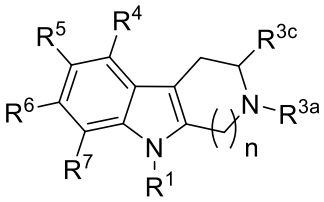
WHAT IS CLAIMED IS:

1. A compound having the following structure:




wherein:

$R^1$ is hydrogen or $C_{1-6}$ alkyl;

$R^{3a}$ is ~~hydrogen,~~ $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, or $C_{4-14}$ alkyl-cycloalkyl;

$R^{3c}$ is hydrogen or $C_{1-6}$ alkyl;

$R^4$, $R^5$~~, $R^6$~~ and $R^7$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $–OR^{8a}$, $-NO_2$, -CN, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, ~~wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H;~~

$R^6$ is F, -OH, -OMe, -OiPr, -Me, $-CF_3$, $-OCF_3$, $-NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me;

alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ heterocycloalkyl;

$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, or $C_{1-6}$ alkyl;

n is 2 or 3;

wherein when n is 2 and $R^6$ is F then at least one of $R^4$, $R^5$, and $R^7$ is not hydrogen; and

wherein when n is 2 and $R^6$ is F, Cl, methyl, or OMe, then $R^{3a}$ is methyl,

or pharmaceutically acceptable salts and isotopically-labeled compounds ~~isomers~~ thereof.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^1$ is hydrogen or methyl.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein $R^1$ is hydrogen.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein $R^{3a}$ is ~~hydrogen or~~ methyl.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein

~~$R^6$ is $C_{1-6}$ alkyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, $-CN$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, or $C_{4-16}$ alkyl-heterocycloalkyl;~~

~~alternatively,~~ $R^5$ and $R^6$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ heterocycloalkyl; and

$R^{8a}$, $R^{8b}$ and$R^{8c}$ are each independently H, or $C_{1-6}$ alkyl.

~~6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein:~~

~~$R^6$ is $C_{1-6}$ alkyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $C_{4-10}$ heterocycloalkyl, or $C_{4-16}$ alkyl-heterocycloalkyl;~~

~~alternatively, $R^5$ and $R^6$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ heterocycloalkyl; and~~

~~$R^{8a}$, $R^{8b}$ and $R^{8c}$ are each independently H, or $C_{1-6}$ alkyl.~~

~~7~~6. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

$R^4$, $R^5$~~, $R^6$~~ and $R^7$ are each independently H, F, Cl, Br, -OH, -OMe, $-CF_3$ $-OCF_3$, -Me, $-NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me,

~~wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H;~~

alternatively, $R^5$ and $R^6$ are combined to form a 1,3-dioxole ring, or 1,4-dioxane ring.

~~8~~7. The compound of any one of claims 1 to ~~7~~6, or a pharmaceutically acceptable salt thereof, wherein:

$R^4$ is H, F, -Me, $-CF_3$, $-OCF_3$, or -OMe;

$R^5$ is H, F, Cl, Br, -Me, $-CF_3$, $-OCF_3$, -OH or -OMe;

$R^6$ is ~~H,~~ F, -OH, -OMe, -OiPr, -Me, $-CF_3$, $-OCF_3$, $-NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me;

alternatively, $R^5$ and $R^6$ are combined to form a 1,3-dioxole ring or 1,4-dioxane ring; and

$R^7$ is H~~, wherein at least one of $R^4$, $R^5$ and $R^6$ is not H~~.

~~9~~8. The compound of any one of claims 1 to ~~8~~7, or a pharmaceutically acceptable salt thereof, wherein

$R^6$ is F, -OH, -OMe, -OiPr, -Me, $-CF_3$, $-OCF_3$, $-NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me;

alternatively, $R^5$ and $R^6$ are combined to form a 1,3-dioxole ring or 1,4-dioxane ring.

~~10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein~~

~~$R^6$ is $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, -CN, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl;~~

~~alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ heterocycloalkyl;~~

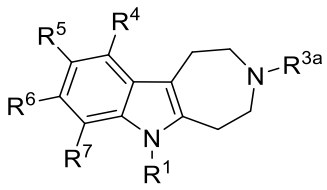
~~$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, or $C_{1-6}$ alkyl; and~~

~~n is 2, or 3;~~

~~wherein when n is 2 and $R^6$ is F then at least one of $R^4$, $R^5$, and $R^7$ is not hydrogen; and~~

~~wherein when n is 2 and $R^6$ is F, Cl, methyl, or OMe, then $R^{3a}$ is methyl.~~

~~11~~9. The compound of any one of claims 1 to ~~10~~8, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



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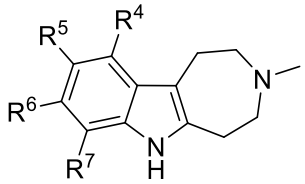
~~12~~10. The compound of any one of claims 1 to ~~11~~9, or a pharmaceutically acceptable salt thereof, wherein $R^{3a}$ is methyl.

~~13~~11. The compound of any one of claims 1 to ~~12~~10, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



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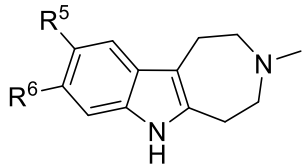
~~14~~12. The compound of any one of claims 1 to ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



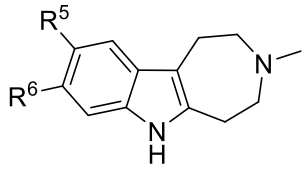
wherein:

$R^5$ ~~and $R^6$ are each independently~~is H, F, Cl, Br, I, -OH, -OMe, -OiPr, -Me, -$CF_3$,-$OCF_3$, -$NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me,

~~wherein at least one of $R^5$ and $R^6$ is not H;~~

alternatively, $R^5$ and $R^6$ are combined to form a 1,3-dioxole ring or 1,4-dioxane ring.

~~15~~13. The compound of any one of claims 1 to ~~14~~12, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:

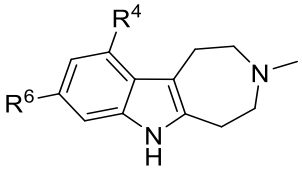


wherein:

$R^5$ ~~and $R^6$ are each independently~~is F, Cl, Br, I, -OH, -OMe, -OiPr, -Me, -$CF_3$,-$OCF_3$, -$NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me;

alternatively, $R^5$ and $R^6$ are combined to form a 1,3-dioxole ring or 1,4-dioxane ring.

~~16~~14. The compound of any one of claims 1 to ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:

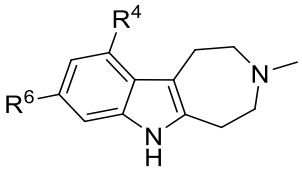


wherein:

$R^4$ ~~and $R^6$ are each independently H,~~is F, Cl, Br, I, -OH, -OMe, -OiPr, -Me, -$CF_3$,-$OCF_3$, -$NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me~~,~~

~~wherein at least one of $R^4$ and $R^6$ is not H~~.

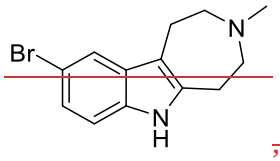
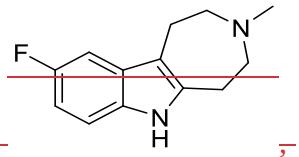
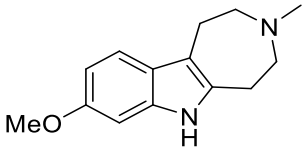
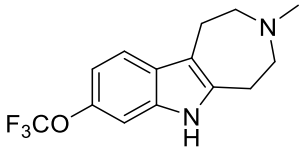
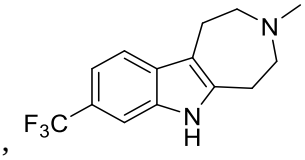
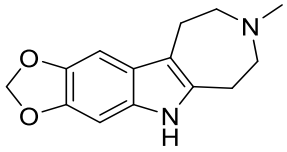
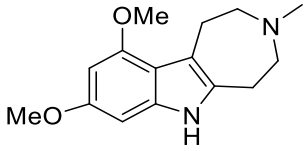
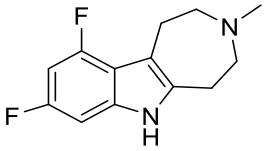
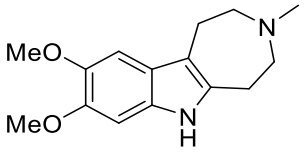
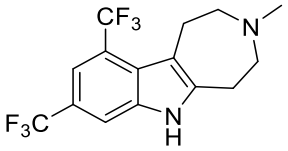
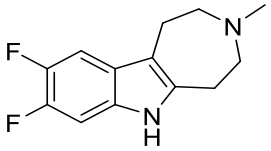
~~17~~15. The compound of any one of claims 1 to ~~13~~ 11 or ~~16~~14, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



wherein:

$R^4$ ~~and $R^6$ are each independently~~is F, Cl, Br, I, -OH, -OMe, -OiPr, -Me, -$CF_3$, -$OCF_3$, -$NMe_2$, -NHC(O)Me, or -N(Me)C(O)Me.

~~18~~16. The compound of any one of claims 1 to ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the compound is

, or



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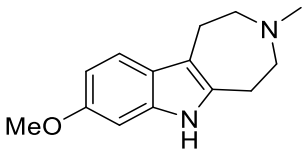
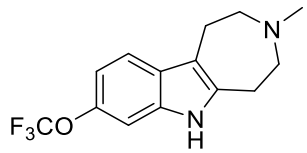
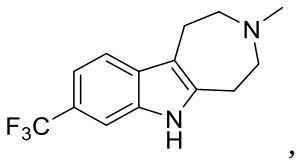
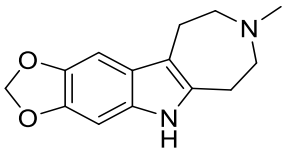
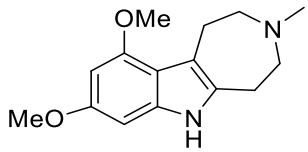
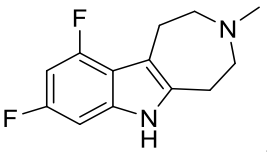
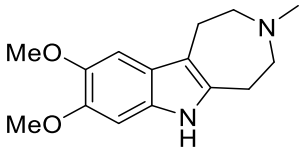
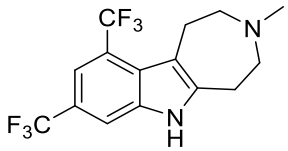
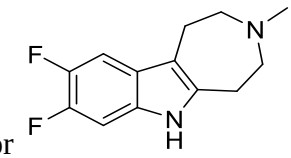
~~19~~17. The compound of any one of claims 1 to ~~13~~ 11 or ~~18~~16, or a pharmaceutically acceptable salt thereof, wherein the compound is

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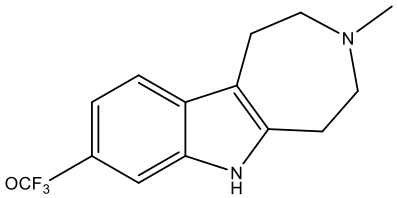
~~20~~18. The compound of any one of claims 1 to ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the compound is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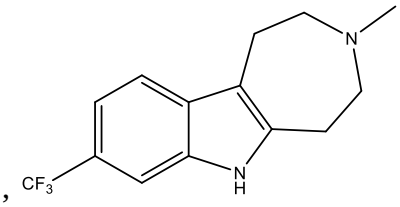
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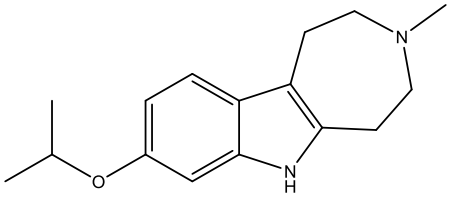
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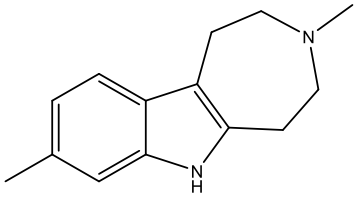
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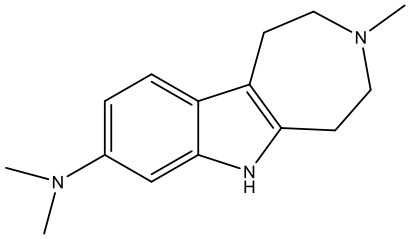
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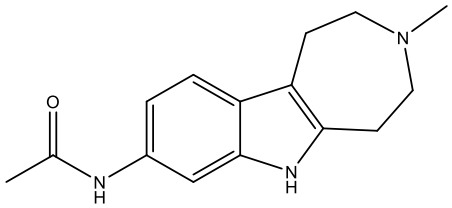
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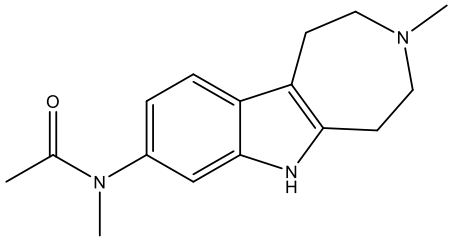
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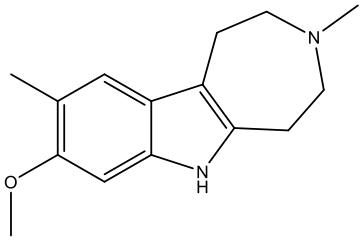
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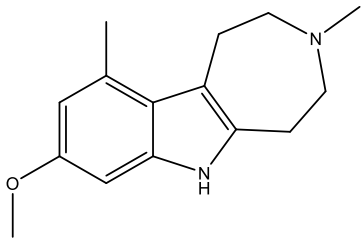
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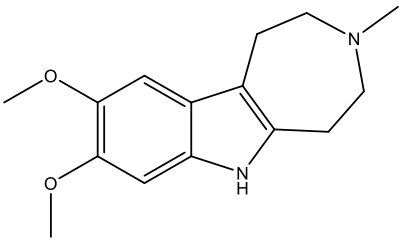
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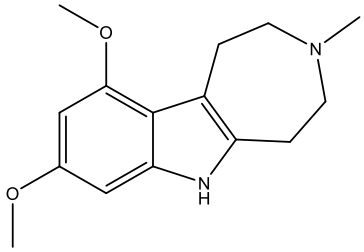
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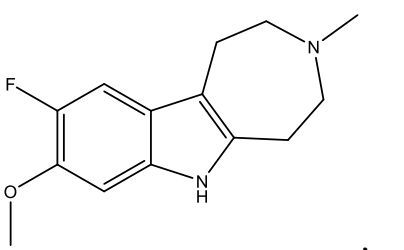
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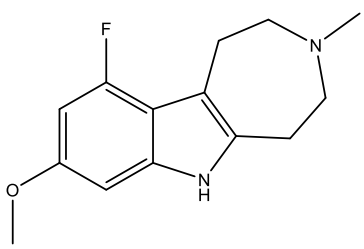
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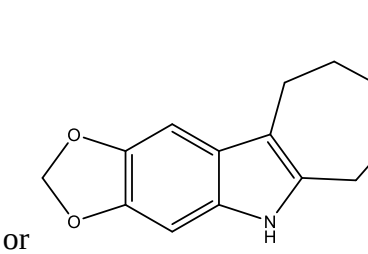
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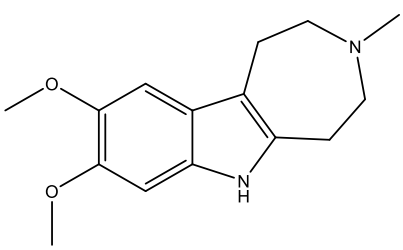
~~21~~19. The compound of any one of claims 1 to ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the compound is



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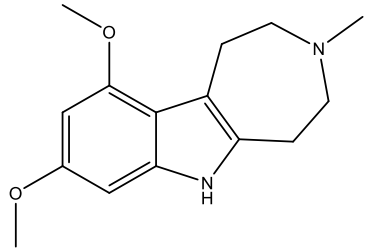

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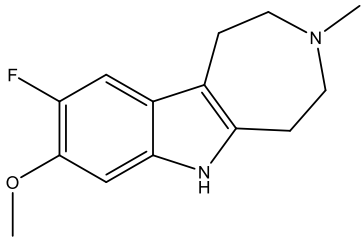
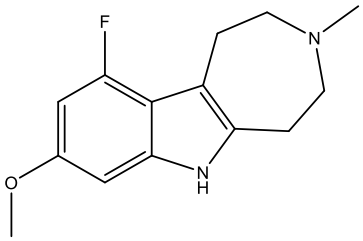
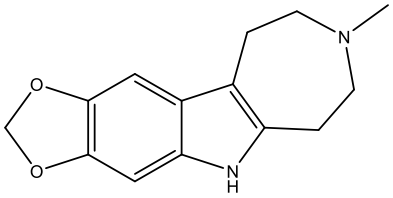


,


, or


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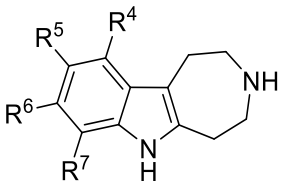
~~22~~20. The compound of any one of claims 1 to ~~11~~9, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



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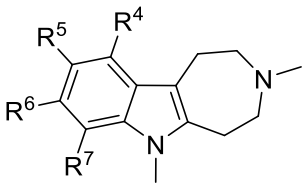
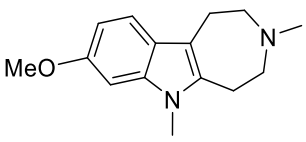
~~23~~21. The compound of any one of claims 1 to ~~9~~8, or a pharmaceutically acceptable salt thereof, wherein the compound has the following structure:



.

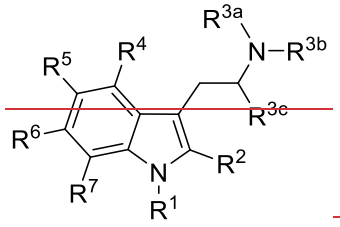
~~24~~22. The compound of claim ~~23~~21, or a pharmaceutically acceptable salt thereof, wherein the compound is



.

~~25~~23. A pharmaceutical composition comprising a compound of any one of claims 1 to ~~24~~22, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

~~26~~24. Use of a compound of any one of claims 1 to 22~~Formula I:~~




~~(I)~~

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing neuronal plasticity of a neuronal cell~~, wherein:~~

~~$R^1$ is hydrogen or $C_{1-6}$ alkyl;~~

~~$R^{3a}$ and $R^{3b}$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, or $C_{4-14}$ alkyl-cycloalkyl;~~

~~$R^{3c}$ is hydrogen or $C_{1-6}$ alkyl;~~

~~alternatively, $R^2$ and $R^{3b}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ heterocycloalkyl substituted with 1 to 3 $R^9$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^9$ groups attached to the same atom are combined to form =O;~~

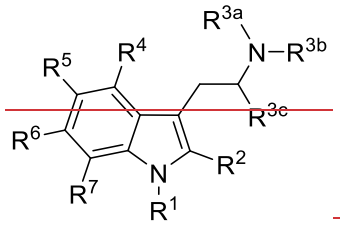
~~alternatively, $R^2$ and $R^{3c}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ cycloalkyl, substituted with 1 to 3 $R^{10}$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^{10}$ groups attached to the same atom are combined to form =O;~~

~~$R^4$, $R^5$, $R^6$ and $R^7$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, $-CN$, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H;~~

~~alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ cycloalkyl, $C_{3-6}$ heterocycloalkyl, $C_{6-12}$ aryl or $C_{5-10}$ heteroaryl; and~~

~~$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, $C_{1-6}$ alkyl~~.

~~27~~25. Use of a compound of any one of claims 1 to 22~~Formula I:~~




~~(I)~~

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a brain disorder~~, wherein:~~

~~$R^1$ is hydrogen or $C_{1-6}$ alkyl;~~

~~$R^{3a}$ and $R^{3b}$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, or $C_{4-14}$ alkyl-cycloalkyl;~~

~~$R^{3c}$ is hydrogen or $C_{1-6}$ alkyl;~~

~~alternatively, $R^2$ and $R^{3b}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ heterocycloalkyl substituted with 1 to 3 $R^9$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^9$ groups attached to the same atom are combined to form =O;~~

~~alternatively, $R^2$ and $R^{3c}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ cycloalkyl, substituted with 1 to 3 $R^{10}$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^{10}$ groups attached to the same atom are combined to form =O;~~

~~$R^4$, $R^5$, $R^6$ and $R^7$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, $-CN$, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H;~~

~~alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ cycloalkyl, $C_{3-6}$ heterocycloalkyl, $C_{6-12}$ aryl or $C_{5-10}$ heteroaryl; and~~

~~$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, $C_{1-6}$ alkyl~~.

~~28~~26. The use of claim ~~27~~25, wherein the brain disorder is a neurodegenerative disorder, Alzheimer's, or Parkinson's disease.

~~29~~27. The use of claim ~~27~~25, wherein the brain disorder is a psychological disorder, depression, addiction, anxiety, or a post-traumatic stress disorder.

~~30~~28. The use of claim ~~29~~27, wherein the brain disorder is depression.

~~31~~29. The use of claim ~~29~~27, wherein the brain disorder is addiction.

~~32~~30. The use of claim ~~27~~25, wherein the brain disorder is treatment resistant depression, suicidal ideation, major depressive disorder, bipolar disorder, or substance use disorder.

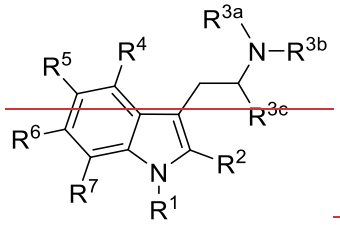
~~33~~31. The use of claim ~~27~~25, wherein the brain disorder is schizophrenia.

~~34~~32. The use of claim ~~27~~ 25, wherein the brain disorder is alcohol use disorder.

~~35~~33. The use of claim 25~~27~~, wherein the brain disorder is stroke or traumatic brain injury.

~~36~~34. The use of any one of claims ~~27~~ 25 to ~~35~~33, wherein one or more additional therapeutic agent that is lithium, Olanzapine (Zyprexa), Quetiapine (Seroquel), Risperidone (Risperdal), Ariprazole (Abilify), Ziprasidone (Geodon), Clozapine (Clozaril), divalproex sodium (Depakote), lamotrigine (Lamictal), valproic acid (Depakene), carbamazepine (Equetro), topiramate (Topamax), levomilnacipran (Fetzima), duloxetine (Cymbalta, Yentreve), venlafaxine (Effexor), citalopram (Celexa), fluvoxamine (Luvox), escitalopram (Lexapro), fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), clomipramine (Anafranil), amitriptyline (Elavil), desipramine (Norpramin), imipramine (Tofranil), nortriptyline (Pamelor), phenelzine (Nardil), tranylcypromine (Parnate), diazepam (Valium), alprazolam (Xanax), or clonazepam (Klonopin) is to be administered.

~~37~~35. Use of a compound of ~~Formula I:~~




~~(I)~~any one of claims 1 to 22

or a pharmaceutically acceptable salt thereof, in an amount sufficient to increase neuronal plasticity of a neuronal cell, in the manufacture of a medicament for increasing at least one of translation, transcription or secretion of neurotrophic factors~~, wherein:~~

~~$R^1$ is hydrogen or $C_{1-6}$ alkyl;~~

~~$R^{3a}$ and $R^{3b}$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, or $C_{4-14}$ alkyl-cycloalkyl;~~

~~$R^{3c}$ is hydrogen or $C_{1-6}$ alkyl;~~

~~alternatively, $R^2$ and $R^{3b}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ heterocycloalkyl substituted with 1 to 3 $R^9$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^9$ groups attached to the same atom are combined to form =O;~~

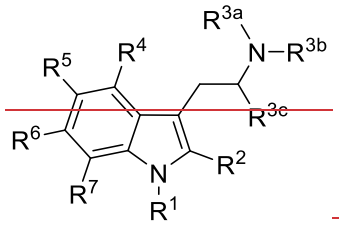
~~alternatively, $R^2$ and $R^{3c}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ cycloalkyl, substituted with 1 to 3 $R^{10}$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^{10}$ groups attached to the same atom are combined to form =O;~~

~~$R^4$, $R^5$, $R^6$ and $R^7$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, $-CN$, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H;~~

~~alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ cycloalkyl, $C_{3-6}$ heterocycloalkyl, $C_{6-12}$ aryl or $C_{5-10}$ heteroaryl; and~~

~~$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, $C_{1-6}$ alkyl~~.

~~38~~36. A compound of ~~Formula I:~~




~~(I)~~any one of claims 1 to 22,

or a pharmaceutically acceptable salt thereof, for use in therapy.~~,~~

~~wherein:~~

~~$R^1$ is hydrogen or $C_{1-6}$ alkyl;~~

~~$R^{3a}$ and $R^{3b}$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, or $C_{4-14}$ alkyl-cycloalkyl;~~

~~$R^{3c}$ is hydrogen or $C_{1-6}$ alkyl;~~

~~alternatively, $R^2$ and $R^{3b}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ heterocycloalkyl substituted with 1 to 3 $R^9$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^9$ groups attached to the same atom are combined to form =O;~~

~~alternatively, $R^2$ and $R^{3c}$ are combined with the atoms to which they are attached to form a $C_{5-8}$ cycloalkyl, substituted with 1 to 3 $R^{10}$ groups which are each independently hydrogen, $C_{1-6}$ alkyl, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, or two $R^{10}$ groups attached to the same atom are combined to form =O;~~

~~$R^4$, $R^5$, $R^6$ and $R^7$ are each independently hydrogen, $C_{1-6}$ alkyl, $C_{2-6}$ alkenyl, $C_{2-6}$ alkynyl, halogen, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamine, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkoxy, $-OR^{8a}$, $-NO_2$, $-CN$, $-C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-OC(O)OR^{8b}$, $-N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)R^{8c}$, $-C(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)OR^{8c}$, $-OC(O)N(R^{8b}R^{8c})$, $-N(R^{8b})C(O)N(R^{8c}R^{8d})$, $-C(O)C(O)N(R^{8b}R^{8c})$, $-S(O_2)R^{8b}$, $-$~~

~~$S(O)_2N(R^{8b}R^{8c})$, $C_{3-8}$ cycloalkyl, $C_{3-14}$ alkyl-cycloalkyl, $C_{4-10}$ heterocycloalkyl, $C_{4-16}$ alkyl-heterocycloalkyl, $C_{6-12}$ aryl, $C_{7-18}$ alkyl-aryl, $C_{5-10}$ heteroaryl, or $C_{4-16}$ alkyl-heteroaryl, wherein at least one of $R^4$, $R^5$, $R^6$ and $R^7$ is not H; alternatively, $R^4$ and $R^5$, $R^5$ and $R^6$, or $R^6$ and $R^7$ are combined with the atoms to which they are each attached to form a $C_{3-6}$ cycloalkyl, $C_{3-6}$ heterocycloalkyl, $C_{6-12}$ aryl or $C_{5-10}$ heteroaryl; and~~

~~$R^{8a}$, $R^{8b}$, $R^{8c}$ and $R^{8d}$ are each independently H, $C_{1-6}$ alkyl.~~

~~39. The use or compound for use of any one of claims 26 to 38, wherein the compound has a structure represented by a compound of any one of claims 1 to 24.~~