**Supplemental Digital Content 3, Supplementary Table 3**: Descriptive statistics of Drug Similarity VAS scores at 12 hours post-dose (secondary endpoints; Completer Set)

|  |  |  | **Cebranopadol** | | | **HMO** | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **PBO** | **200 µg** | **400 µg** | **800 µg** | **8 mg** | **16 mg** |
|  | **Statistic** | **(N = 42)** | **(N = 42)** | **(N = 42)** | **(N = 42)** | **(N = 42)** | **(N = 42)** |
| Overall | Mean (SD) | 68.3 (42.16) | 61.0 (40.86) | 58.3 (40.72) | 58.5 (41.67) | 61.4 (41.44) | 70.3 (36.82) |
| familiarity | Median | 100.0 | 75.5 | 64.0 | 76.5 | 78.5 | 92.5 |
| **Drug or Drug Class** | |  |  |  |  |  |  |
| Placebo | Mean (SD) | 78.1 (39.38) | 61.4 (44.59) | 45.1 (47.44) | 22.7 (40.80) | 22.5 (38.78) | 5.5 (21.58) |
|  | Median | 100.0 | 94.0 | 23.5 | 0.0 | 0.0 | 0.0 |
| Codeine | Mean (SD) | 9.4 (23.69) | 13.2 (26.30) | 26.1 (37.27) | 40.5 (43.56) | 37.3 (40.75) | 62.6 (37.28) |
| or morphine | Median | 0.0 | 0.0 | 1.0 | 7.0 | 15.0 | 75.0 |
| Benzodiazepines | Mean (SD) | 13.1 (29.97) | 5.1 (13.64) | 24.9 (37.29) | 34.5 (41.13) | 28.6 (36.91) | 36.1 (42.59) |
|  | Median | 0.0 | 0.0 | 0.0 | 1.0 | 14.0 | 8.0 |

Other drugs tested for drug similarity were caffeine, cocaine, d-amphetamine, ecstasy (NMDA), pseudoephedrine, nicotine, ketamine, THC (results not shown)

HMO = hydromorphone immediate release; N = number of subjects; PBO = placebo (fully randomized only); SD = standard deviation; THC = tetrahydrocannabinol; VAS = visual analog scale.