

**Clinical and Cognitive Improvement Following Full-Spectrum, High-Cannabidiol
Treatment for Anxiety: An Open-Label, Phase 2 Trial**

Supplemental Materials:

Supplemental Table 1. Changes in Mood, Sleep Disturbance, Sexual Dysfunction, and Quality of Life Over the Course of 4 Weeks of Treatment with a High-Cannabidiol (CBD) Sublingual Study Product: Autoregressive Linear Mixed Models (Two-Tailed)

Supplemental Table 2. Pearson Correlations Assessing the Association Between Positive and Negative Expectancies and the Difference Score (Baseline minus Week 4) of Clinical Outcome Variables

Supplemental Table 1. Changes in Mood, Sleep Disturbance, Sexual Dysfunction, and Quality of Life Over the Course of 4 Weeks of Treatment with a High-Cannabidiol (CBD) Sublingual Study Product: Autoregressive Linear Mixed Models (Two-Tailed)

| Clinical Scale | Mixed Model | Baseline <i>n</i> =14 (ref.) | Week 1 <i>n</i> =14 | Week 2 <i>n</i> =14 | Week 3 <i>n</i> =14 | Week 4 <i>n</i> =14 | Baseline to Week 4 |
|--|-------------------------------------|---------------------------------|--|--|--|--|-----------------------|
| | <i>F</i> <i>p</i> (η_p^2) | Mean [95% CI] | Estimate (<i>p</i>) [95% CI] | Estimate (<i>p</i>) [95% CI] | Estimate (<i>p</i>) [95% CI] | Estimate (<i>p</i>) [95% CI] | Percent Change |
| Depression Scales | | | | | | | |
| Beck Depression Inventory (BDI) | 15.72 <.001 (.65) | 20.07 [16.56, 23.58] | -8.43 (<.001) [-11.28, -5.57] | -11.93 (<.001) [-15.59, -8.27] | -13.57 (<.001) [-17.68, -9.46] | -15.64 (<.001) [-20.03, -11.25] | -77.94% |
| Beck Hopelessness Scale (BHS) | 16.06 .001 (.55) | 8.29 [5.83, 10.74] | - | - | - | -5.36 (.001) [-8.25, -2.47] | -64.66% |
| Beck Scale for Suicide Ideation (BSS) | 3.06 .104 (.19) | 0.64 [-0.29, 1.57] | - | - | - | -0.29 (.104) [-0.64, 0.07] | -44.44% |
| Profile of Mood States (POMS) | | | | | | | |
| Total Mood Disturbance | 10.95 <.001 (.63) | 65.86 [51.02, 80.69] | -26.57 (<.001) [-36.05, -17.09] | -36.14 (<.001) [-48.76, -23.52] | -34.93 (<.001) [-49.54, -20.31] | -41.93 (<.001) [-57.95, -25.91] | -63.67% |
| Positive and Negative Affect Schedule (PANAS) | | | | | | | |
| Positive Affect | 1.88 .129 (.14) | 29.36 [25.18, 33.53] | -0.36 (.844) [-3.98, 3.27] | -2.21 (.338) [-6.80, 2.37] | -1.29 (.616) [-6.38, 3.81] | 3.21 (.238) [-2.18, 8.60] | 10.95% |
| Negative Affect | 7.49 <.001 (.44) | 26.21 [22.41, 30.02] | -8.00 (.001) [-12.72, -3.28] | -12.29 (<.001) [-17.51, -7.07] | -11.57 (<.001) [-16.91, -6.23] | -12.71 (<.001) [-18.09, -7.34] | -48.50% |
| Sleep Disturbance | | | | | | | |
| Pittsburgh Sleep Quality Index (PSQI) | 20.27 .001 (.61) | 9.21 [7.57, 10.86] | - | - | - | -3.36 (.001) [-4.97, -1.75] | -36.43% |
| Sexual Dysfunction | | | | | | | |
| Arizona Sexual Experiences Scale (ASEX) ^a | 1.55 .237 (.11) | 15.08 [12.03, 18.12] | - | - | - | -0.54 (.237) [-1.48, 0.40] | -3.57% |
| Medical Outcomes Survey Short Form (SF-36) | | | | | | | |
| Physical Function | 4.10 .064 (.24) | 78.57 [66.17, 90.97] | - | - | - | 5.36 (.064) [-0.36, 11.07] | 6.82% |
| Role Limitations: Physical Health | 2.58 .133 (.17) | 60.71 [39.51, 81.91] | - | - | - | 16.07 (.133) [-5.57, 37.71] | 26.47% |
| Role Limitations: Emotional Problems | 32.50 <.001 (.71) | 26.19 [7.33, 45.05] | - | - | - | 47.62 (<.001) [29.57, 65.67] | 181.82% |
| Energy/Fatigue | 8.50 .012 (.40) | 30.36 [18.54, 42.18] | - | - | - | 16.79 (.012) [4.35, 29.22] | 55.29% |
| Emotional Well-Being | 56.52 <.001 (.81) | 49.14 [42.10, 56.19] | - | - | - | 24.86 (<.001) [17.71, 32.00] | 50.58% |
| Social Function | 37.16 <.001 (.74) | 52.68 [41.57, 63.79] | - | - | - | 29.46 (<.001) [19.02, 39.91] | 55.93% |
| Pain | 4.74 .049 (.27) | 59.82 [45.53, 74.12] | - | - | - | 10.18 (.049) [0.07, 20.28] | 17.01% |
| General Health | 2.98 .108 (.19) | 55.00 [45.93, 64.07] | - | - | - | 6.43 (.108) [-1.61, 14.47] | 11.69% |

Bold numbers are significant at $p \leq .010$ for 5 timepoints and $p \leq .025$ for 2 timepoints.

Significance is only noted for estimates relative to the baseline reference group.

Note: For the BDI, BHS, BSS, POMS, PANAS negative affect, PSQI, and ASEX scales, reduced estimates indicate clinical improvement. For the PANAS positive affect, and SF-36 scales, increased estimates indicate clinical improvement.

^a $n=13$: one patient was not sexually active and therefore did not complete the ASEX

Supplemental Table 2. Pearson Correlations Assessing the Association Between Positive and Negative Expectancies and the Difference Score (Baseline minus Week 4) of Clinical Outcome Variables

| Clinical Outcome Variables | Marijuana Effect Expectancy Questionnaire-Brief (MEEQ-B) | |
|---|--|-----------------------------------|
| | Positive Expectancies | Negative Expectancies |
| Anxiety Scales | | |
| Beck Anxiety Inventory (BAI) | <i>r</i> =.048 <i>p</i> =.871 | <i>r</i> =-.185 <i>p</i> =.526 |
| Overall Anxiety Severity and Impairment Scale (OASIS) | <i>r</i> =-.377 <i>p</i> =.184 | <i>r</i> =-.056 <i>p</i> =.849 |
| Hamilton Anxiety Rating Scale (HAM-A) | <i>r</i> =-.002 <i>p</i> =.994 | <i>r</i> =-.086 <i>p</i> =.770 |
| State-Trait Anxiety Inventory (STAI): State | <i>r</i> =-.125 <i>p</i> =.670 | <i>r</i> =.137 <i>p</i> =.641 |
| State-Trait Anxiety Inventory (STAI): Trait | <i>r</i> =-.161 <i>p</i> =.583 | <i>r</i> =.100 <i>p</i> =.735 |
| Depression Scales | | |
| Beck Depression Inventory (BDI) | <i>r</i> =-.067 <i>p</i> =.820 | <i>r</i> =.043 <i>p</i> =.883 |
| Beck Hopelessness Scale (BHS) | <i>r</i> =-.193 <i>p</i> =.509 | <i>r</i> =.265 <i>p</i> =.360 |
| Beck Scale for Suicide Ideation (BSS) | <i>r</i> =.283 <i>p</i> =.328 | <i>r</i> =-.274 <i>p</i> =.343 |
| Profile of Mood States (POMS) | | |
| Total Mood Disturbance | <i>r</i> =-.267 <i>p</i> =.356 | <i>r</i> =.186 <i>p</i> =.524 |
| Positive and Negative Affect Schedule (PANAS) | | |
| Positive Affect | <i>r</i> =.148 <i>p</i> =.613 | <i>r</i> =-.352 <i>p</i> =.217 |
| Negative Affect | <i>r</i> =-.017 <i>p</i> =.953 | <i>r</i> =-.168 <i>p</i> =.566 |
| Sleep Disturbance | | |
| Pittsburgh Sleep Quality Index (PSQI) | <i>r</i> =.136 <i>p</i> =.644 | <i>r</i> =.177 <i>p</i> =.545 |
| Sexual Dysfunction | | |
| Arizona Sexual Experiences Scale (ASEX) ^a | <i>r</i> =-.432 <i>p</i> =.140 | <i>r</i> =-.625 <i>p</i> =.022 |
| Medical Outcomes Survey Short Form (SF-36) | | |
| Physical Function | <i>r</i> =.400 <i>p</i> =.157 | <i>r</i> =-.426 <i>p</i> =.128 |
| Role Limitations: Physical Health | <i>r</i> =.563 <i>p</i> =.036 | <i>r</i> =-.282 <i>p</i> =.329 |
| Role Limitations: Emotional Problems | <i>r</i> =.371 <i>p</i> =.191 | <i>r</i> =-.148 <i>p</i> =.615 |
| Energy/Fatigue | <i>r</i> =.501 <i>p</i> =.068 | <i>r</i> =-.056 <i>p</i> =.849 |
| Emotional Well-Being | <i>r</i> =.083 <i>p</i> =.779 | <i>r</i> =.014 <i>p</i> =.962 |
| Social Function | <i>r</i> =.227 <i>p</i> =.436 | <i>r</i> =.079 <i>p</i> =.788 |
| Pain | <i>r</i> =.191 <i>p</i> =.514 | <i>r</i> =.224 <i>p</i> =.442 |
| General Health | <i>r</i> =.429 <i>p</i> =.126 | <i>r</i> =-.437 <i>p</i> =.118 |

Unless otherwise noted, n=14

Bold numbers are significant at $p \leq .010$ ^a n=13: one patient was not sexually active and therefore did not complete the ASEX