Cognitive Performance and Adverse Effects Following Single and Multiple Ascending Doses of a New Cannabis Formulation (PPP001) Administered by Smoking/Inhalation in Male and Female Volunteers

Beatrice Setnik1, Jade Huguet1, Catherine Mills1, Randy Ringuette2, Charles Campbell1, Aurelia De Pauw2, Eric Sicard1, Guy Chemberland2

1Altasciences, Quebec, Canada; 2Tiera Bio-Pharma, Quebec, Canada

Abstract
Background: PPP001 is a novel cannabis product for medical indication, being developed for the treatment of chronic pain. It is a low-THC (1.4% THC), high-CBD (6% CBD) with a high CBD/CBDv (1:4) ratio and a novel ratio of 1:50 of tetrahydrocannabinol-9-carboxylic acid (THCA) over THC. An increasing number of cannabis users are reporting subjective and cognitive impairment upon smoking PPP001. The objective of this study was to evaluate the safety, tolerability, and cognitive effects of PPP001 in healthy volunteers, and to determine the no-observed-adverse-effect level (NOAEL) of PPP001 administration via smoked inhalation over 1 to 7 consecutive days (including 5-Day inhaled). Only the cognitive effects of PPP001 are discussed in this presentation.

Objectives
The objectives of this study were to evaluate the safety, tolerability, and cognitive effects of PPP001 with smoked inhalation in healthy male and female volunteers. The study was conducted in two parts (A and B).

Methods

Part A: Single Dose Study – Design and Single and Multiple Ascending Dosing of PPP001 Formulation

- **Subjects:** 21 healthy male and female volunteers (13 males and 8 females) with a mean age of 26.1 ± 4.7 years.
- **Design:** Single dose study with escalating doses of PPP001 formulation (100 mg THC/300 mg CBD/puff).
- **Procedure:** Volunteers smoked PPP001 formulation using a custom-designed smoking device. Cognitive and psychomotor performance was assessed using computerized tasks validated by Cambridge Cognition and psychometric properties of CANTAB.

Results (Abstract)

- **Cognitive and Psychomotor Performance:** Following single dose administration of PPP001, there were no significant changes observed in cognitive performance compared to placebo across Part A.
- **Subjective Effects:** PPP001 formulation is not expected to accentuate the observed impairment on cognitive performance as compared to placebo.

Part B: Dose-Dependent Study – Design and Single and Multiple Ascending Dosing of PPP001 Formulation

- **Subjects:** 70 healthy male and female volunteers (43 males and 27 females) with a mean age of 25.8 ± 5.3 years.
- **Design:** Dose-Dependent Study (73.75 mg THC/211 mg CBD/puff, 100 mg THC/300 mg CBD/puff, 150 mg THC/450 mg CBD/puff).
- **Procedure:** Volunteers smoked PPP001 formulation using a custom-designed smoking device. Cognitive and psychomotor performance was assessed using computerized tasks validated by Cambridge Cognition and psychometric properties of CANTAB.

Results (Abstract)

- **Cognitive and Psychomotor Performance:** For Part B, cognitive effects were observed following administration of PPP001. The highest effect was seen with the 150 mg THC/450 mg CBD dose, with the lowest effect seen with the 73.75 mg THC/211 mg CBD dose. The differences between placebo and active treatment were lower for Part A, single day of exposure compared to Part B, multiple-day exposure.
- **Subjective Effects:** PPP001 formulation is not expected to accentuate the observed impairment on cognitive performance as compared to placebo.

Conclusion
In general, the differences between placebo and active treatment were lower for Part A, single day of exposure compared to Part B, multiple-day exposure. The reduction in the magnitude of the observed impairment on cognitive performance is consistent with the low sample size, therefore it is suggested to interpret these results with great caution.

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