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Behavioural Outcomes of Treatment With Cannabidiol Oral Solution in Individuals With Seizures Associated With Tuberous Sclerosis Complex: Design of an Ongoing Phase 4 Trial (EpiCom)

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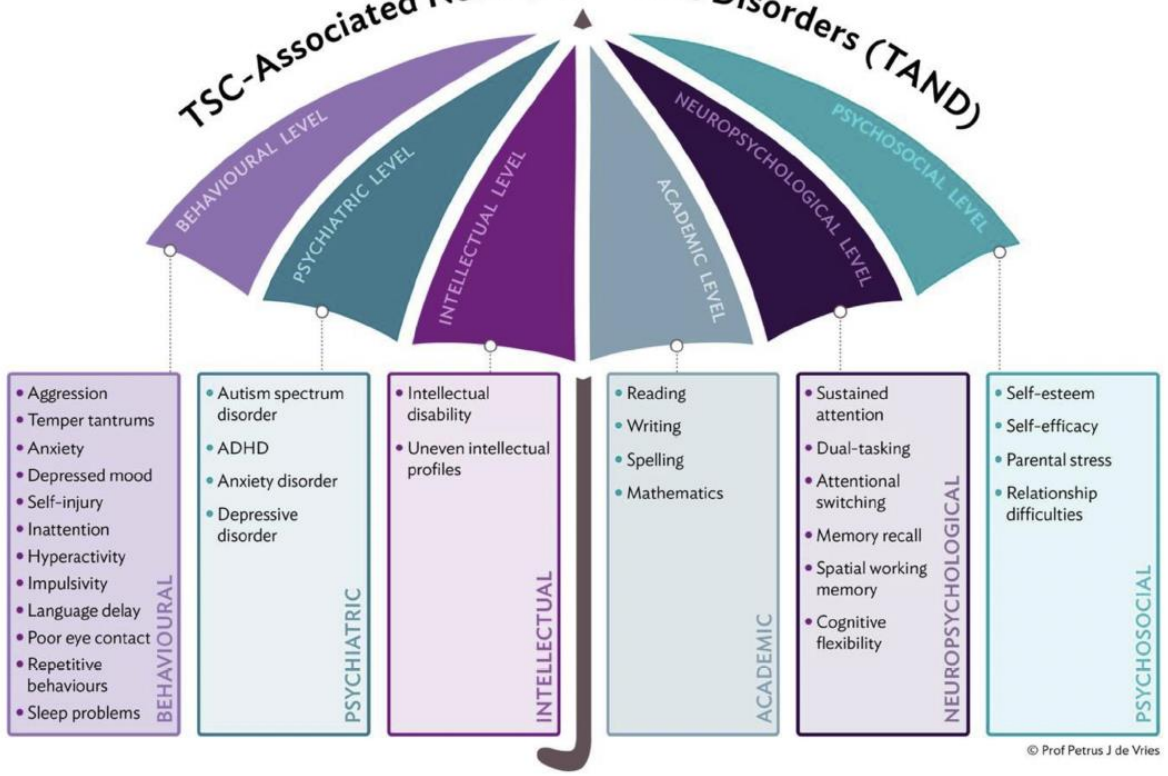
Background

Cannabidiol (CBD; Epidiolex®/Epidyolex®, 100 mg/mL oral solution) is **approved for the treatment of seizures** associated with LGS, DS, and TSC in several countries[2]

Although anecdotal reports suggest positive effect of CBD on nonseizure outcomes, **reliable clinical evidence is lacking**



Limited treatments for TAND[1]

CBD treatment improved participants' overall clinical condition in clinical trials[3]

Personalized outcomes measures necessary

The TAND figure is presented here with permission from Prof Petrus J. de Vries.

ADHD, Attention-deficit/hyperactivity disorder; CBD, cannabidiol; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; TAND, tuberous sclerosis complex associated neuropsychiatric disorders; TSC, tuberous sclerosis complex.

1. Vanclooster S, et al. *J Neurodev Disord*. 2022;14:13; **2.** The US Food and Drug Administration. 2023. EPIDIOLEX® prescribing information. Accessed July 27, 2023. https://www.epidiolex.com/sites/default/files/pdfs/1120/EPX-03645-1120_EPIDIOLEX_(cannabidiol)_USPI.pdf; **3.** Thiele EA, et al. *JAMA Neurol*. 2021;78:285-292.

The EpiCom Trial is designed in collaboration with:

PATIENT ADVISORY GROUPS (PAGs)

GABRIELLE RUSHING[1]

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France

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VICENTE VILLANUEVA
Spain

HCP, health care professional.
1. TSC Alliance (USA); **2.** European-Tuberous Sclerosis Association (E-TSC; Europe – Portugal/Italy); **3.** Epilepsy Research UK (UK); **4.** Tuberous Sclerosis Association (UK); **5.** Association Sclérose Tubéreuse French de Bourneville.

Co-creation strategy for trial design

Engage the TSC community of HCPs, patients, and their caregivers

Co-create the advisory board agenda

Patient Advisory Board

HCP Advisory Board

Integration of feedback from both groups into study design

Formation of an ongoing patient-HCP steering committee to guide trial execution

TSC, tuberous sclerosis complex; HCP, health care professional.

The EpiCom Trial

Clinical Trial Number: NCT05864846

EpiCom is a multicentre, open-label, phase 4 study

AIMS TO EVALUATE

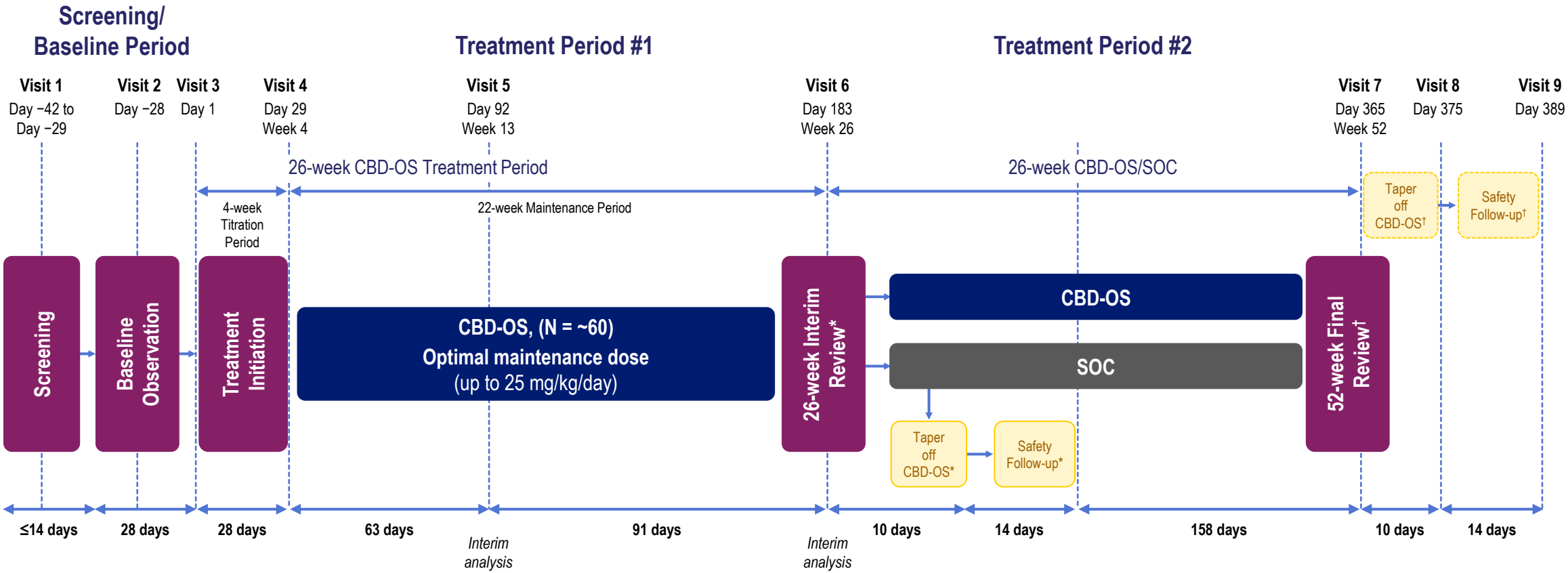
- **Changes in various aspects of TAND**
- **Other co-occurring outcomes**

DECENTRALIZED STUDY DESIGN

- **Flexibility**
- **Virtual** or **in-person visits**

CBD, cannabidiol; TAND, tuberous sclerosis complex associated neuropsychiatric disorders; TSC, tuberous sclerosis complex.

Trial design



CBD-OS, cannabidiol oral solution; SOC, standard of care.
*Participants who decide to discontinue CBD-OS after the 26-week interim review visit but remain on study will form the SOC treatment arm. These participants will taper off CBD-OS and complete a safety follow-up.
†Participants who decide to discontinue CBD-OS after the 52-week interim review visit will taper off CBD-OS and complete a safety follow-up. For participants who wish to remain on CBD-OS after the study, the 52-week final review visit is the last study visit.

Key eligibility criteria

INCLUSION

- **Confirmed diagnosis of TSC** with history of associated seizures
- **Moderate/severe behavioural challenges** (eg, aggression, impulsivity, temper tantrum, self-injury, and hyperactivity), with a most problematic behaviour score of ≥6 on the TAND-SQ at baseline
- Aged **1–65 years**
- On **≥1 antiseizure medication**
- **Naive to CBD** or has been off CBD for ≥3 months before screening

EXCLUSION

- **Any medical condition that could affect the study outcomes**
- **Felbamate initiation within the year before screening**
- **Recreational or medicinal cannabis use within the 3 months before screening if they refuse a 1-month washout period**
- **Significant hepatic impairment and any history of suicidal behaviour or ideation of type 4 or 5 as evaluated with C-SSRS**

CBD, cannabidiol; C-SSRS, Columbia-Suicide Severity Rating Scale; TSC, Tuberous Sclerosis Complex; TAND-SQ, Tuberous Sclerosis Complex Associated Neuropsychiatric Disorders Self-report

Endpoints

TAND outcomes

- TAND-SQ
- Most problematic behaviour NRS score
- ABC, ABCL/CBCL and ASR
- BRIEF
- CSHQ or PSQI
- PROMIS

QOL and family functioning

- PedsQL
- PedsQL FIM

Symptom severity and seizure outcomes

- Treatment responder rates
- Change in seizure frequency
- Seizure-free days
- CareGI-S/PGI-S/CGI-S
- Retention

Safety and tolerability of CBD

- Adverse events
- Discontinuations due to AEs
- Inpatient hospitalisations
- Abnormal clinical laboratory parameters

ABC, Aberrant Behavior Checklist; ABCL, Adult Behavior Checklist; AEs, adverse events; ASR, Adult Self-Report; BRIEF, Behavior Rating Inventory of Executive Function; CareGI-S, Caregiver Global Impression of Severity; CBD, cannabidiol; CBCL, Child Behavior Checklist; CGI-S, Clinician Global Impression of Severity; CSHQ, Children's Sleep Habits Questionnaire; NRS, Numerical Rating Scale; PedsQL, Pediatric Quality of Life Inventory; PedsQL FIM, Pediatric Quality of Life Survey Family Impact Module; PGI-S, Physician Global Impression of Severity; PROMIS, Patient-Reported Outcomes Measurement Information System; PSQI, Pittsburgh Sleep Quality Index; TAND-SQ, Tuberous Sclerosis Complex Associated Neuropsychiatric Disorders Self-report.

Participating countries

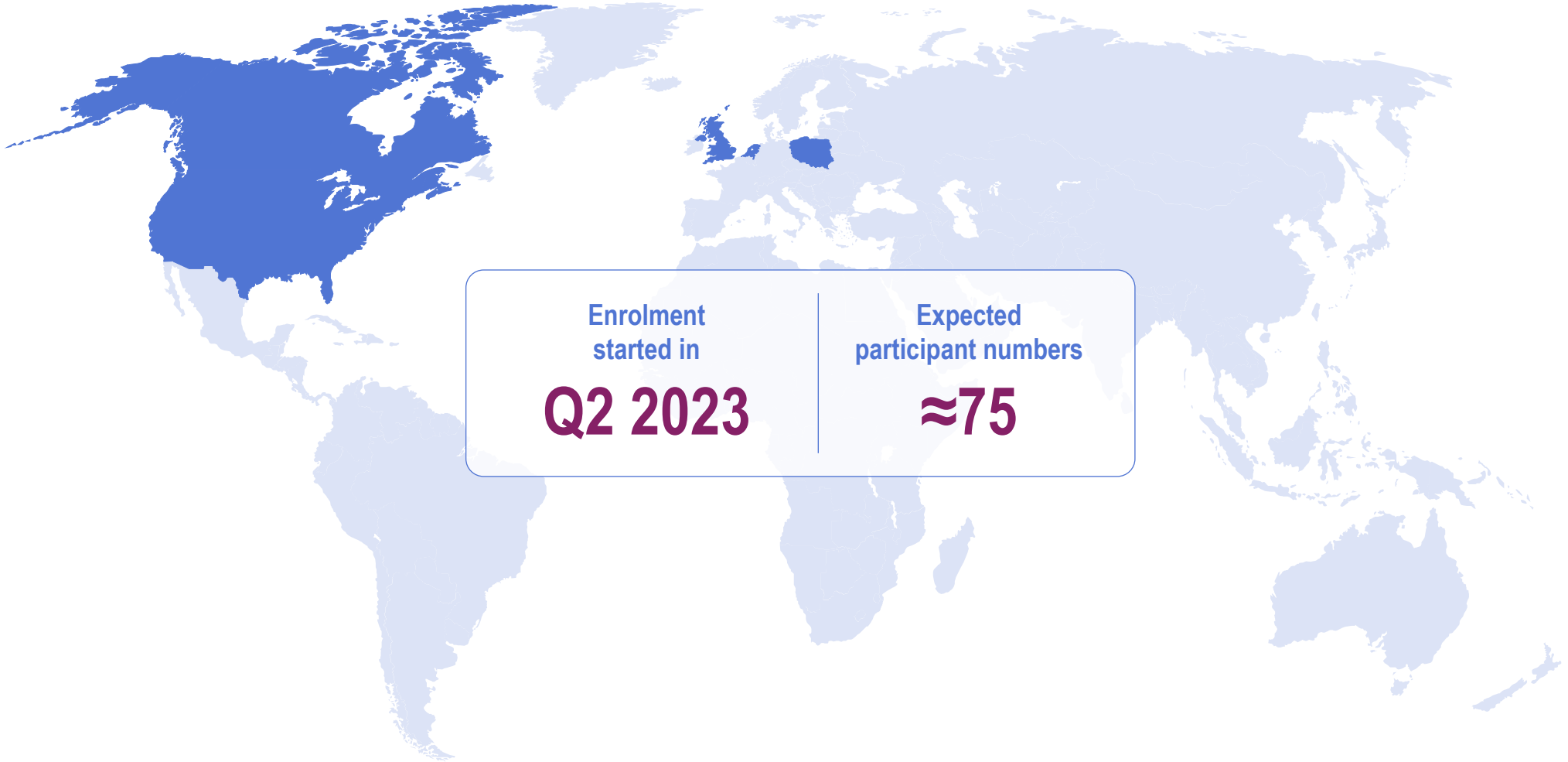
United States

United Kingdom

Canada

The Netherlands

Poland



Enrolment started in	Expected participant numbers
Q2 2023	≈75

Q2, second quarter.

Conclusions

Integrative and holistic approach to managing TSC and TAND

Collaborative approach to design with patients, caregivers and HCPs

Decentralized trial approach

New Innovative Tools

TAND-SQ

HCP, health care professional; TSC, tuberous sclerosis complex; TAND, tuberous sclerosis complex neuropsychiatric disorders; TAND-SQ, tuberous sclerosis complex associated neuropsychiatric disorders self-report.

Disclosures

This study was sponsored by Jazz Pharmaceuticals, Inc.

Author disclosures:

- **Agnies M. van Eeghen** serves as the principal investigator for the EpiCom trial and has received funding from Jazz Pharmaceuticals, Inc.
- **Elizabeth A. Thiele** serves as a principal investigator on clinical trials for Jazz Pharmaceuticals, Inc.
- **Sam Amin** and **Debopam Samanta** have received funding from Jazz Pharmaceuticals, Inc.
- **Petrus J. de Vries** is a consultant for Jazz Pharmaceuticals, Inc.
- **Lisa Moore-Ramdin** and **Joanne Stevens** are full-time employees of Jazz Pharmaceuticals, Inc. who, in the course of this employment, have received stock options and/or other stock awards or ordinary shares of Jazz Pharmaceuticals, Inc.

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Thank You

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