

Longer Term Tolerability and Efficacy of ZYN002 Cannabidiol Transdermal Gel in Children and Adolescents with Autism Spectrum Disorder (ASD): An Open-Label Phase 2 Study (BRIGHT [ZYN2-CL-030])

Helen Heussler^{1,2}, Michael Duhig^{1,2}, Terry Hurst³, Carol O'Neill⁴, Donna Gutterman⁴, Joseph M. Palumbo⁴

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

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Disclaimers

- This presentation is intended to communicate scientific and medical information about data from clinical trials involving ZYN002. ZYN002 is an experimental treatment which has not been approved by any government regulatory bodies, including the United States Food and Drug Administration (FDA), and has not been determined by the FDA to be a safe or effective treatment for any disease or condition. This presentation is not designed or intended to promote the use of ZYN002 or any other Company product in order to impact prescribing.
- This slide presentation is based on an abstract submitted and accepted for presentation at the 2021 annual meeting of the American Academy of Child and Adolescent Psychiatry.

Background

- Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by difficulties with behaviors, communication, and reciprocal social interaction^{1,2}
- 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 population²
- The endocannabinoid system is a key modulator of emotion and social behavior and is dysregulated in ASD³
- It is therefore possible that cannabidiol may provide therapeutic benefit in ASD; however, the efficacy and safety of cannabidiol in patients with ASD have not been well established³
- BRIGHT (ZYN2-CL-030) is an exploratory, single-center, open-label, Phase 2 study evaluating the safety and tolerability and efficacy of ZYN002 in children and adolescents with ASD who are 3 to <18 years old
- ZYN002 is a pharmaceutically manufactured transdermal cannabidiol gel

1. Masi A et al. *Neurosci Bull.* 2017;33(2):183-193.

2. Sanchack KE, Thomas CA. *Am Fam Physician.* 2016;94(12):972-979.

3. Poleg S et al. *Prog Neuropsychopharmacol Biol Psychiatry.* 2019;89:90-96.

Methods

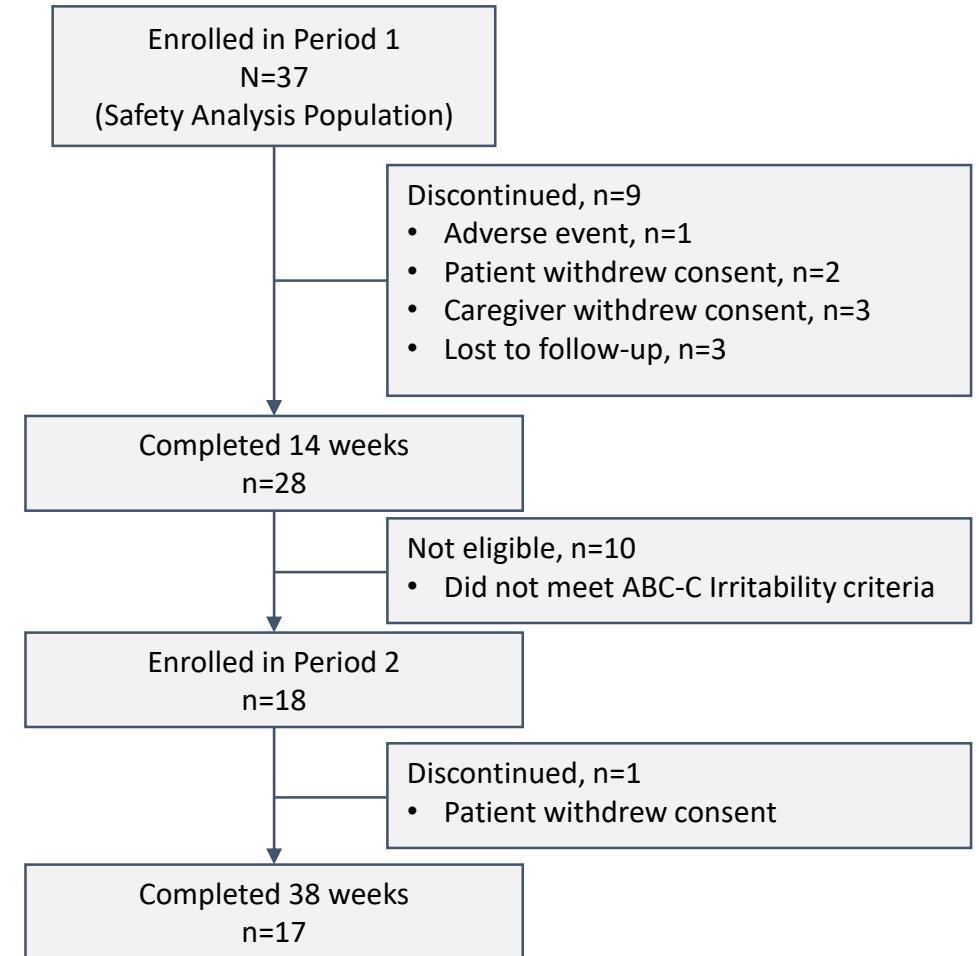
- The study enrolled patients with an Aberrant Behavior Checklist-Community (ABC-C) Irritability score ≥ 18 and a Clinical Global Impression (CGI)–Severity score ≥ 4 (moderate or greater)
- Primary objective: To evaluate the safety and tolerability of ZYN002 for up to 38 weeks (14-week treatment period [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 assessments included ABC-C and CGI
- Secondary objectives comprised evaluation of the efficacy of ZYN002 in the treatment of symptoms of ASD, including measuring parental/caregiver stress (APSI[†]), Parent Rated Anxiety Scale (PRAS), Autism 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 antipsychotic agents, when prescribed)
- Patients demonstrating $\geq 35\%$ improvement in the ABC-C irritability subscale at week 14 were allowed to continue treatment for an additional 24 weeks
- The focus of this presentation is data from patients who entered Period 2 and completed 38 weeks of treatment

[†]APSI=Autism Parenting Stress Index.

Baseline Demographics and Patient Disposition

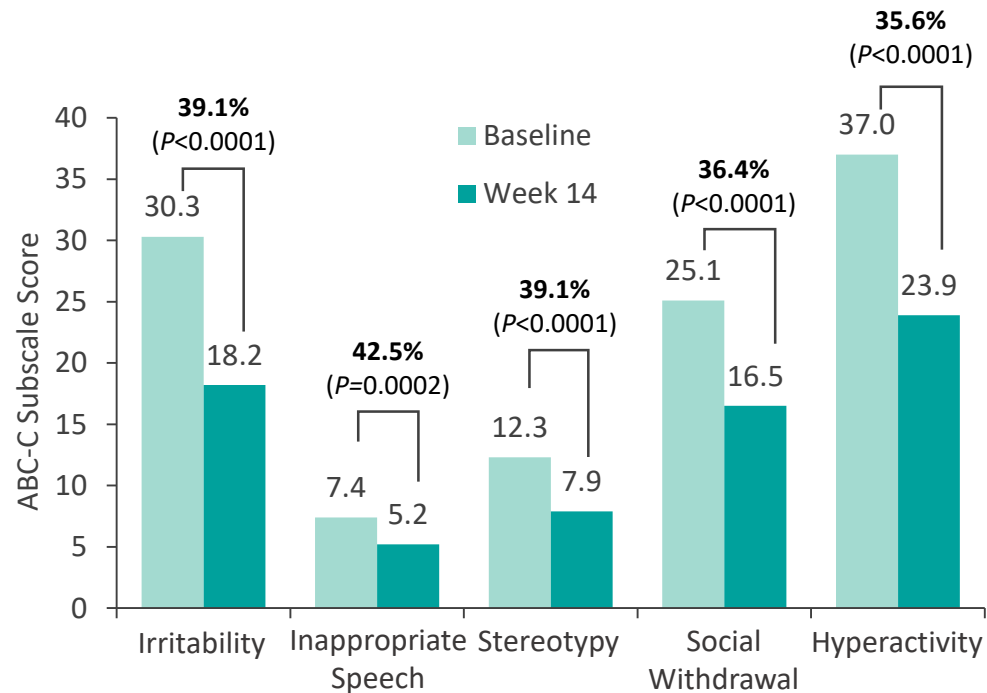
Demographics were similar for patients in Period 1 and Period 2

Characteristic	BRIGHT Participants Period 1 N=37	BRIGHT Participants Period 2 n=18
Age, mean years (range)	9.2 (3-16)	9.2 (3-16)
Sex, n (%)		
Male	34 (91.9)	16 (89)
Female	3 (8.1)	2 (11)
Race, %		
White	75.7	77.8
Indigenous Australian	5.4	0
Asian	8.1	5.6
Other	10.8	16.7

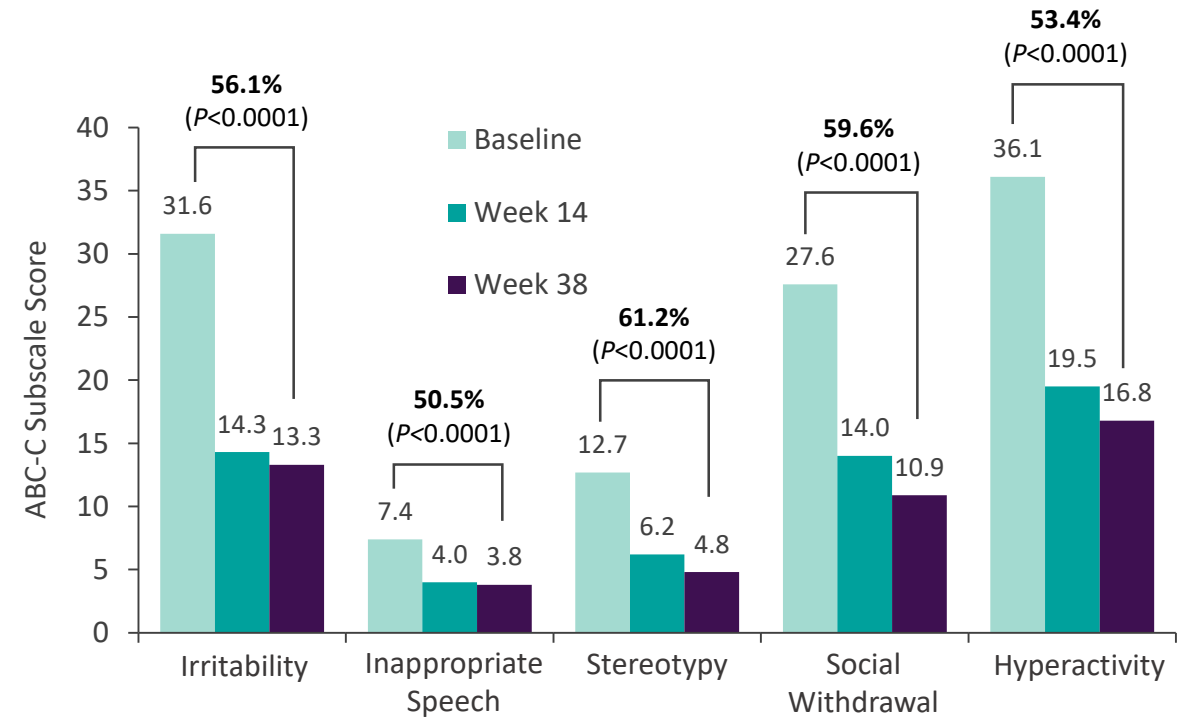


Efficacy: Statistically Significant Improvements From Baseline in all ABC-C Subscale Scores* Sustained Through Week 38

Mean Scores and Percent Improvement Period 1
(n=28 [n=26 for Inappropriate Speech])



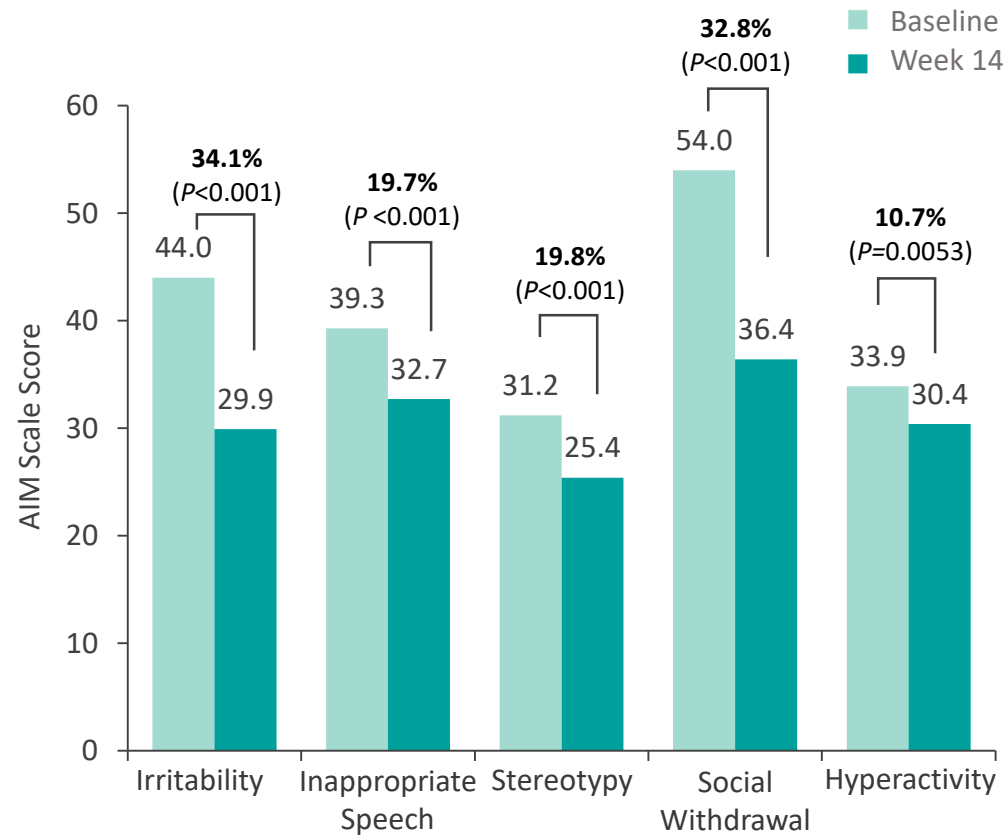
Mean Scores and Percent Improvement Period 2
(n=18)



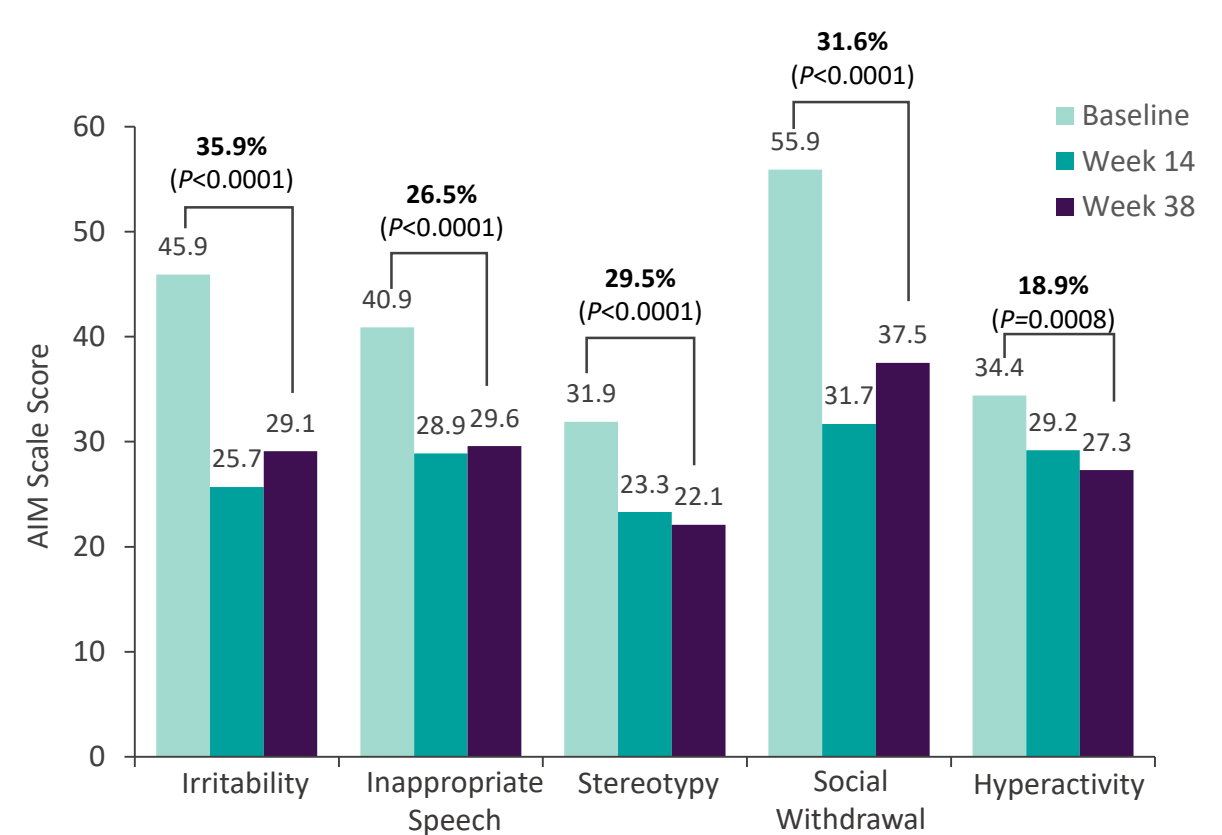
*Lower values reflect improvement in each ABC-C subscale.

Efficacy: Statistically Significant Improvements From Baseline in Autism Impact Measure Scores^a Sustained Through 38 weeks

Mean Scores and Percent Improvement Period 1 (n=28)



Mean Scores and Percent Improvement Period 2 (n=18)

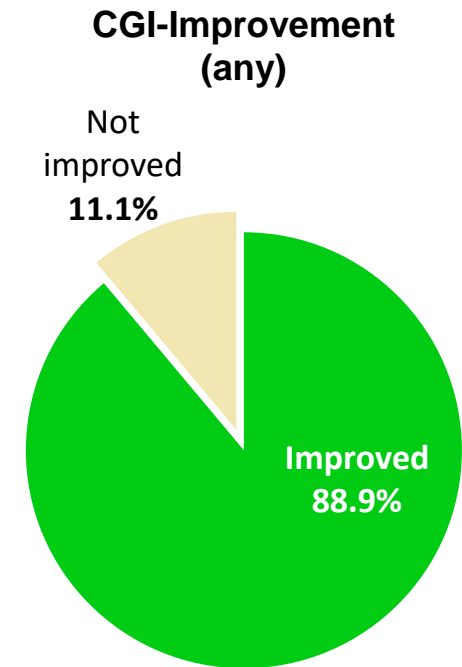
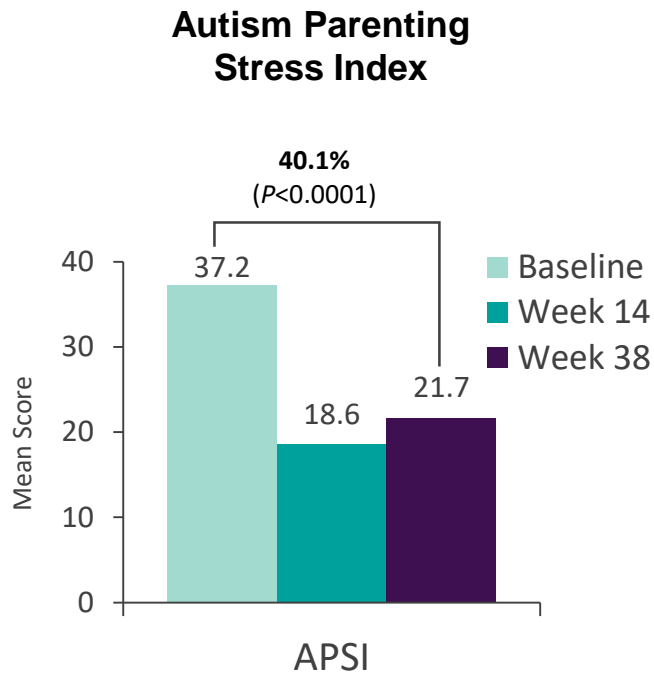
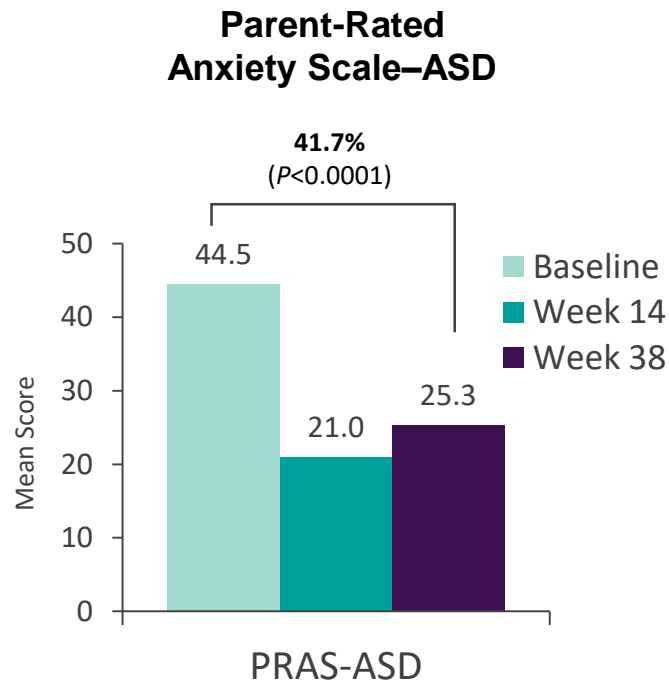


^aThe AIM score has been shown to be sensitive to change as a measure of core ASD symptoms.¹

1. Mazurek MO, et al. *Autism Res.* 2020;13(11):1867-1879.

Efficacy: Statistically Significant Improvements From Baseline in PRAS-ASD, APSI, and CGI-I Sustained Through Week 38

Mean Scores and Percent Improvement Through Week 38



n=18

ASD=Autism Spectrum Disorder; CGI=Clinical Global Impression.

Summary of Overall Safety/Tolerability

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

Summary of Results: BRIGHT

- Through 38 weeks of treatment, BRIGHT 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 showed improvement in all ASD efficacy measures (ABC-C, AIM, PRAS-ASD, CGI-I)
- Further controlled studies are warranted in this difficult-to-treat population