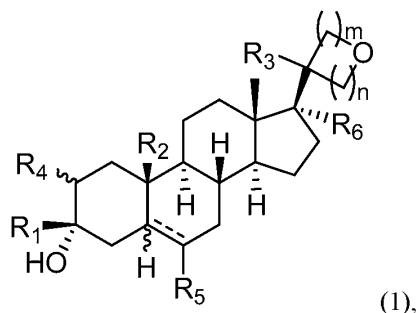


CLAIMS

What is claimed is:

1. A neuroactive steroid (NAS) according to formula (1):



one or more isomers thereof, a deuterium labeled variant thereof, or a combination thereof,

wherein:

R₁ is H, D, substituted or unsubstituted C1-C10 alkyl, C1-C5 deuterated alkyl; substituted or unsubstituted C2-C10 alkenyl, substituted or unsubstituted C2-C10 alkynyl, substituted or unsubstituted C3-C10 cycloalkyl, substituted or unsubstituted C3-C10 cycloalkenyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

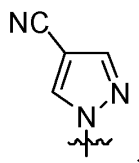
R₂, R₄ and R₅ each is independently H, halogen, -CN, substituted or unsubstituted C1-C10 alkyl, substituted or unsubstituted C2-C10 alkenyl, substituted or unsubstituted C2-C10 alkynyl, substituted or unsubstituted C3-C10 cycloalkyl, substituted or unsubstituted C3-C10 cycloalkenyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or a combination thereof;

R₃ is H, D, halogen, -CN, substituted or unsubstituted C1-C10 alkyl, -CD₃, substituted or unsubstituted C2-C10 alkenyl, substituted or unsubstituted C2-C10 alkynyl, substituted or unsubstituted C3-C10 cycloalkyl, substituted or unsubstituted C3-C10 cycloalkenyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or a combination thereof;

R₆ is H or D; and

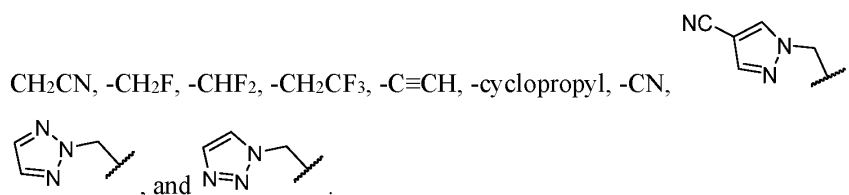
m and n each is independently 0, 1, 2 or 3, with the proviso that at least one of m and n is not 0.

2. The neuroactive steroid of claim 1, wherein at least one of said R₁, R₂, R₃, R₄ and R₅ is a C1-C10 haloalkyl, wherein said halogen is one or more Cl, F, Br or I.
3. The neuroactive steroid of claim 1 or 2, wherein at least one of said R₁, R₂, R₃, R₄ and R₅ is a substituted or unsubstituted C3-C10 cycloalkyl, substituted or unsubstituted C3-C10 cycloalkenyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.
4. The neuroactive steroid of any one of claims 1-3, wherein R₁ is H or C1-C5 alkyl.
5. The neuroactive steroid of any one of claims 1-4, wherein R₁ is H.
6. The neuroactive steroid of any one of claims 1-4, wherein R₁ is methyl or ethyl.
7. The neuroactive steroid of any one of claims 1-4, wherein R₁ is methyl.
8. The neuroactive steroid of any one of claims 1-7, wherein R₂ is H or C1-C5 alkyl.
9. The neuroactive steroid of any one of claims 1-7, wherein R₂ is H.
10. The neuroactive steroid of any one of claims 1-7, wherein R₂ is methyl or ethyl.
11. The neuroactive steroid of any one of claims 1-7, wherein R₂ is methyl.
12. The neuroactive steroid of any one of claims 1-11, wherein R₃ is H, -D, -CH₃, -CD₃, -CN, substituted or unsubstituted cyclopropyl, substituted or unsubstituted C1-C10 haloalkyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -X,



wherein X is selected from the group consisting of Cl, F, Br and I.

13. The neuroactive steroid of any one of claims 1-12, wherein R₃ is selected from the group consisting of H, -D, F, -CH₃, -CD₃, -CH₂-cyclopropyl, -CH₂OH, -COOH, -



14. The neuroactive steroid of any one of claims 1-13, wherein R₃ is H, D, F, -CH₃, -CD₃, and -CN.

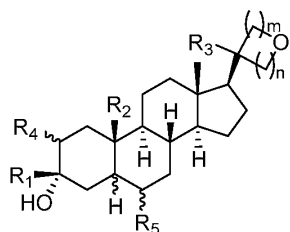
15. The neuroactive steroid of any one of claims 1-14, wherein R₄ is H or substituted or unsubstituted C1-C5 alkyl.

16. The neuroactive steroid of any one of claims 1-14, wherein R₄ is H.

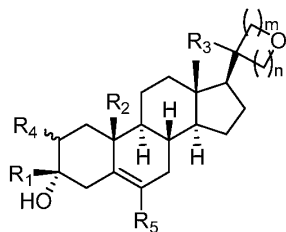
17. The neuroactive steroid of any one of claims 1-16, wherein R₅ is H or substituted or unsubstituted C1-C5 alkyl.

18. The neuroactive steroid of any one of claims 1-17, wherein R₅ is H.

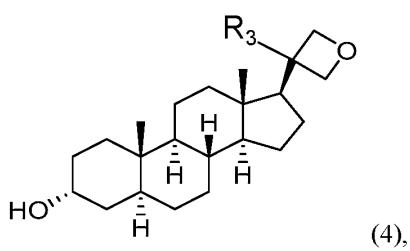
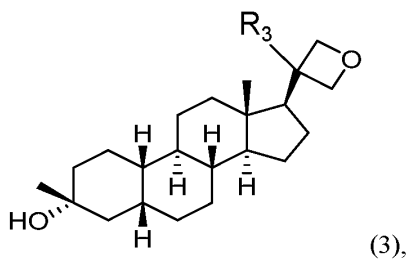
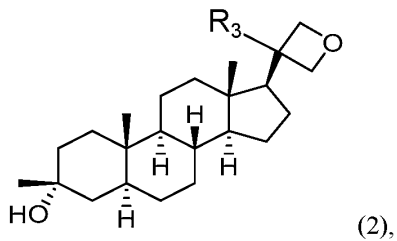
19. The neuroactive steroid of any one of claims 1-18, wherein said neuroactive steroid is:

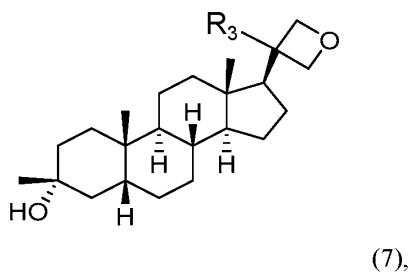
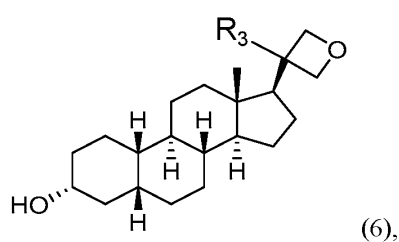
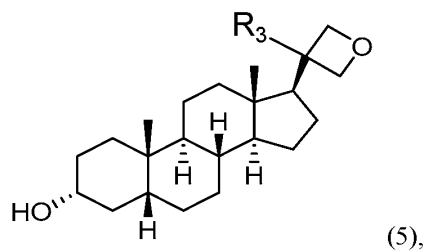


20. The neuroactive steroid of any one of claims 1-18, wherein said neuroactive steroid is:



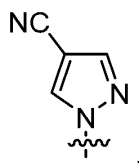
21. The neuroactive steroid of claim 1, wherein said neuroactive steroid is:





one or more isomers thereof, or a combination thereof.

22. The neuroactive steroid of claim 21, wherein said R_3 is H, -D, -CH₃, -CD₃, -CN, substituted or unsubstituted cyclopropyl, substituted or unsubstituted C1-C10 haloalkyl, substituted or unsubstituted C3-C10 heterocycloalkyl, substituted or unsubstituted C3-C10 heterocycloalkenyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, -X, or

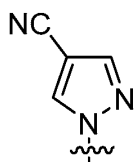


wherein said X is Cl, F, Br or I.

23. The neuroactive steroid of claim 22, wherein said C1-C10 haloalkyl is -CXH₂, -CX₂H, -CX₃, -CH₂CXH₂, -CH₂CX₂H, or -CH₂CX₃, and wherein X is Cl, F, Br, I.

24. The neuroactive steroid of claim 23, wherein said C1-C10 haloalkyl is -CFH₂, -CF₂H, -CF₃, -CH₂CFH₂, -CH₂CF₂H or -CH₂CF₃.

25. The neuroactive steroid of claim 21, wherein said R₃ is:



26. The neuroactive steroid of claim 21, wherein said R₃ is H, D, F, -CH₃, -CD₃, and -CN.

27. A pharmaceutical composition comprising a neuroactive steroid (NAS) any one of claims 1-26; and a pharmaceutically acceptable excipient.

28. A method for treating a disease in a subject in need thereof, said method comprising administering said subject an effective dosage of the pharmaceutical composition of claim 27.

29. The method of claim 28, wherein said pharmaceutical composition is administered to said subject via intramuscular (IM) injection, subcutaneous (SC) injection, intravenous (IV) injection, oral administration, topical application, implant application or a combination thereof.

30. The method of any one of claims 28 or 29, wherein said disease comprises sleep disorders, insomnia, mood disorders, depression, dysthymic disorder, mild depression, bipolar disorder, anxiety disorders, generalized anxiety disorder (GAD), social anxiety disorder, stress, post-traumatic stress disorder (PTSD), compulsive disorders, obsessive compulsive disorder (OCD), schizophrenia spectrum disorders, schizophrenia, schizoaffective disorder, convulsive disorders, epilepsy, status epilepticus (SE), seizures, disorders of memory and/or cognition, attention disorders, attention deficit hyperactivity disorder (ADHD), dementia, Alzheimer's type dementia, Lewis body type dementia, vascular type dementia, movement disorders, Huntington's

disease, Parkinson's disease, personality disorders, anti-social personality disorder, obsessive compulsive personality disorder, autism spectrum disorders (ASD), autism, monogenetic causes of autism, synaptophathy's, Rett syndrome, Fragile X syndrome, Angelman syndrome, neuropathic pain, injury related pain syndromes, acute pain, chronic pain, traumatic brain injury (TBI), vascular diseases, stroke, ischemia, vascular malformations, substance abuse disorders and/or withdrawal syndromes, addition to opiates, addition to cocaine, addition to alcohol, tinnitus, or a combination thereof.

31. The method of any one of claims 28-30, wherein said disease comprises CDD, MDD, PPD, essential tremor, PTSD, SE, ESE, Fragile X syndrome, Parkinson's Disease, or treatment resistant depression.

32. Use of the neuroactive steroid of any one of claims 1-26 for manufacturing a medicament for treating a disease, wherein said disease comprises sleep disorders, insomnia, mood disorders, depression, dysthymic disorder, mild depression, bipolar disorder, anxiety disorders, generalized anxiety disorder (GAD), social anxiety disorder, stress, post-traumatic stress disorder (PTSD), compulsive disorders, obsessive compulsive disorder (OCD), schizophrenia spectrum disorders, schizophrenia, schizoaffective disorder, convulsive disorders, epilepsy, status epilepticus (SE), seizures, disorders of memory and/or cognition, attention disorders, attention deficit hyperactivity disorder (ADHD), dementia, Alzheimer's type dementia, Lewy body type dementia, vascular type dementia, movement disorders, Huntington's disease, Parkinson's disease, personality disorders, anti-social personality disorder, obsessive compulsive personality disorder, autism spectrum disorders (ASD), autism, monogenetic causes of autism, synaptophathy's, Rett syndrome, Fragile X syndrome, Angelman syndrome, neuropathic pain, injury related pain syndromes, acute pain, chronic pain, traumatic brain injury (TBI), vascular diseases, stroke, ischemia, vascular malformations, substance abuse disorders and/or withdrawal syndromes, addition to opiates, addition to cocaine, addition to alcohol, tinnitus, or a combination thereof.

33. The use of claim 32, wherein said disease comprises CDD, MDD, PPD, essential tremor, PTSD, SE, ESE, Fragile X syndrome, Parkinson's Disease, or treatment resistant depression.