concentration) of about 100 ng/ml or greater for approximately 70% or more for a 24 hour-day.

**[0011]** This disclosure is directed in part to the use of ganaxolone in the manufacture of a medicament for treating tuberous sclerosis complex-related epilepsy in a subject in need thereof, wherein the ganaxolone is to be administered orally as an oral suspension three times per day in an amount of up to 63 mg/kg/day that produces a ganaxolone plasma concentration of at least 100 ng/ml for at least 70% or more for a period of a 24 hour-day. To achieve a ganaxolone plasma concentration of about 100 ng/ml or greater for approximately 70% or more over a 24 hour-day, ganaxolone can be administered three times daily (or more) at a maximum amount of about 1,800 mg per day. In subjects' that weigh less than 40 kg ganaxolone can be administered three times daily (or more) at a maximum amount of 63 mg/kg/day is Typically, up to about 1,500 mg per day of ganaxolone can produce a plasma concentration of about 100 ng/ml or greater for approximately 70% or more over a 24 hour-day when administered three times a day. Ganaxolone can be administered at a dose of about 500 mg three times a day. A skilled clinician will understand that the amount of ganaxolone administered three times a day (e.g., orally) can be adjusted to achieve the desired ganaxolone trough level so long as the total amount does not exceed the maximum daily dose of ganaxolone.

**[0012]** Preferably ganaxolone is administered orally (e.g., as an oral suspension or an oral capsule). Without being bound by theory, the inventors believe that three time dosing results in improved antiseizure activity (i.e., reduces seizure frequency and/or severity of seizures) because of increased plasma ganaxolone exposure. This is contrary to prior treatment protocols that teach administering ganaxolone at high dose (e.g., per day dose) to achieve therapeutic efficacy. For example, administering ganaxolone at a higher dose two times a day.

**[0013]** Administering ganaxolone at an amount to achieve a ganaxolone plasma concentration of at least about 100 ng/ml or greater for approximately about 70% or more for a period of 24 hours reduces the frequency of seizure and/or severity of seizure in the subject relative to baseline. Typically, a reduction in seizure frequency of at least about 20% or greater relative to baseline seizure frequency can be achieved. During treatment

# CLAIMS

1. Use of ganaxolone in the manufacture of a medicament for treating tuberous sclerosis complex-related epilepsy in a subject in need thereof, wherein the ganaxolone is to be administered orally as an oral suspension three times per day in an amount of up to 63 mg/kg/day that produces a ganaxolone plasma concentration of at least 100 ng/ml for at least 70% or more for a period of a 24 hour-day.

2. The use of claim 1, wherein ganaxolone is to be administered in an amount of up to 1,800 mg per day.

3. The use of claim 1 or claim 2, wherein ganaxolone is to be administered in an amount of up to 1,500 mg per day.

4. The use of any one of claims 1 to 3, wherein the tuberous sclerosis complex-related epilepsy is a infantile spasm, a focal impaired awareness seizure, a focal seizure, or a generalized seizure.

5. The use of any one of claims 1 to 4, wherein the administered ganaxolone reduces the frequency of seizure and/or severity of seizure in the subject relative to baseline.

6. The use of any one of claims 1 to 4, wherein the administered ganaxolone reduces major motor frequency in the subject relative to baseline.

7. The use of any one of claims 1 to 4, wherein the administered ganaxolone results in a reduction in seizure frequency of 20% or greater relative to baseline seizure frequency.

8. The use of any one of claims 1 to 4, wherein the administered ganaxolone results in a reduction in seizure frequency of at least 35% or greater relative to baseline seizure frequency.

9. The use of any one of claims 1 to 8, wherein the subject is monitored by electroencephalogram (EEG).

10. The use of any one of claims 1 to 8, wherein seizure activity in the subject is monitored by electroencephalogram (EEG).