

GW Pharmaceuticals RCT Inclusion and Exclusion Criteria

Appendix D

** See <https://clinicaltrials.gov/> for up to date information on available trials

Lennox-Gastaut Syndrome

Key Inclusion Criteria:

- Subject must be male or female aged between two and 55 years (inclusive).
- Subject must have a documented history of Lennox-Gastaut syndrome. This includes written documentation of having met electroencephalogram (EEG) diagnostic criteria during the patient's history and evidence of at least one type of generalized seizure, including drop seizures (atonic, tonic, tonic-clonic or myoclonic) for at least six months.
- Subjects who have a history of slow (<2.5 Hz) spike-and-wave pattern in an EEG prior to the enrollment into the baseline period.
- Subjects must have at least two drop seizures each week during the 28-day baseline period.
- Subjects should be refractory; that is having documented failures on more than one antiepileptic drug (AED).
- Subject must be taking one or more AEDs at a dose which has been stable for at least four weeks prior to screening.
- All medications or interventions for epilepsy (including ketogenic diet and vagus nerve stimulation [VNS]) must have been stable for four weeks prior to screening and patient is willing to maintain a stable regimen throughout the study. The ketogenic diet and VNS treatments are not accounted as an AED.

Key Exclusion Criteria:

- Etiology of subject's seizures is a progressive neurologic disease. Subjects with tuberous sclerosis will not be excluded from study participation, unless there is a progressive tumor.
- Subject has had an anoxic episode requiring resuscitation within six months of screening.
- Subject has clinically significant unstable medical conditions other than epilepsy.
- Subject has had clinically relevant symptoms or a clinically significant illness in the four weeks prior to screening or randomization, other than epilepsy.
- Subject is currently using or has in the past used recreational or medicinal cannabis, or synthetic cannabinoid based medications (including Sativex®) within the three months prior to study entry and is unwilling to abstain for the duration of the study.
- Subject has any known or suspected hypersensitivity to cannabinoids or any of the excipients of the Investigational Medicinal Product (IMP), such as sesame oil.
- Subject has been part of a clinical trial involving another IMP in the previous six months.
- Subject has significantly impaired hepatic function at screening (Visit 1) or randomization (Visit 2) (Alanine aminotransferase [ALT] >5 x upper limit of normal [ULN] or total bilirubin [TBL] >2 x ULN) OR the ALT or Aspartate aminotransferase (AST) >3 x ULN and (TBL >2 x ULN or international normalized ratio >1.5). This criterion can only be confirmed once the laboratory results are available; subjects randomized into the study who are later found not to meet this criterion should be withdrawn from the study.
- Any history of suicidal behavior or any suicidal ideation of type four or five on the Columbia Suicide Severity Rating Scale in the last month or at screening.
- Subject is taking more than four concurrent AEDs.

- *Subject has taken corticotropins in the six months prior to screening.*
- *Subject is currently taking long-term systemic steroids (excluding inhaled medication for asthma treatment) or any other daily medication known to exacerbate epilepsy. An exception will be made of prophylactic medication, for example, idiopathic nephrotic syndrome or asthma.*
- *Subject is taking felbamate, and they have been taking it for less than one year prior to screening.*

Dravet Syndrome

Key Inclusion Criteria:

- *Subject must be male or female aged between 2 and 18 years (inclusive).*
- *Subject must have a documented history of Dravet syndrome which is not completely controlled by current antiepileptic drugs.*
- *Subject must be experiencing four or more convulsive seizures (tonic-clonic, tonic, clonic, atonic seizures) during the 28-day baseline observation period.*
- *Subject must be taking one or more antiepileptic drugs at a dose which has been stable for at least four weeks.*
- *All medications or interventions for epilepsy (including ketogenic diet and vagus nerve stimulation) must have been stable for four weeks prior to screening and subject is willing to maintain a stable regimen throughout the study.*

Key Exclusion Criteria:

- *Subject has clinically significant unstable medical conditions other than epilepsy.*
- *Subject has had clinically relevant symptoms or a clinically significant illness in the four weeks prior to screening or randomization, other than epilepsy.*
- *Subject is currently using or has in the past used recreational or medicinal cannabis, or synthetic cannabinoid based medications (including Sativex®) within the three months prior to study entry and is unwilling to abstain for the duration for the study.*
- *Subject has any known or suspected hypersensitivity to cannabinoids or any of the excipients of the investigational medicinal products.*
- *There are plans for the subject to travel outside their country of residence during the study.*
- *Subjects previously randomized into this study. In particular, subjects who participated in Part A of the study cannot enter Part B.*
- *Any history of suicidal behavior or any suicidal ideation of type four or five on the Columbia-Suicide Severity Rating Scale (Children's) at screening.*