T-CALM is a new clinical trial for patients with essential tremor that will evaluate whether an investigational oral drug decreases the severity of tremors by reducing abnormal activity in certain regions of the brain.

Contact our study center to see if you qualify to participate in T-CALM.

Learn more at www.TCALMstudy.com

If you are interested in T-CALM, please call 833-TCALM11 (833-822-5611) or email ettrial@cavionpharma.com

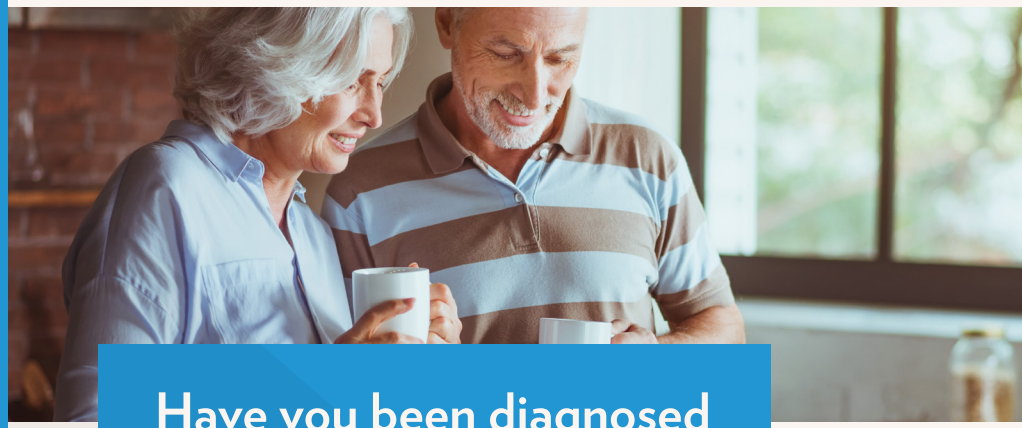
The safety and effectiveness of CX-8998 for treatment of essential tremor have not been established.

T-CALM

Tremor-CAv3 Modulation Study

Study Sponsor

Cavion



Have you been diagnosed with essential tremor?

Consider joining this new clinical study.

T-CALM will evaluate whether an investigational oral drug decreases the severity of tremors by reducing abnormal activity in certain regions of the brain.

You may be eligible for this study researching a new drug to reduce tremors if you:

- ✓ **Are 18-75 years old**
- ✓ **Been diagnosed with essential tremor**
- ✓ **Have uncontrolled tremor in at least one hand and arm due to essential tremor**
- ✓ **Have no history of brain surgery, focused ultrasound or deep brain stimulation for tremor**
- ✓ **No history of other causes of tremor, such as Parkinson's disease, hyperthyroidism, multiple sclerosis, or head trauma or brain disease in the 3 months before the tremor began**

You may be eligible for T-CALM even if you are already taking one medication for tremor. (However, people using Primidone will be asked to discontinue it prior to starting the study).

About T-CALM

The T-CALM clinical study will evaluate whether investigational oral drug, CX-8998, decreases the severity of tremors by reducing abnormal activity in certain regions of the brain. The study will also assess side effects of the drug, measure its impact on quality of life and further examine how the drug works.

Participating in T-CALM

The study is being conducted with more than 90 participants at multiple medical research centers in the United States. People with essential tremor will participate in the study for 5 weeks. Participants in the study will be randomly assigned to one of two groups – half will receive the study drug and the other half will be given a placebo (sugar pill). In order to scientifically assess the effects of the drug, neither the participants nor the clinical team will know during the study what group each patient is in.

Study participation, testing and medication are all free to participants. Some people may receive stipends to cover meals and travel related to study visits.

Eligibility requirements for the T-CALM Study include:

- Men and women (not pregnant or breastfeeding) 18 to 75 years old
- Diagnosis of essential tremor affecting both hands and arms
- No previous brain surgery, focused ultrasound or deep brain stimulation for tremor
- No known history of other causes of tremor, such as Parkinson's disease, hyperthyroidism, multiple sclerosis, or head trauma or brain disease in the three months before the tremor began

You may be able to participate in the study even if you are already taking one medication for tremor. (However, people using Primidone will be asked to discontinue it prior to starting the study.) Other eligibility criteria will be reviewed with the study clinical team before proceeding with enrollment.

www.TCALMstudy.com

What does the study involve?

- **SCREENING VISIT** – Participants will start with a screening visit to confirm if they have essential tremor and to measure the severity of tremor.
- **INFORMED CONSENT** – People who are eligible to participate will be provided with a consent form to review carefully to ensure they fully understand the risks and benefits of participation.
- **STUDY GROUP ASSIGNMENT** – Participants in the study will be randomly assigned to one of two groups – half will receive the study drug (CX-8998) and the other half will be given a sugar pill.
- **STUDY INITIATION** – The first day of the study, participants will take the first dose of the study medication and undergo testing.
- **STUDY VISITS** – Participants will take the study medication for 28 days with incremental increases in dosing and will make multiple clinic visits for assessments.
- **STUDY COMPLETION** – After the 28 days on study medication, participants will continue for 7 days without taking the study medication and then return for final evaluation.

About CX-8998

The brain's neural network utilizes certain calcium channels, called Cav3, that help control neuronal firing and signaling between brain regions. Some neurological diseases, such as essential tremor, are associated with abnormal activity of these signals. CX-8998 is an oral drug that was designed to selectively modulate Cav3 calcium channel activity in the brain's neurons, acting as a biological 'pacemaker' to help restore the brain's natural rhythms. Scientific data suggest that CX-8998 reduces tremor by suppressing abnormal Cav3 activity and restoring normal neural signaling in relevant brain regions.

CX-8998 has been studied in nearly 200 people, mostly healthy volunteers and some people with other neurological conditions. CX-8998 is being developed by Cavion, Inc., a company developing T-type calcium channel (Cav3) modulating therapies for a range of neurological diseases.