Title: Efficacy of a Nonhormonal Neurokinin B Inhibiting Supplement for Reducing Vasomotor Symptoms

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Objective: The primary objective was to evaluate the effects of a nonhormonal, botanical blend (VMS-BH02; Thermella™), on hot flashes and night sweats in women who experience menopausal vasomotor symptoms (VMS). Preclinical studies showed that the combination of these ingredients synergistically inhibited the neurokinin B pathway and did not raise estrogen levels nor induce cell proliferation in MCF-7 cells. This was the first clinical study conducted to evaluate clinical benefits.

Design: This is an ongoing open-label study in women 45-65 years of age. Thirty peri- and post-menopausal women were recruited if they reported a daily average of 5 or more VMS, regardless of severity. Participants were instructed to consume 2 capsules of the supplement daily. To date, participants have completed 8 weeks. The primary endpoint was the percent change in total VMS, collected using daily diaries. Secondary endpoints were assessed using various validated monthly questionnaires including the Menopause Specific Quality of Life (MENQOL), the Hot Flash Related Daily Interference Scale (HFRDIS), the Greene Climacteric Scale (GCS), and the Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b (PROMIS). Participants completed all questionnaires at Baseline, and weeks 2, 4, and 8, with the exception of the MENQOL, which was not administered at week 2.

Results: Thirty women completed 8 weeks (55.5 ± 3.7 yrs) of supplementation. There was a significant decrease in self-reported total VMS occurrences (all severities) noted across the time points (Baseline: 10.7 ± 6.0; Week 4: 6.2 ± 4.2; Week 8: 5.1 ± 4.4; $p < 0.01$). Combined, moderate and severe hot flashes were significantly decreased at all weeks when compared to baseline (Baseline: 5.1 ± 2.6; Week 4: 2.9 ± 2.6; Week 8: 2.5 ± 2.9; $p < 0.01$). Night sweats significantly decreased from baseline at weeks 4 and 8 (Baseline: 2.9 ± 2.1; Week 4: 1.5 ± 1.2, $p = 0.002$; Week 8: 1.4 ± 1.3, $p < 0.01$). Significant improvements were also noted in the MENQOL total sum at weeks 4 and 8 compared to baseline (Baseline: 3.8 ± 1.2; Week 4: 3.0 ± 1.1; Week 8: 2.7 ± 1.4; $p < 0.01$), the HFRDIS total sum at all timepoints compared to baseline (Baseline: 42.7 ± 18.2; Week 2: 31.03 ± 18.3; Week 4: 26.1 ± 20.4; Week 8: 18.4 ± 18.4; $p < 0.001$), and the GCS total sum at weeks 2, 4, and 8 compared to baseline (Baseline: 20.3 ± 8.6; Week 2: 16.3 ± 8.3, $p < 0.001$; Week 4: 14.1 ± 8.5, $p = 0.001$; Week 8: 12.5 ± 10.3, $p < 0.001$). There were also significant improvements in PROMIS total score at weeks 2, 4, and 8 compared to baseline (Baseline: 30.3 ± 7.0; Week 2: 26.4 ± 8.3; Week 4: 25.5 ± 8.1; Week 8: 23.4 ± 8.3; $p < 0.01$).

Conclusion: The eight-week daily supplementation with Thermella™, which has a high affinity for inhibition of the NK3 receptor, resulted in significant and consistent reductions in vasomotor symptoms, including hot flashes and night sweats. These improvements were observed as early as two weeks into

the study and continued throughout the investigation period. Notably, the frequency and severity of these symptoms decreased over time. Supplementation also showed positive effects on menopause-specific quality of life related outcomes and sleep disturbances. Overall, these findings underscore the promising clinical efficacy of this novel botanical blend in effectively managing vasomotor symptoms experienced by women throughout their menopausal transition.

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