Effects of COMP360 on Anhedonia-Related Items of the Montgomery-Asperg Depression Rating Scale (MADRS) and Positive and Negative Affect Scales (PANAS)

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Request for Proposals Psychedelics

Abstract: Background: Both depressed mood and anhedonia are core symptoms for diagnosis of major depressive disorder (MDD). Although patients voice the importance of improvements in anhedonia and positive affect, both pharmacological and non-pharmacological antidepressant treatments (ADT) have historically addressed negative affect better than positive affect, and anhedonia is a common residual symptom in treatment-resistant depression (TRD). Recent studies suggest that psilocybin may impact anhedonia symptoms in individuals with TRD, including a 233-patient randomized controlled double-blind study of investigational COMP360 psilocybin (COMP 001). To address the paucity of data on the effects of psilocybin on measures of anhedonia, we undertook additional post-hoc analyses of data from the COMP 001 study.

Methods: Data from COMP 001 were used to assess the effect of 25 mg, 10 mg or 1 mg (n=79, 75, 79; N=233) investigational COMP360 psilocybin on items of the Montgomery-Asperg Depression Rating Scale (MADRS) and the Positive and Negative Affect Scales (PANAS) most relevant to anhedonia. These include the MADRS Anhedonia Factor (MADRS-AF; Items 1, 2, 6, 7, 8) and the PANAS positive (PANAS-P) scale, which correlate with changes on the Snaith-Hamilton Pleasure Scale (SHAPS) and/or the Dimensional Anhedonia Rating Scale (DARS). For MADRS-AF, least squares (LS) mean change from baseline (CFB) are reported for Day 2 and Weeks 1, 3, 6 and 12 after treatment administration (Day 1). For PANAS total scores, LS mean CFB is reported for Day 2 and Week 3. Mean CFBs are also reported for individual items of the MADRS-AF and PANAS-P at the same time points as their respective total scores. All analyses were conducted on observed cases without explicit imputations for missing data or control over Type-I error.

Results: Mean CFB MADRS-AF total score was numerically greater in the 25 mg group than the 10mg and 1mg groups at 1 day, 1 week, 3 weeks and 6 weeks after a single administration of COMP360. Mean CFB in MADRS-AF total score in the 25mg group stabilized from Week 1 to Week 12. Numerically greater mean CFB in all 5 items of the MADRS-AF were observed in the 25 mg

group compared to the 10 mg and 1 mg groups up to Week 12. The LS Mean Difference in CFB between 25 mg and 1 mg in MADRS-AF total score were nominally significant at Day 2 (LS Mean Difference [95% Confidence Interval] (-3.9 [-6.2, -1.7]), Week 1 (-4.2 [-6.3, -2.0]), Week 3 (-4.3 [-6.4, -2.1]) and Week 6 (-2.6 [-4.9, -0.3]). Numerically greater LS Mean CFB differences were seen at Week 9 and 12 for the COMP360 25 mg vs 1 mg comparisons, but these were not nominally significant. The mean difference CFB at Day 2 and Week 3 demonstrated numerical superiority of 25 mg but not 10 mg over 1 mg for both PANAS-P and PANAS-N total scores. For PANAS-P, the LS mean differences in CFB between the 25 mg and 1 mg groups were 6.3 (95% confidence interval [CI] [3.4, 9.2]) at Day 2 and 6.2 (95% CI [3.5, 8.8]) at Week 3. For PANAS-N, the LS mean differences in CFB between the 25 mg and 1 mg groups were -3.3 (95% CI [-5.3, -1.2]) at Day 2 and -3.2 (95% CI [-5.6, -0.8]) at Week 3. Only the 25mg group sustained improvements the day after treatment at Week 3. Individual items most improved in 25mg group compared to the 10mg or 1mg group included ‘Interested’, ‘Enthusiastic’, ‘Inspired’, ‘Proud’, and ‘Determined’

Conclusion: In a post-hoc analysis of a large (N=233) Phase 2b study of participants with TRD, treatment with COMP360 25 mg improved items of the MADRS and PANAS that are most relevant to anhedonic symptoms of depression. COMP360 25 mg appeared to have nominally greater efficacy than 10 and 1 mg, suggesting a dose-related effect. Given the post-hoc nature of this analysis, future studies should prospectively study these effects.

Learning Objectives:

Learning Objective 1 Impact of COMP360 psilocybin on measures of anhedonia in patients with treatment resistant depression

Learning Objective 2 Impact of COMP360 psilocybin on measures of positive affect

DISCLOSURE

Financial Relationships

Disclosure Yes, I do have a financial relationship(s) to disclose.

Financial Relationships Details

Ineligible Company	Type of Financial Interest
Compass Pathways, PLC	Employee, Stock Shareholder