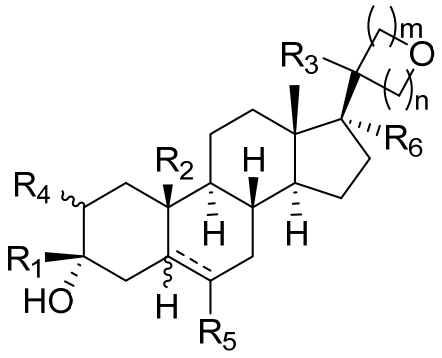
CLAIMS

What is claimed is:

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



(1),

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

R_1 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;

R_2, R_4 and R_5 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;

R_3 is H, D, halogen, -CN, substituted or unsubstituted C1-C10 alkyl, $-CD_3$, 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;

R_6 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 R_1, R_2, R_3, R_4 and R_5 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 R_1, R_2, R_3, R_4 and R_5 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 R_1 is H or C1-C5 alkyl.

5. The neuroactive steroid of any one of claims 1-4, wherein R_1 is H.

6. The neuroactive steroid of any one of claims 1-4, wherein R_1 is methyl or ethyl.

7. The neuroactive steroid of any one of claims 1-4, wherein R_1 is methyl.

8. The neuroactive steroid of any one of claims 1-7, wherein R_2 is H or C1-C5 alkyl.

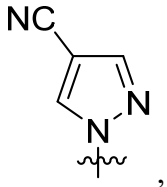
9. The neuroactive steroid of any one of claims 1-7, wherein R_2 is H.

10. The neuroactive steroid of any one of claims 1-7, wherein R_2 is methyl or ethyl.

11. The neuroactive steroid of any one of claims 1-7, wherein R_2 is methyl.

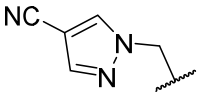
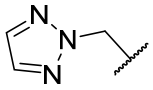
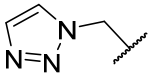
12. The neuroactive steroid of any one of claims 1-11, wherein R_3 is H, -D, $-CH_3$, $-CD_3$, -CN, substituted or unsubstituted cyclopropyl, substituted or unsubstituted C1-C10 haloalkyl,

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 R_3 is selected from the group consisting of H, -D, F, $-CH_3$, $-CD_3$, $-CH_2$-cyclopropyl, $-CH_2OH$, -COOH, $-CH_2CN$, $-CH_2F$, $-CHF_2$, $-CH_2CF_3$, -C≡CH, -cyclopropyl, -CN, , , and .

14. The neuroactive steroid of any one of claims 1-13, wherein R_3 is H, D, F, $-CH_3$, $-CD_3$, ~~and~~ or -CN.

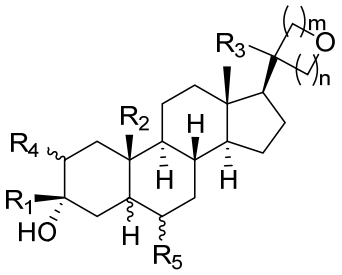
15. The neuroactive steroid of any one of claims 1-14, wherein R_4 is H or substituted or unsubstituted C1-C5 alkyl.

16. The neuroactive steroid of any one of claims 1-14, wherein R_4 is H.

17. The neuroactive steroid of any one of claims 1-16, wherein R_5 is H or substituted or unsubstituted C1-C5 alkyl.

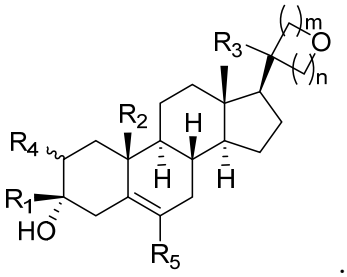
18. The neuroactive steroid of any one of claims 1-l7, wherein R_5 is H.

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



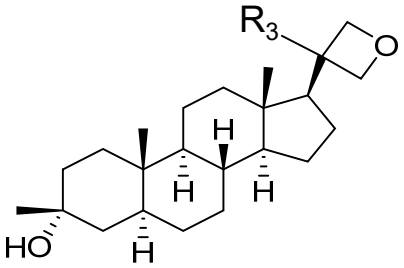
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20. The neuroactive steroid of any one of claims 1-18, wherein said neuroactive steroid is:

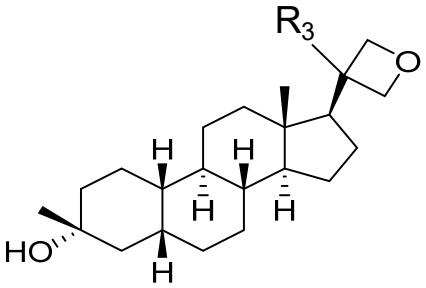


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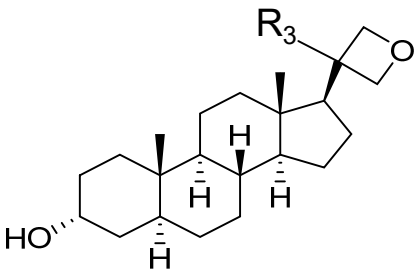
21. The neuroactive steroid of claim 1, wherein said neuroactive steroid is:



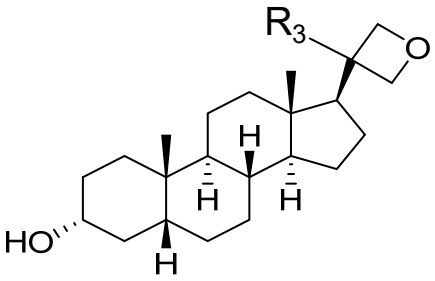
(2),



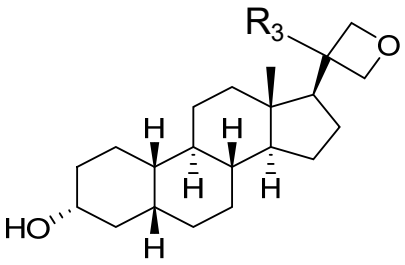
(3),



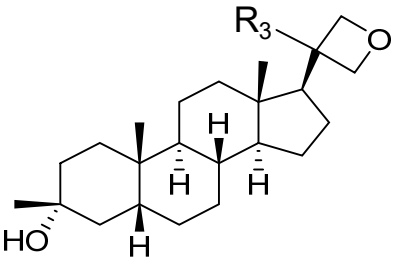
(4),



(5),



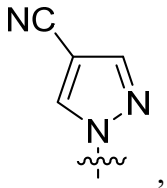
(6),



(7),

one or more isomers thereof, or a combination thereof.

22. The neuroactive steroid of claim 21, wherein said R_3 is H, -D, $-CH_3$, $-CD_3$, -CN, substituted or unsubstituted cyclopropanyl, 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



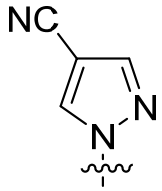
,

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

23. The neuroactive steroid of claim 22, wherein said C1-C10 haloalkyl is -CXH_2, -CX_2H, -CX_3, -CH_2CXH_2, -CH_2CX_2H, or -CH_2CX_3, and wherein X is Cl, F, Br, or I.

24. The neuroactive steroid of claim 23, wherein said C1-C10 haloalkyl is -CFH_2, -CF_2H, -CF_3, -CH_2CFH_2, -CH_2CF_2H or -CH_2CF_3.

25. The neuroactive steroid of claim 21, wherein said R_3 is:



.

26. The neuroactive steroid of claim 21, wherein said R_3 is H, D, F, -CH_3, -CD_3, ~~and~~ or -CN.

27. A pharmaceutical composition comprising a neuroactive steroid (NAS) of 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.~~

28~~32~~. Use of the neuroactive steroid of any one of claims 1-26 or the pharmaceutical composition of claim 27 ~~for manufacturing~~in the manufacture of a medicament for the treatment of ~~treating~~ a disease in a subject, 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, and wherein an effective dosage of the neuroactive steroid or the pharmaceutical composition is to be administered to the subject.

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

3033. The use of claim 28 or 2932, wherein said disease comprises CDD, MDD, PPD, essential tremor, PTSD, SE, ESE, Fragile X syndrome, Parkinson's Disease, or treatment resistant depression.

31. The neuroactive steroid of any one of claims 1-26 or the pharmaceutical composition of claim 27 for use in therapy.