



# Post Hoc Analysis—An Open-Label Study of Transdermal Cannabidiol (ZYN002) for the Treatment of Fragile X Syndrome in Children and Adolescents: Estimating Health State Utility Scores

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# Disclaimer

- This presentation is for educational purposes only.
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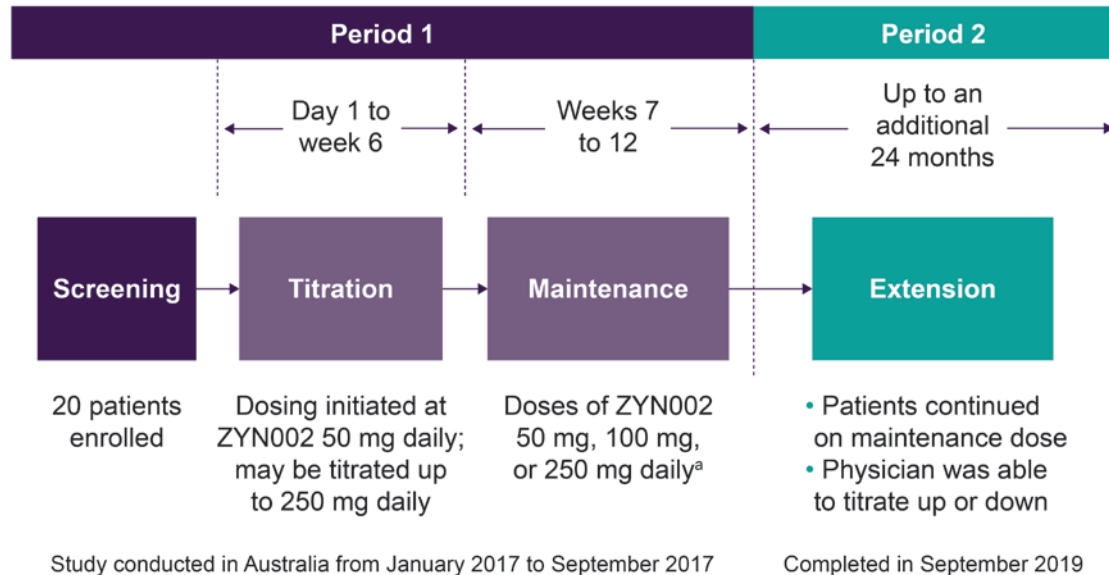
# Background

- ZYN002 is a pharmaceutically manufactured CBD transdermal gel in clinical development for the treatment of behavioral symptoms associated with FXS
- Safety, tolerability, and efficacy of ZYN002 were evaluated in a 12-week, phase 2 open-label study (ZYN2-CL-009) in patients aged 6-17 years with FXS<sup>1</sup>
- Health state utility indices are commonly employed in clinical and economic analyses of therapies with potential impact on HRQoL and enable comparison of HRQoL across conditions<sup>2,3</sup>
  - Health state utility is measured on a 0-1 scale in which 0 represents death and 1 represents complete health
- The ABC-UI—a utility index specific to FXS—was derived from the ABC-C<sub>FXS</sub> to measure the HRQoL benefit of treatments for FXS<sup>4</sup>

Objective: To evaluate the potential benefit of ZYN002 on ABC-UI in pediatric and adolescent patients with FXS through post hoc analysis of ZYN2-CL-009

# ZYN2-CL-009 Study Design & Post Hoc Analysis

- ZYN-CL-009 was a multicenter, open-label, phase 2 study to evaluate the safety, tolerability, and efficacy of ZYN002 in pediatric and adolescent patients with FXS



## Key Inclusion Criteria

- Male or female patients aged 6-17 years
- Documented FXS diagnosis with full *FMR1* mutation
- PARS-R score  $\geq 11$
- CGI-S score  $\geq 3$

- Individual patient-level data from ZYN-CL-009 were mapped to the ABC-UI algorithm to generate a utility index score for each patient
- ABC-C<sub>FXS</sub> items included in the ABC-UI algorithm:<sup>1</sup>

Social avoidance	<ul style="list-style-type: none"> <li>ABC-C:30, "Isolates him/herself from other children or adults"</li> </ul>
Irritability	<ul style="list-style-type: none"> <li>ABC-C:4, "Aggressive to other children or adults (verbally or physically)"</li> <li>ABC-C:36, "Mood changes quickly"</li> </ul>
Socially unresponsive/lethargic	<ul style="list-style-type: none"> <li>ABC-C:58, "Shows few social reactions to others"</li> </ul>
Inappropriate speech	<ul style="list-style-type: none"> <li>ABC-C:22 "Repetitive speech"</li> </ul>
Stereotypy	<ul style="list-style-type: none"> <li>ABC-C:35, "Repetitive hand, body, or head movements"</li> </ul>
Hyperactivity	<ul style="list-style-type: none"> <li>ABC-C:13, "Impulsive (acts without thinking)"</li> <li>ABC-C:15, "Restless, unable to sit still"</li> <li>ABC-C:44, "Being easily distractible"</li> </ul>

<sup>a</sup>Total daily dose, administered twice daily.

ABC-C<sub>FXS</sub>, Aberrant Behavior Checklist–Community for FXS; ABC-UI, Aberrant Behavior Checklist–Community Utility Index; CGI-S; Clinical Global Impression–Severity; *FMR1*, *Fragile X Mental Retardation 1*; FXS, fragile X syndrome; PARS-R, Pediatric Anxiety Rating Scale–Revised.

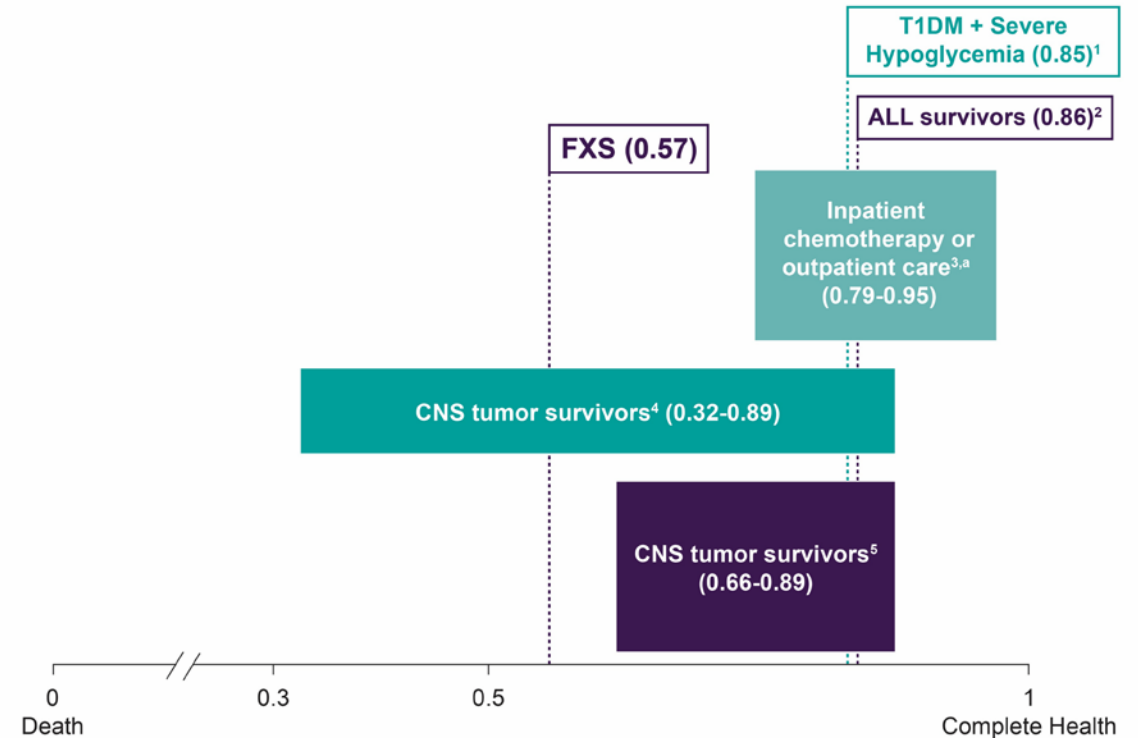
1. Kerr C et al. *Qual Life Res.* 2015;24(2):305-314.

# ABC-UI Score at Screening and Reference to Other Conditions

- 20 patients enrolled in the study, received treatment, and were included in the post hoc analysis
- The mean age was 10.4 (SD, 3.88) and most patients were male (75.0%) and white (90.0%)
- The mean ABC-UI score at screening was 0.57 (SD, 0.16)

Mean ABC-UI score of 0.57 in patients with FXS enrolled in ZYN2-CL-009 appears to reflect a poor baseline level of HRQoL, despite standard of care

## ABC-UI Score at Screening With Reference to Literature Describing HUI in Other Childhood Conditions



<sup>a</sup>Outpatient care was received from rheumatology, hemophilia, or bone marrow transplantation clinics.

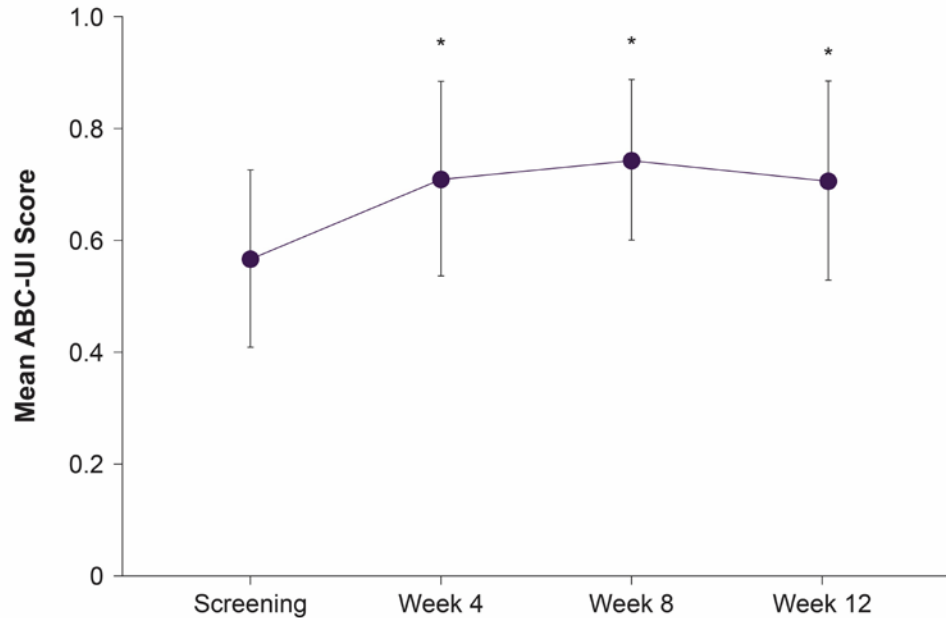
ABC-UI, Aberrant Behavior Checklist–Community Utility Index; ALL, acute lymphoblastic leukemia; CNS, central nervous system; FXS, fragile X syndrome; SD, standard deviation; T1DM, type 1 diabetes mellitus.

1. Nordfeldt S, Jonsson D. *Acta Paediatr.* 2001;90(2):137-142. 2. Wright MJ et al. *Phys Ther.* 2005;85(8):782-790. 3. Sung L et al. *J Clin Epidemiol.* 2004;57(11):1161-1166. 4. Barr RD et al. *Eur J Cancer.* 1999;35(2):248-255.

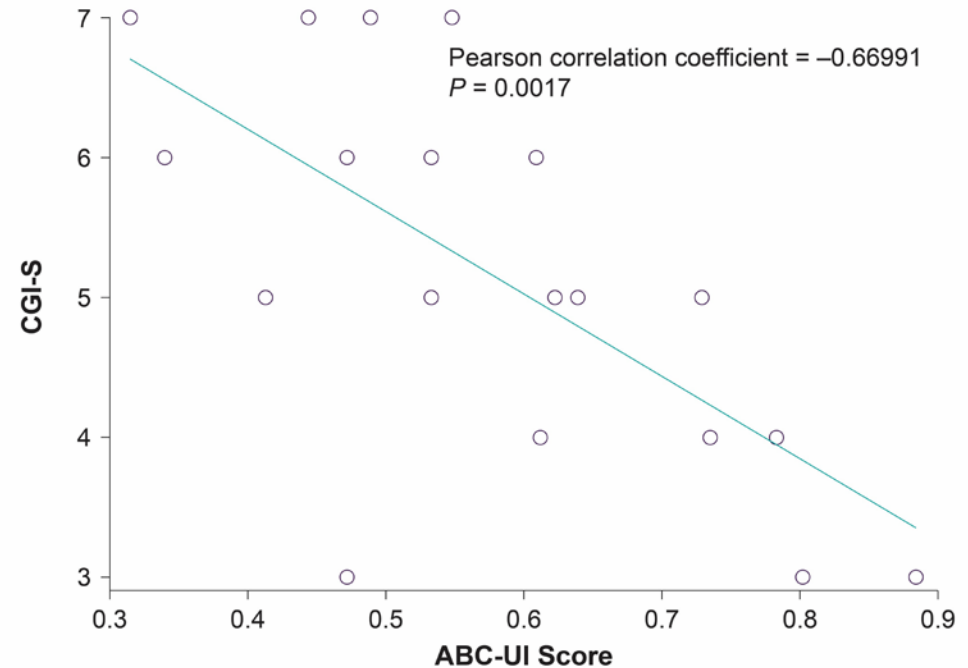
5. Glaser AW et al. *Eur J Cancer.* 1999;35(2):256-261.

# Improvement in ABC-UI Score With ZYN002 Treatment

Mean ABC-UI Score at Each Timepoint During Treatment With ZYN002



Scatter Plot of ABC-UI Score and CGI-S Score at Screening



- Significant improvement with treatment in ABC-UI was observed at the first postscreening assessment and was maintained through week 12 (mean ABC-UI at week 12, 0.71; SD, 0.18)
- ABC-UI score at screening was significantly correlated with CGI-S score, suggesting that the ABC-UI is a meaningful measure in FXS

\* $P < 0.01$ .

Data on left represent mean  $\pm$  standard deviation.

ABC-UI, Aberrant Behavior Checklist–Community Utility Index; CGI-S; Clinical Global Impression–Severity; FXS, fragile X syndrome.

# Conclusions

- In this post hoc analysis, treatment with ZYN002 significantly improved health state utility index scores in pediatric and adolescent patients with FXS, suggesting a potential broad spectrum of activity of ZYN002 in the important domains of the ABC-C<sub>FXS</sub> that were incorporated into the utility index
- The correlation of the ABC-UI scores with CGI-S scores in these patients suggests that the ABC-UI appropriately reflects symptom severity in FXS
- The estimated health state utility index score of 0.57 in patients with FXS enrolled in ZYN2-CL-009 appears to describe a poor baseline level of HRQoL, despite standard of care, highlighting the considerable impact of FXS symptoms on patient HRQoL