# Phase 2 BRIGHT (an Exploratory Open-Label Tolerability and Efficacy Study of ZYN002 Administered as a Transdermal Gel to Children and Adolescents With Autism Spectrum Disorder): Baseline Characteristics

**Helen Heussler,[1,2] Michael Duhig,[1,2] Terry Hurst,[3] Carol O'Neill,[4] Wendy Agnese,[4] Joseph M. Palumbo[4]**

[1]Centre for Clinical Trials in Rare Neurodevelopmental Disorders (CCTRND), Children's Health Queensland, Brisbane, QLD, Australia;
[2]Centre for Child Health Research, University of Queensland, Brisbane, QLD, Australia; [3]Zynerba Pharmaceuticals, Pty Ltd, Brisbane, QLD, Australia; [4]Zynerba Pharmaceuticals, Devon, PA, USA

## BACKGROUND

- Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by difficulties with behaviors, communication, and reciprocal social interaction[1,2]
  - Initial signs and symptoms of ASD may appear in the first 6-12 months of life, and the disorder can be clinically diagnosed by age 2 years[2]
- In an analysis of the 2011 Survey of Pathways to Diagnosis and Services, rates of parent-reported mild, moderate, and severe ASD were 50.3%, 37.9%, and 11.8%, respectively[3]
- Patients with ASD of any severity require long-term supportive care, and ASD imposes considerable economic and medical burdens on patients and caregivers[1,4]
- Adding to disease burden, patients with ASD frequently experience comorbid conditions including anxiety disorders[1,5]
- Current management options for ASD symptoms are restricted to cognitive behavioral therapy and a limited number of approved pharmacologic treatments, highlighting the substantial unmet need for novel therapies in this population[2]
- As the endocannabinoid system—a key modulator of emotion and social behavior—is dysregulated in ASD, cannabidiol (CBD) may provide therapeutic benefit; however, the efficacy and safety of CBD in patients with ASD have not been well established[6]
- ZYN002 is a pharmaceutically manufactured transdermal CBD gel currently in clinical development for the treatment of behavioral symptoms in ASD

## OBJECTIVES

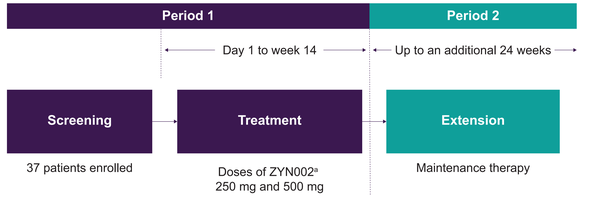
- To describe the baseline demographic and clinical characteristics of the study population (n = 37 patients) with ASD enrolled in BRIGHT

## METHODS

### STUDY DESIGN AND TREATMENT

- BRIGHT is a 14-week, phase 2, open-label, single-center study being conducted in Australia with a 24-week open-label extension (**Figure 1**)

**Figure 1. BRIGHT study design.**




ABC-C, Aberrant Behavior Checklist–Community.

[a]Total daily dose, administered twice daily. Dose is dependent on body weight. The investigator may increase dosage at week 6 in patients with <25% improvement from baseline in ABC-C Irritability Subscale score.

### PATIENTS

- Key inclusion criteria
  - Male or female patients aged 4 through 17 years
  - Confirmed diagnosis of ASD by *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition, criteria
  - Clinical Global Impression–Severity score ≥4
  - Aberrant Behavior Checklist–Community (ABC-C) Irritability Subscale score ≥18
- Key exclusion criteria
  - Use of any tetrahydrocannabinol- or CBD-containing product ≤3 months before screening
  - Diagnosed with a genetic disorder (eg, Fragile X syndrome, Rett syndrome)
  - Primary psychiatric diagnosis of a condition other than ASD or anxiety
  - Treated with >2 psychoactive medications at screening or during study

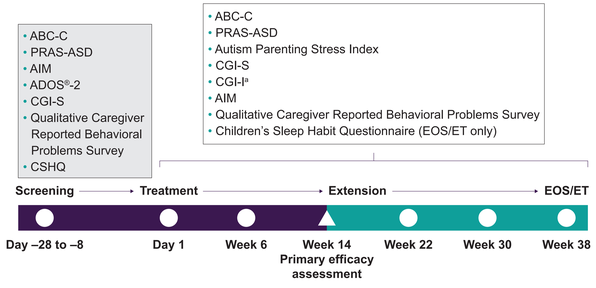
### STUDY OBJECTIVES

- Primary objective
  - To evaluate the safety and tolerability of transdermal ZYN002 in the treatment of symptoms of ASD in patients aged 4 through 17 years
- Secondary objectives
  - To evaluate the efficacy of ZYN002 in the treatment of symptoms of ASD
  - To evaluate CBD and tetrahydrocannabinol plasma level exposure
- Exploratory objective
  - To identify plasma levels of CBD metabolite(s)

### EFFICACY ASSESSMENTS

- Efficacy assessments administered at screening and throughout the study will provide information regarding the baseline severity of ASD and anxiety symptoms and their improvement with treatment (**Figure 2**, **Table 1**)
- At week 14, change in ABC-C Irritability Subscale score (primary efficacy assessment) will be evaluated

**Figure 2. Schedule of screening and efficacy assessments.**




ABC-C, Aberrant Behavior Checklist–Community; ADOS®-2, Autism Diagnostic Observation Schedule®, 2nd edition; AIM, Autism Impact Measure; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impression–Severity; CSHQ, Children's Sleep Habit Questionnaire; EOS, end of study; ET, end of treatment; PRAS-ASD, Parent Rated Anxiety Scale–Autism Spectrum Disorder.

[a]Not completed on day 1.

**Table 1. Key Scales Used for Screening and Efficacy Assessment in BRIGHT**

| Assessment | Description |
|---|---|
| ABC-C[7] | • 58-item caregiver-rated scale measuring behaviors across 5 subscales: irritability/agitation (maximum score: 45), lethargy/social withdrawal (maximum score: 48), stereotypic behavior (maximum score: 21), hyperactivity/noncompliance (maximum score: 48), inappropriate speech (maximum score: 12)<br>• Each behavior is scored from 0 ("not at all a problem") to 3 ("the problem is severe in degree")<br>• Higher scores indicate greater severity of aberrant behavior |
| ADOS®-2[8-11] | • Diagnostic tool consisting of 5 age- and verbal ability–dependent modules that assess social communication and core behaviors of ASD<br>• Each item is scored by a trained test administrator from 0 ("no abnormality of type specified") to 3 ("moderate to severe abnormality")<br>• ADOS total scores are diagnostic; however, standardized comparison scores can be used to measure severity<br>• Comparison scores range from 0-10, with scores of <5 indicating mild ASD, scores of 5-7 indicating moderate ASD, and scores of 8-10 indicating severe ASD |
| PRAS-ASD[12,13] | • 25-item parent-rated scale assessing anxiety in ASD<br>• Each item is scored from 0 ("not present") to 3 ("very frequent and a major problem")<br>• Maximum score is 75, with scores >52 indicating possible clinical anxiety |

ABC-C, Aberrant Behavior Checklist–Community; ADOS®-2, Autism Diagnostic Observation Schedule®, 2nd edition; PRAS-ASD, Parent Rated Anxiety Scale–Autism Spectrum Disorder.

## RESULTS

### BASELINE DEMOGRAPHICS

- BRIGHT enrolled 37 patients, the majority of whom are male (91.9%) and white (75.7%), with a mean age of 9.2 years (**Table 2**)

**Table 2. Baseline Demographics of Patients Enrolled in BRIGHT**

| Demographic | BRIGHT Patients N = 37 |
|---|---|
| Age, years | |
| Mean (range) | 9.2 (3-16) |
| Sex, n (%) | |
| Male | 34 (91.9) |
| Female | 3 (8.1) |
| Race, % | |
| White | 75.7 |
| Aboriginal | 5.4 |
| Asian | 8.1 |
| Other | 10.8 |

### DISEASE CHARACTERISTICS

- The majority of patients had moderate or severe ASD at baseline as measured by the ADOS®-2 comparison score (94.4%) and *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition, severity levels (91.9%) (**Table 3**)
- The mean ABC-C Irritability score was 30.0, and 9 patients (24.3%) had PRAS-ASD scores indicative of possible clinical anxiety, further highlighting the severity of symptoms in the enrolled patient population

**Table 3. Baseline Disease Characteristics of Patients Enrolled in BRIGHT**

| Disease Characteristic | BRIGHT Patients N = 37 |
|---|---|
| ABC-C Irritability Subscale score | |
| n | 37 |
| Mean (range) | 30.0 (18-43) |
| PRAS-ASD score | |
| n | 37 |
| Mean (range) | 40.9 (21-68) |
| >52, n (%) | 9 (24.3) |
| DSM-5 severity level[a] | |
| Level 1 (mild), n (%) | 3 (8.1) |
| Level 2 (moderate), n (%) | 15 (40.5) |
| Level 3 (severe), n (%) | 19 (51.4) |
| ADOS®-2 total score | |
| n | 36[b] |
| Mean (range) | 17.5 (7-25) |
| ADOS®-2 comparison score | |
| n | 36[b] |
| Mean (range) | 7.5 (4-10) |
| <5, n (%) | 2 (5.6) |
| 5-7, n (%) | 19 (52.8) |
| 8-10, n (%) | 15 (41.7) |

ABC-C, Aberrant Behavior Checklist–Community; ADOS®-2, Autism Diagnostic Observation Schedule®, 2nd edition; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition; PRAS-ASD, Parent Rated Anxiety Scale–Autism Spectrum Disorder.

[a]DSM-5 severity levels are based on degree of social communication impairment and behavioral flexibility. The levels indicate patients "requiring support" (level 1), "requiring substantial support" (level 2), and "requiring very substantial support" (level 3).[2]
[b]One patient had missing data.

## CONCLUSIONS

- BRIGHT is an ongoing, exploratory, phase 2, open-label study to evaluate the safety, tolerability, and efficacy of ZYN002 in children and adolescents with ASD, a patient population with high unmet needs
- BRIGHT enrolled a broad and inclusive patient population and was enriched for disease severity to avoid floor effects on outcome measures
- Baseline characteristics indicate a patient population with predominantly moderate-to-severe ASD, with a high burden of anxiety

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