**BACKGROUND**

- Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by difficulties with behaviors, communication, and reciprocal social interaction.
- Current management options for symptoms of ASD are restricted to behavioral therapies and a limited number of approved pharmacologic treatments, which have been associated with serious potential adverse effects.
- There is therefore substantial unmet need for novel therapies in this population.
- The endocannabinoid system (ECS) is found in diverse species, indicating that it is highly evolutionarily conserved, and may play central roles in physiology and pathophysiology.
- Evidence indicates that the ECS has an important role in the central nervous system (CNS) and appears to regulate neuronal development and function, particularly synaptic homeostasis and plasticity, and may be a key modulator of emotion and social behavior that is dysregulated in ASD.
- It is therefore reasonable to explore the question of whether cannabidiol may have broader effects on multiple behavioral target symptoms in ASD; however, the efficacy and safety of cannabidiol in patients with ASD have not been well established.
- **BRIGHT**, ZYN002 (42%) vs placebo (P<0.0001) (Figure 2) and the AIM (19%) to 38% across domains; Ps<0.0001 (Figure 3).

**METHODS**

- The trial enrolled patients with an Aberrant Behavior Checklist-Community (ABC)-C subscale scores of 15 or higher (moderate or greater).
- Primary objective: To evaluate the safety and tolerability of ZYN002 for up to 38 weeks (14-week treatment period [Period 1] and a 24-week extension period [Period 2]).
- Safety assessments included adverse events (AEs), skin assessments, laboratory tests, and electrocardiograms (ECGs).
- The primary efficacy assessment included ABC-C and CGI-I.
- Secondary objectives comprised evaluation of the efficacy of ZYN002 in the treatment of symptoms of ASD, including measuring parental/caregiver stress index (APSI), Parent Rated Anxiety Scale (PRAS), Autistic Impact Measure (AIM), and qualitative caregiver-reported behavioral problems, assisting us to appreciate the voice of the patient and family.
- Patients received ZYN002 250 mg or 500 mg (weight-based dose) daily for up to 38 weeks in addition to stable standard of care medications (including antipsychotics and/or anticonvulsants), when prescribed.
- Patients demonstrating >25% improvement in the ABC-C irritability subscale at week 14 were allowed to continue treatment for an additional 24 weeks.

**OBJECTIVE**

- To examine longer-term safety, tolerability, and efficacy of ZYN002 in BRIGHT treatment responders through 38 weeks.

**RESULTS**

- The baseline demographics were similar between the overall population in Period 1 and patients who entered Period 2.
- At week 38, improvements were demonstrated in the ABC-C subscale scores (50% to 61% across domains; Ps<0.0001; Figure 1), the PRAS-ASD (42%; Ps<0.0001) (Figure 2) and the AIM (19%) to 38% across domains; Ps<0.0001 (Figure 3).

**OVERALL SAFETY/ TOLERABILITY**

- **ZYN002** was generally well tolerated, and the safety profile was consistent with data from previous **ZYN002** clinical trials.
- Over the 38-week treatment period, slightly more than half (54.1%) of patients experienced any AE (whether unrelated or related to study drug).
- Throughout the trial, all AEs were mild (80%) or moderate (20%) and transient.
- Only 7 patients (19%) experienced an AE that was deemed to be treatment-related.
- Of the 10 treatment-related AEs reported, 7 were application-site-related (application site reaction, pruritus, and dryness), 1 patient experienced a sleep disorder, 1 patient had an increased appetite, and 1 patient experienced photophobia.
- There were no severe or serious AEs reported during the trial.
- There were no clinically significant changes in vital signs, laboratories, or ECG parameters.

**SUMMARY AND CONCLUSIONS**

- The **BRIGHT** trial provides initial evidence suggesting a positive benefit-risk profile for **ZYN002** when administered in addition to stable standard of care in children and adolescents with moderate-to-severe ASD.
- **ZYN002**-induced improvement in all ASD efficacy measures (ABC-C, AIM, PRAS-ASD, CGI-I).
- Further controlled studies are warranted in this difficult-to-treat population.

**REFERENCES**


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