CLAIMS

1. Use of ganaxolone for the manufacture of a medicament ~~A method~~ for ~~treating~~ the treatment of status epilepticus (SE), ~~comprising administering to~~in a subject in need thereof comprising:

a) an intravenous bolus of ganaxolone in an amount sufficient to suppress SE, and

b) a continuous intravenous infusion of ganaxolone in an amount sufficient for continued SE suppression, wherein the continuous intravenous infusion i) is initiated periprocedural with the intravenous bolus, ii) is administered for a target concentration period of at least about 8 hours, and iii) produces a ganaxolone plasma concentration in the subject of at least about 425 ng/ml, at least about 450 ng/ml, at least about 475 ng/ml or at least about 500 ng/ml throughout the target concentration period.

2. The ~~method~~ use of claim 1, wherein the continuous intravenous infusion is initiated concurrently with the administration of the intravenous bolus.

3. The ~~method~~ use of claim 1, wherein the intravenous bolus and the continuous intravenous infusion does not result in anesthesia of the subject.

4. The ~~method~~ use of any one of claims 1-3, wherein the intravenous bolus produces a ganaxolone plasma concentration in the subject of at least about 500 ng/ml to about 1000 ng/ml.

5. The ~~method~~ use of any one of claims 1-3, wherein the continuous intravenous infusion produces a ganaxolone plasma concentration in the subject of at least about 500 ng/ml to about 1000 ng/ml throughout the treatment period.

6. The ~~method~~ use of any one of claims 1-5, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased over a period of about 24 hours from the initiation of the continuous intravenous infusion.

7. The ~~method~~ use of any one of claims 1-6, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased about 2 hours after the initiation of the continuous intravenous infusion.

8. The ~~method~~ use of claim 7, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased by about 50%, relative to the amount administered per hour at the initiation of the continuous intravenous infusion, about 2 hours after the initiation of the continuous intravenous infusion.

9. The ~~method~~ use of any one of claims 1-8, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased about 10 hours to about 14 hours after the initiation of the continuous intravenous infusion.

10. The ~~method~~ use of claim 9, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased by about 75%, relative to the amount administered per hour at the initiation of the continuous intravenous infusion,

about 10 hours to about 14 hours after the initiation of the continuous intravenous infusion.

11. The ~~method~~ use of any one of claims 1-10, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased about 2 hours after the initiation of the continuous intravenous infusion, and then about 10 hours to about 14 hours after the initiation of the continuous intravenous infusion.

12. The ~~method~~ use of claim 11, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased by about 50%, relative to the amount administered per hour at the initiation of the continuous intravenous infusion, about 2 hours after the initiation of the continuous infusion, and then by about 75%, relative to the amount administered per hour at the initiation of the continuous intravenous infusion, about 10 hours to about 14 hours after the initiation of the continuous infusion.

13. The ~~method~~ use of any of the preceding claims, wherein the continuous intravenous infusion is administered for a treatment period of about 36 hours after the initiation of the continuous intravenous infusion.

14. The ~~method~~ use of any of the preceding claims, wherein the treatment period of the continuous intravenous infusion is for a period of at least about 8 hours to about 36 hours after the initiation of the continuous intravenous infusion.

15. The ~~method~~ use of any one of the preceding claims, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is increased after about 24 hours from the initiation of the continuous intravenous infusion.

16. The ~~method~~ use of claim 15, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is increased by up to about 45%, relative to the amount administered per hour starting after about 24 hours after initiation of the continuous intravenous infusion.

17. The ~~method~~ use of claim 15 or 16, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is increased for a period up to about 12 hours.

18. The ~~method~~ use of any one of the preceding claims, further comprising c) continuing to administer the continuous intravenous infusion for a taper period following the target concentration period.

19. The ~~method~~ use of any one of the preceding claims, wherein the taper period starts at about 36 hours from the initiation of the continuous intravenous infusion.

20. The ~~method~~ use of claim 18 or 19, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion during the taper period is reduce by about one third about every 4 hours.

21. The ~~method~~ use of any one of the preceding claims, wherein the amount of ganaxolone administered to the subject per hour by continuous intravenous infusion is decreased by decreasing the infusion rate.

22. The ~~method~~ use of any one of the preceding claims, wherein about 5 mg to about 40 mg of ganaxolone is administered to the subject at the initiation of the intravenous bolus.

23. The ~~method~~ use of any one of the preceding claims, wherein about 30 mg of ganaxolone is administered to the subject at the initiation of the intravenous bolus.

24. The ~~method~~ use of any one of the preceding claims, wherein the intravenous bolus is administered to the subject for about 1 minute to about 5 minutes.

25. The ~~method~~ use of any one of the preceding claims, wherein about 20 mg of ganaxolone per hour to about 80 mg of ganaxolone per hour are infused into the subject during the continuous infusion treatment period.

26. The ~~method~~ use of any one of the preceding claims, wherein about 80 mg of ganaxolone per hour are infused into the subject at the initiation of the continuous intravenous infusion.

27. The ~~method~~ use of any one of the preceding claims, wherein the amount of ganaxolone infused into the subject by the continuous intravenous infusion is decreased to

about 40 mg ganaxolone per hour and then to about 20 mg ganaxolone per hour during the treatment period.

28. The ~~method~~ use of any one of the preceding claims, wherein about 80 mg of ganaxolone per hour is administered to the subject by the continuous intravenous infusion from initiation and for at least about 2 hours thereafter.

29. The use~~method~~ of any one of the preceding claims, wherein about 40 mg of ganaxolone per hour is administered to the subject by continuous intravenous infusion starting about 2 hours after initiation and for about 6 hours to about 10 hours thereafter.

30. The ~~method~~ use of any one of the preceding claims, wherein about 20 mg of ganaxolone per hour is administered to the subject by continuous intravenous infusion starting about 12 hours after initiation and for about 12 hours to about 24 hours thereafter.

31. The ~~method~~ use of any one of the preceding claims, wherein the amount of ganaxolone infused into the subject by continuous intravenous infusion is increased up to about 45 mg of ganaxolone per hour starting about 24 hours after initiation and for up to about 12 hours thereafter.

32. The ~~method~~ use of claim 31, wherein the amount of ganaxolone administered to the subject by continuous intravenous infusion does not exceed 45 mg ganaxolone per hour.

33. The ~~method~~ use of any one of the preceding claims, wherein the continuous infusion is administered before or after the intravenous bolus.

34. The ~~method~~ use of any one of the preceding claims, wherein the subject failed first-line seizure treatment, second-line seizure treatment, or third-line seizure treatment.

35. The ~~method~~ use of any one of the preceding claims, wherein the first-line seizure treatment is benzodiazepine.

36. The ~~method~~ use of claim 35, wherein the second-line seizure treatment is fosphenytoin, valproic acid or levetiracetam.

37. The ~~method~~ use of claim 35, whereon the third-line seizure treatment is thiopental, midazolam, pentobarbital, or propofol.

38. The ~~method~~ use of any one of the preceding claims, wherein the subject has failed at least one anti-seizure drug.

39. The ~~method~~ use of any one of the preceding claims, wherein the subject has failed treatment with benzodiazepine and at least one anti-seizure drug.

40. The ~~method~~ use of any one of the preceding claims, wherein the status epilepticus is convulsive status epilepticus.

41. The ~~method~~ use of any one of the preceding claims, wherein the status epilepticus is non-convulsive status epilepticus.

42. The ~~method~~ use of any one of the preceding claims, wherein the subject as refractory status epilepticus.

43. The ~~method~~ use of any one of the preceding claims, wherein the subject has super-refractory status epilepticus.

44. The ~~method~~ use of any one of the preceding claims, wherein the subject is monitored by electroencephalogram (EEG).

45. The ~~method~~ use of any one of the preceding claims, wherein seizure activity in the subject is monitored by EEG.

46. The ~~method~~ use of any of the preceding claims, wherein the intravenous administration of ganaxolone further comprises sulfobutylether-β-cyclodextrin.

47. The ~~method~~ use of claim 45, wherein ganaxolone and sulfobutylether-β-cyclodextrin are administered in one formulation.

48. The ~~method~~ use of any one of the preceding claims, wherein one or more intravenous bolus of ganaxolone can be administered to the subject during the continuous intravenous infusion.

49. The use~~method~~ of any one of the preceding claims wherein the bolus results is a reduction of seizure burden to about 20% or less, or a reduction of seizure burden of at least about 50% relative to the seizure burden during the 30 minutes immediately prior to administration of the bolus.

50. The ~~method~~ use of claim 49, wherein the continuous infusion maintains seizure burden at about 20% or less, or maintain seizure burden at least about 50% less than the seizure burden during the 30 minutes immediately prior to administration of the bolus.

~~51. Use ganaxolone for treating status epilepticus in a subject in need thereof, wherein~~

~~a) an intravenous bolus of ganaxolone in an amount sufficient to stop seizure, and~~

~~b) a continuous intravenous infusion of ganaxolone in an amount sufficient to prevent seizure re-lapse, wherein the continuous intravenous infusion i) is initiated periprocedural with the intravenous bolus, ii) is administered for a treatment period of at least about 8 hours, and iii) produces a ganaxolone plasma concentration in the subject of at least about 425 ng/ml, at least about 450 ng/ml, at least about 475 ng/ml or at least about 500 ng/ml throughout the treatment period.~~

~~52. A pharmaceutical composition for treating status epilepticus comprising ganaxolone as an active ingredient, wherein the pharmaceutical formulation is for intravenous administration as an intravenous bolus of ganaxolone in an amount sufficient to stop seizure, and a continuous intravenous infusion of ganaxolone in an amount sufficient to prevent seizure re-lapse, wherein the continuous intravenous infusion i) is initiated periprocedural with the intravenous bolus, ii) is administered for a treatment~~

~~period of at least about 8 hours, and iii) produces a ganaxolone plasma concentration in the subject of at least about 425 ng/ml, at least about 450 ng/ml, at least about 475 ng/ml or at least about 500 ng/ml throughout the treatment period.~~

~~53. The use of ganaxolone for the manufacture of a medicament for the treatment of status epilepticus in a subject in need thereof comprising:~~

~~a) an intravenous bolus of ganaxolone in an amount sufficient to stop seizure, and~~

~~b) a continuous intravenous infusion of ganaxolone in an amount sufficient to prevent seizure re-lapse, wherein the continuous intravenous infusion i) is initiated periprocedural with the intravenous bolus, ii) is administered for a treatment period of at least about 8 hours, and iii) produces a ganaxolone plasma concentration in the subject of at least about 425 ng/ml, at least about 450 ng/ml, at least about 475 ng/ml or at least about 500 ng/ml throughout the treatment period.~~

~~54. A method of treating status epilepticus, comprising administering a therapeutic dose of ganaxolone to a subject experiencing status epilepticus in a manner which achieves and maintains a plasma concentration of ganaxolone from about 50 ng/ml to about 3500 ng/ml over a time period from about 30 minutes to about 120 hours, and wherein the administration reduces or eliminates seizure activity and/or reduces or eliminates convulsions and/or completely suppresses status epilepticus.~~