38 |
| Week 24 Change from BL | (n = 8) | (n = 11) | (n = 12) | (n = 10) | (n = 41) |
| Mean | 0.6 | -4.0 | -5.4 | -6.3 | -4.1 |
| SD | 6.63 | 5.48 | 11.09 | 7.78 | 8.30 |
| Median | 1.5 | -3.0 | -6.0 | -6.5 | -4.0 |
| Minimum, Maximum | -10, 11 | -17, 2 | -19, 16 | -15, 12 | -19, 16 |
| p value change from 002 BL | 0.7975 | 0.0359 | 0.1214 | 0.0306 | 0.0032 |
| MMRM p value vs. Group 1 |  | 0.0635 | 0.1283 | 0.0114 |  |
| \*Includes early termination value for Subject who early terminated at Week 15.  Abbreviations: 002 = VBP15-002; BL = Baseline; MMRM = mixed model for repeated measures | | | | | |

**Supplemental Table 13. Summary of Insulin Resistance Biomarkers (Safety Population).**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Group 1  0.25 mg/kg/d  (N = 12) | Group 2  0.75 mg/kg/d  (N = 12) | Group 3 2.0 mg/kg/d (N = 12) | Group 4 6.0 mg/kg/d  (N = 12) | Total  (N = 48) |
| **Fasting Glucose (mg/dL)** |  |  |  |  |  |
| VBP15-002 Baseline | (n = 12) | (n = 12) | (n = 12) | (n = 10) | (n = 46) |
| Mean | 87.5 | 88.9 | 89.3 | 92.3 | 89.4 |
| SD | 9.44 | 18.71 | 7.91 | 8.19 | 11.79 |
| Median | 88.5 | 84.5 | 87.0 | 95.0 | 88.0 |
| Minimum, Maximum | 70, 106 | 77, 146 | 81, 101 | 74, 104 | 70, 146 |
| VBP15-003 Week 24 | (n = 10) | (n = 10) | (n = 10) | (n = 11) | (n = 41) |
| Mean | 80.8 | 80.8 | 81.3 | 84.6 | 82.0 |
| SD | 6.56 | 4.08 | 7.94 | 6.53 | 6.41 |
| Median | 82.0 | 82.0 | 80.5 | 84.0 | 82.0 |
| Minimum, Maximum | 71, 90 | 72, 85 | 69, 94 | 76, 94 | 69, 94 |
| Week 24 Change from BL | (n = 10) | (n = 10) | (n = 10) | (n = 10) | (n = 40) |
| Mean | -6.3 | -9.0 | -8.1 | -7.8 | -7.8 |
| SD | 11.97 | 20.87 | 10.28 | 9.44 | 13.40 |
| Median | -9.5 | -1.5 | -8.0 | -6.5 | -6.5 |
| Minimum, Maximum | -24, 13 | -65, 8 | -28, 9 | -22, 6 | -65, 13 |
| p value change from 002 BL | 0.1305 | 0.2058 | 0.0343 | 0.0281 | 0.0007 |
| MMRM p value vs. Group 1 |  | 0.9449 | 0.8944 | 0.3453 |  |
| **Fasting Insulin (µIU/mL)** |  |  |  |  |  |
| VBP15-002 Baseline | (n = 11) | (n = 8) | (n = 12) | (n = 12) | (n = 43) |
| Mean | 5.54 | 3.09 | 3.40 | 3.96 | 4.04 |
| SD | 3.651 | 2.033 | 1.548 | 2.027 | 2.539 |
| Median | 4.50 | 2.35 | 3.35 | 3.65 | 3.50 |
| Minimum, Maximum | 1.7, 14.6 | 1.2, 6.4 | 1.1, 5.6 | 1.7, 9.7 | 1.1, 14.6 |
| VBP15-003 Week 24 | (n = 11) | (n = 9) | (n = 9) | (n = 7) | (n = 36) |
| Mean | 4.23 | 3.12 | 4.82 | 7.21 | 4.68 |
| SD | 2.560 | 1.788 | 3.393 | 2.374 | 2.860 |
| Median | 4.00 | 2.80 | 2.80 | 7.80 | 3.80 |
| Minimum, Maximum | 0.9, 9.2 | 1.1, 6.5 | 1.3, 9.4 | 3.0, 10.6 | 0.9, 10.6 |
| Week 24 Change from BL | (n = 10) | (n = 5) | (n = 9) | (n = 7) | (n = 31) |
| Mean | ‑1.67 | 0.34 | 1.36 | 3.26 | 0.65 |
| SD | 4.478 | 2.898 | 3.262 | 2.862 | 3.893 |
| Median | ‑0.85 | ‑0.60 | 1.20 | 3.30 | 0.00 |
| Minimum, Maximum | -12.4, 3.3 | -3.2, 4.1 | -3.1, 6.6 | -1.2, 8.1 | -12.4, 8.1 |
| p value change from 002 BL | 0.2685 | 0.8060 | 0.2478 | 0.0237 | 0.3635 |
| MMRM p value vs. Group 1 |  | 0.4712 | 0.1414 | 0.0023 |  |
| Abbreviations: 002 = VBP15-002; BL = Baseline; MMRM = mixed model for repeated measures | | | | | |