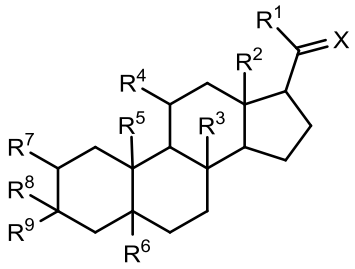
CLAIMS

What is claimed is:

1. An injectable neurosteroid formulation comprising nanoparticles having a D50 of less than 2000 nm, the nanoparticles comprising

a) a neurosteroid of the Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

X is O, S, or NR^{10};

R^1 is hydrogen, hydroxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R^4 is hydrogen, hydroxyl, oxo, optionally substituted alkyl, or optionally substituted heteroalkyl,

R^2, R^3, R^5, R^6, and R^7 are each independently hydrogen, hydroxyl, halogen, optionally substituted alkyl, or optionally substituted heteroalkyl;

R^8 is hydrogen or alkyl and R^9 is hydroxyl; or

R^8 and R^9 are taken together to form an oxo group;

R^{10} is hydrogen, hydroxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted aryl, or optionally substituted arylalkyl where

each alkyl is a C_1-C_{10}alkyl, C_3-C_6cycloalkyl, (C_3-C_6cycloalkyl)C_1-C_4alkyl, and optionally contains a single bond replaced by a double or triple bond;

each heteroalkyl group is an alkyl group in which one or more methyl group is replaced by an independently chosen -O-, -S-, -N(R^{10})-, -S(=O)- or -S(=O)$_2$-, where R^{10} is hydrogen, alkyl, or alkyl in which one or more methylene group is replaced by -O-, -S-, -NH, or -N-alkyl;

b) at least one polymeric surface stabilizer selected from hydroxyethyl starch, dextran, povidone, or a mixture of any of the foregoing, wherein the (wt:wt) ratio of the neurosteroid to the polymeric surface stabilizer is about 4:1 to about 0.5:1; and

c) an ionic surfactant selected from sodium cholate, sodium deoxycholate, and sodium cholesterol sulfate, and a mixture of any of the foregoing.

2. The injectable neurosteroid formulation of Claim 1, comprising nanoparticles having a D50 of less than 500 nm; wherein the formulation is an intravenous formulation; and the neurosteroid is ganaxolone.

3. The injectable neurosteroid formulation of Claim 2, wherein the formulation additionally comprises an antifoaming agent.

4. The injectable neurosteroid formulation of Claim 2, wherein the polymeric surface stabilizer is hydroxyethyl starch; and the surfactant is sodium deoxycholate.

5. The injectable neurosteroid formulation of Claim 2 additionally comprising a cryoprotectant, wherein the cryoprotectant is sucrose, dextrose, lactose, D-sorbitol, or a mixture of any of the foregoing.

6. The injectable neurosteroid formulation of Claim 2 additionally comprising one or more of the following

(a) 0.5% to 1.5% sodium chloride (weight percent);

(b) a buffer;

(c) a preservative, wherein the preservative is benzyl alcohol, chlorbutanol, 2-ethoxyethanol, parabens (including methyl, ethyl, propyl, butyl, and combinations), benzoic acid, sorbic acid, chlorhexidene, phenol, 3-cresol, thimerosal, a phenylmercurate salt, or a mixture of any of the foregoing.

7. The injectable neurosteroid formulation of Claim 1, wherein the neurosteroid is ganaxolone or allopregnanolone;

the (wt:wt) ratio of the neurosteroid to the polymeric surface stabilizer is about 4:1 to about 1:1; and

the ionic surfactant is sodium deoxycholate and the ratio of neurosteroid to sodium deoxycholate (w:w) is about 10:1.5 to about 10:0.1.

8. The formulation of Claim 7, wherein the formulation is in the form of a lyophilized powder.

9. The formulation of Claim 2, wherein the formulation is an aqueous suspension and the neurosteroid concentration is about 0.1 mg/mL to about 300 mg/mL.

10. The injectable neurosteroid formulation of Claim 1, wherein the formulation is an aqueous ganaxolone formulation comprising

(a) nanoparticles having a D50 of less than 500 nm, the nanoparticles comprising ganaxolone, wherein the weight percent of the ganaxolone is 1 to 10%;

(b) a polymeric surface stabilizer selected from hydroxy ethyl starch, dextran, and povidone, wherein the weight percent of the polymeric surface stabilizer is 2 to 20%; and

(c) sodium deoxycholate, wherein the weight percent of sodium deoxycholate is 0.1% to 2.0 %; and

(d) an antifoaming agent.

11. The injectable neurosteroid formulation of Claim 1 wherein the formulation is an aqueous formulation comprising

(a) nanoparticles having a D50 of less than 500 nm, the nanoparticles comprising ganaxolone, wherein the weight percent of the ganaxolone is about 5%;

(b) a polymeric surface stabilizer selected from hydroxy ethyl starch 130/0.4 and plasdone C-12, wherein the weight percent of the polymeric surface stabilizer is about 5% to about 10%;

(c) sodium deoxycholate, wherein the weight percent of the sodium deoxycholate is about 0.75%; and optionally

(d) simethicone, wherein the weight percent of simethicone is 0.009%.

12. A method for sterilizing the injectable neurosteroid nanoparticle formulation of Claim 2, comprising subjecting the formulation to ebeam radiation, wherein the method produces a sterilized neurosteroid nanoparticle formulation containing a degradant concentration of not more than 0.2% w/w of neurosteroid.

13. The injectable neurosteroid formulation of Claim 2, wherein the formulation has been sterilized by ebeam irradiation and wherein the formulation contains a degradant concentration of not more than 0.2% w/w of the neurosteroid.

14. The injectable neurosteroid formulation of Claim 13, wherein the ebeam irradiation is a cumulative dose of about 25kGray.

15. The injectable ganaxolone formulation of Claim 2 for use in the treatment of a seizure disorder, stroke, or traumatic brain injury in a patient.

16. The injectable ganaxoloneformulation of Claim 15, wherein the seizure disorder is status epilepticus, refractory status epilepticus, super refractory status epilepticus, or PCDH19 female pediatric epilepsy.

17. The injectable ganaxolone formulation of Claim 15 wherein at least one additional active agent is an anticonvulsant or anesthetic/sedative.