Neuropsychological Effects of ZYN002 (Synthetic Cannabidiol) Transdermal Gel in Healthy Subjects and Patients With Epilepsy: Phase 1, Randomized, Double-Blind, Placebo-Controlled Studies

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Background
- Cannabinoid (CBD), the main non-psychotropic component of cannabis, has shown initial therapeutic efficacy in a myriad of chronic medical conditions, including epilepsy.
- Early clinical work has indicated that CBD does not elicit euphoric or negative neuropsychological effects commonly associated with Δ9-tetrahydrocannabinol (THC).
- ZYN002 is the first and only patent-protected permeation-enhanced synthetic CBD gel, formulated for transdermal delivery.
- Due to limitations of existing CBD studies (e.g., not well controlled; oral routes of administration, which can convert to THC in an acidic environment), the potential neuropsychological effects of ZYN002 are unknown.

Objective
- To characterize the neuropsychological effects of ZYN002, a synthetic CBD transdermal gel, in healthy subjects and patients with epilepsy.

Methods
- Phase 1, 7-day randomized, double-blind, placebo-controlled study in (1) healthy adults and (2) epilepsy patients
- Healthy Adults - Multiple-dose study with 4 treatment groups:
  - Placebo (N=18)
  - 250 mg/10 mL, 1% ZYN002 BID (N=18)
  - 250 mg/10 mL, 1.5% ZYN002 BID (N=18)
  - 500 mg/10 mL, 1.5% ZYN002 BID (N=18)
- Epilepsy Patients (EPI) - 2 treatment groups:
  - Placebo (N=3)
  - 500 mg/d, 10 g x 2.5% ZYN002 BID (N=6)
- Treatment was applied to clean, dry, intact skin of the upper arms and shoulders.

Assessments:
- Trail Making Test (visual attention and task switching)
- Stroop Color-Word Interference Test (information processing)
- Delays Depression (25 items)
- Positive and Negative Affect Schedule (14 items)
- Inventory of Depression and Anxiety Symptoms

Results
- Repeated Measures ANCOVAs were conducted for time, dose, and dose by time interactions (key measures of drug effect).
- Among healthy adults, study drug did not impact the speed or flexibility that participants processed information over time. However, among epilepsy patients, there was a non-significant trend toward improved performance among those who received ZYN002 over time.

Conclusions
- Results indicate that ZYN002 does not produce impairment in critical areas of cognitive functioning often impacted by CNS drugs in healthy subjects and patients with epilepsy.
- Results also indicate that ZYN002 is not associated with declines in psychological health in healthy subjects and patients with epilepsy.
- Unlike THC, ZYN002 may provide therapeutic benefit for chronic medical conditions while minimizing neuropsychological risk.

References

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