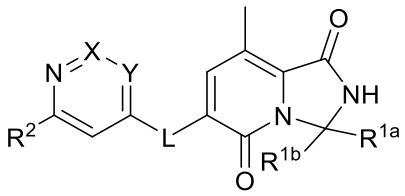
CLAIMS

1. A compound having the following Structure (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof, wherein

R^{1a} is C_1-C_6 alkyl or aryl;

R^{1b} is C_1-C_6 alkyl or aryl,

or R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form cycloalkyl, cycloalkenyl, heterocyclyl, aryl, or heteroaryl;

R^2 is $–NHR^{3a}$, $–NHC(=O)R^{3b}$, $–NHC(=S)R^{3b}$, or $–C(=O)R^{3c}$;

R^{3a} is hydrogen, C_1-C_6 alkyl, or C_3-C_6 cycloalkyl, each of which is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, C_3-C_6 cycloalkyl, $-NHS(O)_2CH_3$, heterocyclyl, $-C(=O)OH$, $-C(=O)N(R^{3d})R^{3d}$, or $-N(R^{3d})R^{3d}$;

R^{3b} is C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or heterocyclyl each of which is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, halo, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, $-NHS(O)_2CH_3$, $-N(R^{3d})R^{3d}$, heterocyclyl, $-C(=O)OH$, $-C(=O)N(R^{3d})R^{3d}$, $-NHC(=O)CH_3$, $-CH_2C(=O)OH$,

R^{3c} is $-N(R^{3d})R^{3d}$ or heterocyclyl;

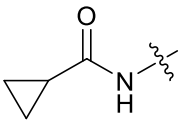
R^{3d} is, at each occurrence, independently hydrogen, C_1-C_6 alkyl, or C_3-C_6 cycloalkyl;

L is $–NH–$ or $–CH_2NH–$; and

X is N and Y is CH or X is CH and Y is N,

provided that:

when R^{1a} and R^{1b} are both $–CH_3$ or when R^{1a} and R^{1b} join to form a 5- or 6-membered cycloalkyl or heterocyclyl, then R^2 does not have the following structure:

$–NH_2$ or  .

2. The compound of claim 1, wherein R^{1a} is C_1-C_6 alkyl, preferably methyl.

~~3. The compound of any one of claims 1 or 2, wherein R^{1a} is methyl.~~

~~4~~3. The compound of claim 1, wherein R^{1a} is aryl, preferably phenyl.

~~5. The compound of any one of claims 1 or 4, wherein R^{1a} is phenyl.~~

~~6~~4. The compound of any one of claims 1-~~5~~3, wherein R^{1b} is C_1-C_6 alkyl, preferably methyl.

~~7. The compound of any one of claims 1-6, wherein R^{1b} is methyl.~~

~~8~~5. The compound of claim 1, wherein R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form cycloalkyl, preferably cyclopentyl or cyclohexyl.

~~9. The compound of claim 8, wherein the cycloalkyl is cyclopentyl or cyclohexyl.~~

~~10~~6. The compound of claim 1, wherein R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form cycloalkenyl, preferably cyclopentenyl, cyclohexenyl, or cycloheptenyl.

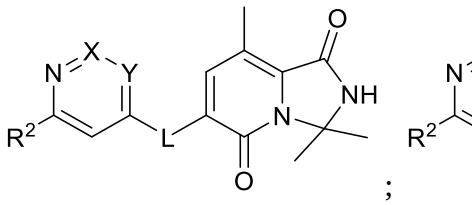
~~11. The compound of claim 10, wherein the cycloalkenyl is cyclopentenyl, cyclohexenyl, or cycloheptenyl.~~

~~12~~7. The compound of claim 1, wherein R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form heterocyclyl, aryl, or heteroaryl.

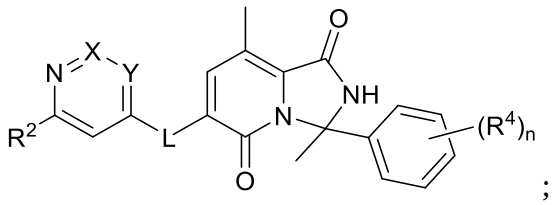
~~13. The compound of claim 1, wherein R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form aryl.~~

~~14. The compound of claim 1, wherein R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form heteroaryl.~~

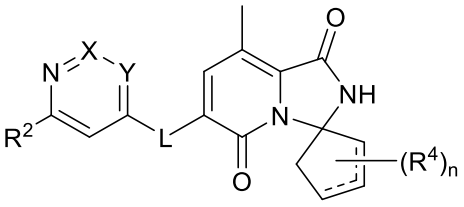
~~15~~8. The compound of any one of claims 1-~~14~~7, wherein the compound has one of the following structures:



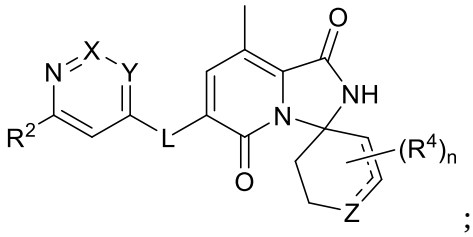
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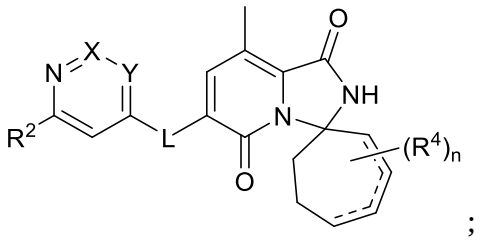
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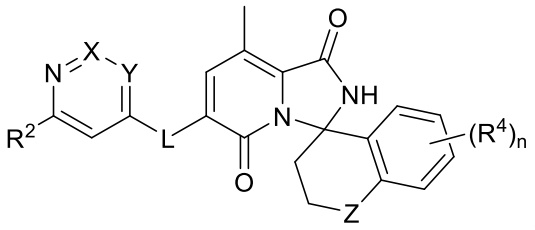


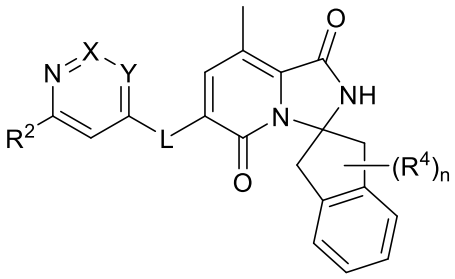
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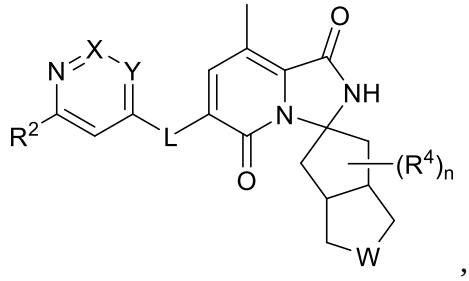


;



;


;


or


,

or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof, wherein

---- indicates a double or single bond;

R^4 is, at each occurrence, independently C_1-C_6 alkyl, C_3-C_6 cycloalkyl, halo, haloalkyl, hydroxyl, -$NHS(O)_2CH_3$, or -C(O)OH,

or two R^4, together with the carbon to which they are both attached, join to form a cycloalkyl;

W is N or O;

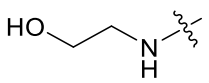
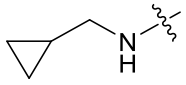
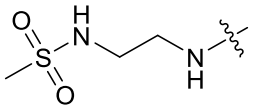
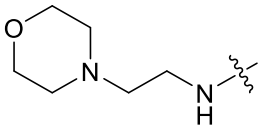
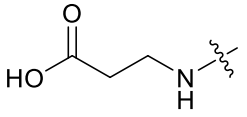
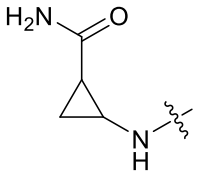
Z is C or O; and

n is 0, 1, 2, 3, or 4.

~~16~~9. The compound of claim ~~15~~8, wherein n is 0, 1, or 2.

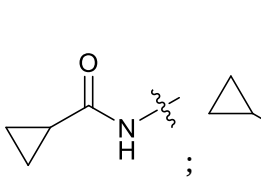
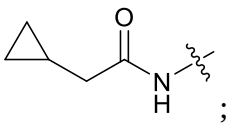
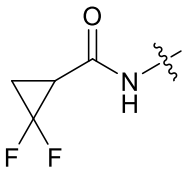
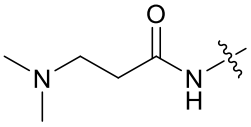
~~17~~10. The compound of any one of claims 1-~~16~~9, wherein R^2 is –NHR^{3a}~~.~~; or

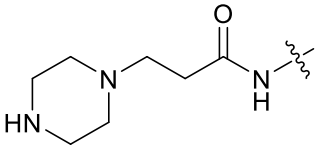
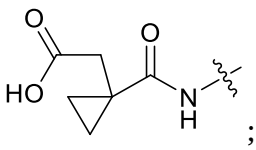
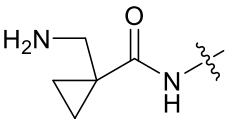
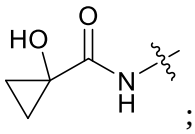
~~18. The compound of any one of claims 1-17, wherein~~ R^2 has one of the following structures:

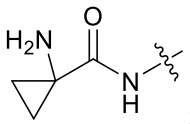
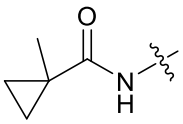
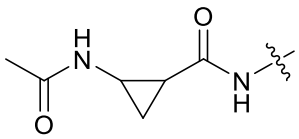
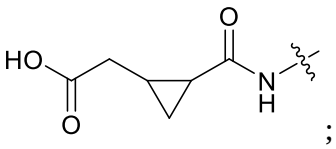
-NH_2;  ;  ;  ;  ;  or  -; or

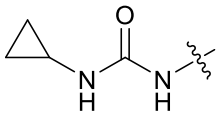
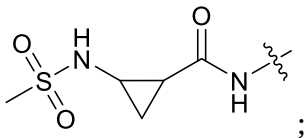
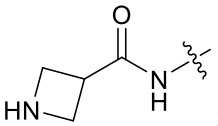
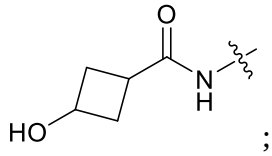
~~19. The compound of any one of claims 1-16, wherein~~ R^2 is –NHC(=O)R^{3b} ~~-~~; or

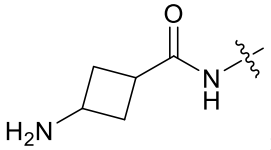
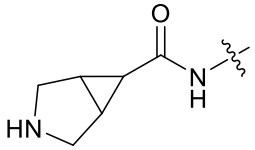
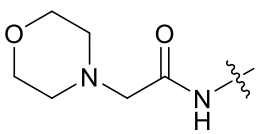
~~20. The compound of any one of claims 1-16, wherein~~ R^2 has one of the following structures:

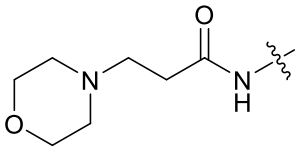
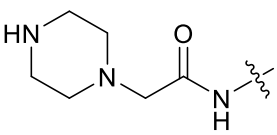
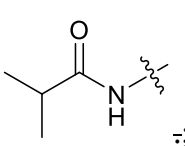
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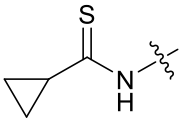
 ;  ;  ;  ;

 ;  ;  ;

 ;  or  -; or

~~21. The compound of any one of claims 1-16, wherein~~ R^2 is –$NHC(=S)R^{3b}$~~.~~; or

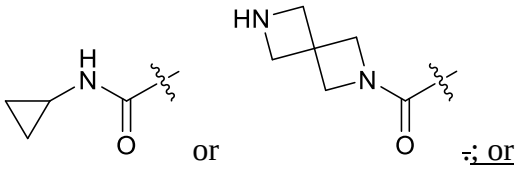
~~22. The compound of any one of claims 1-16, wherein~~ R^2 has the following structure:



~~.~~; or

~~23. The compound of any one of claims 1-16, wherein~~ R^2 is –$C(=O)R^{3c}$~~.~~; or

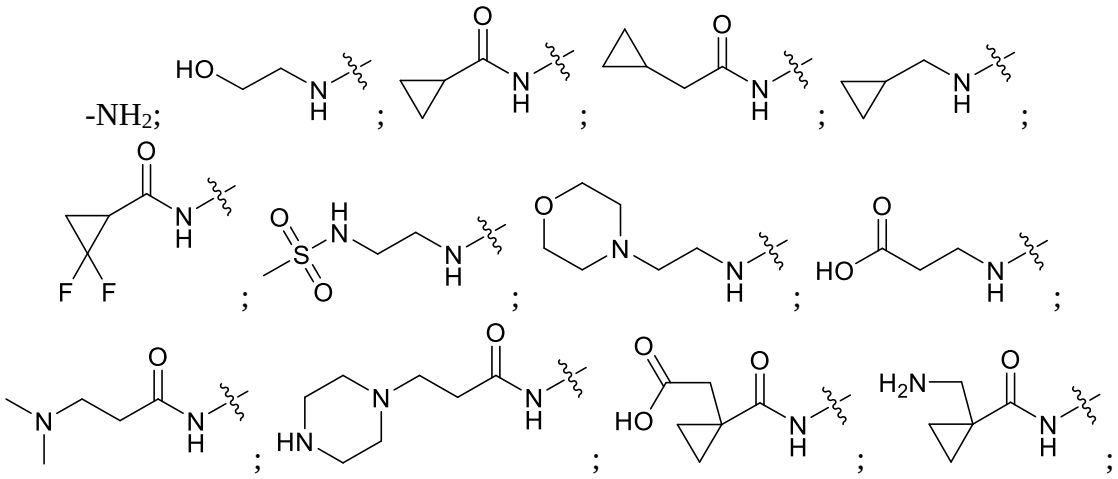
~~24. The compound of any one of claims 1-16, wherein~~ R^2 has one of the following structures:



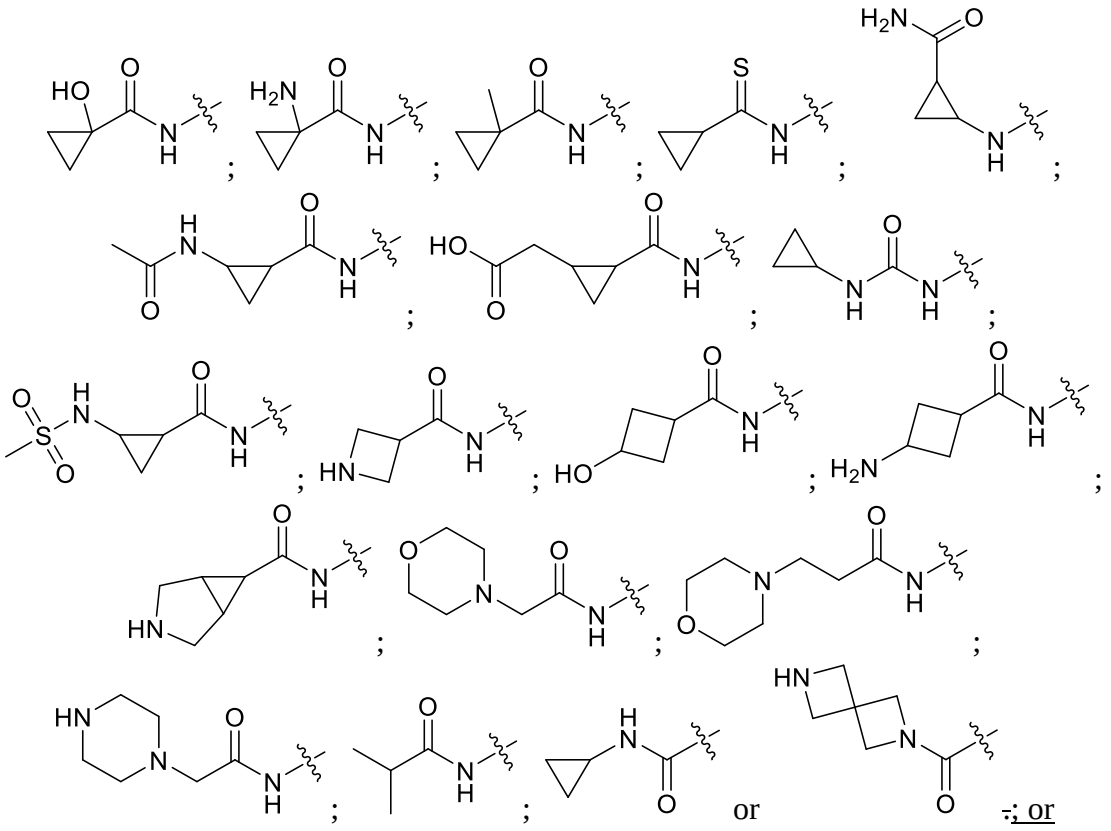
or

~~.~~; or

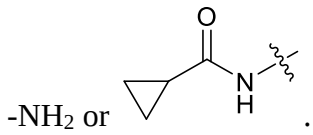
~~25. The compound of any one of claims 1-24, wherein~~ R^2 has one of the following structures:



-NH_2;



~~26. The compound of any one of claims 1-24, wherein~~ R^2 has one of the following structures:



.

~~27~~11. The compound of any one of claims 1-~~26~~10, wherein X is CH and Y is N.

~~28~~12. The compound of any one of claims 1-~~26~~10, wherein X is N and Y is CH.

~~29~~13. The compound of any one of claims 1-~~28~~12, wherein L is –NH–.

~~30~~14. The compound of any one of claims 1-~~28~~12, wherein L is –CH_2NH–.

~~31~~15. The compound of any one of claims 1-~~30~~14, wherein the compound is selected from Table 1, or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof.

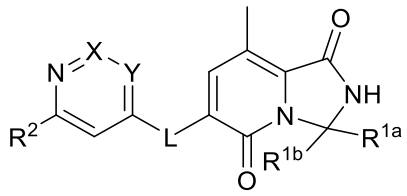
~~32~~16. A pharmaceutical composition comprising the compound of any one of claims 1-~~31~~15, and a pharmaceutically acceptable carrier, diluent or excipient.

~~33~~17. A compound of any one of claims 1-15, or the pharmaceutical composition of claim 16 for use in ~~method of~~ treating a disease or disorder~~, comprising administering a therapeutically effective amount of a compound of any one of claims 1-32, or the pharmaceutical composition of claim 32, to a subject in need thereof~~.

~~34. The method of claim 33, wherein the disorder is neuropathic pain.~~

~~35~~18. Use of a compound of any one of claims 1-15, or the pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a disease or a disorder~~The method of claim 34~~, wherein the disease or disorder is Huntington’s disease, Alzheimer's, high fat induced obesity, Fragile X Symdrome, lupus, Covid19 related acute respiratory distress syndrome (ARDS), non-alcoholic fatty liver disease (NAFLD), or viral induced pain.

~~36~~19. A compound for use in ~~method for~~ treating neuropathic pain, the ~~method comprising administering a therapeutically effective amount of a~~ compound having the following Structure (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof, wherein

R^{1a} is C_1-C_6 alkyl or aryl;

R^{1b} is C_1-C_6 alkyl or aryl,

or R^{1a} and R^{1b}, together with the carbon to which they are both attached, join to form cycloalkyl, cycloalkenyl, heterocyclyl, aryl, or heteroaryl;

R^2 is heterocyclyl, $–NHR^{3a}$, $–NHC(=O)R^{3b}$, $–NHC(=S)R^{3b}$, or $–C(=O)R^{3c}$;

R^{3a} is hydrogen, C_1-C_6 alkyl, or C_3-C_6 cycloalkyl, each of which is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, C_3-C_6 cycloalkyl, $-NHS(O)_2CH_3$, heterocyclyl, $-C(=O)OH$, $-C(=O)N(R^{3d})R^{3d}$, or $-N(R^{3d})R^{3d}$;

R^{3b} is C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or heterocyclyl each of which is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, halo, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, $-NHS(O)_2CH_3$, $-N(R^{3d})R^{3d}$, heterocyclyl, $-C(=O)OH$, $-C(=O)N(R^{3d})R^{3d}$, $-NHC(=O)CH_3$, $-CH_2C(=O)OH$,

R^{3c} is $-N(R^{3d})R^{3d}$ or heterocyclyl;

R^{3d} is, at each occurrence, independently hydrogen, C_1-C_6 alkyl, or C_3-C_6 cycloalkyl;

L is –NH– or $–CH_2NH–$; and

X is N and Y is CH or X is CH and Y is N, to a subject in need thereof.

~~37~~20. A compound from Table 1 or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof for use in~~method for~~ treating neuropathic pain~~, the method comprising administering a therapeutically effective amount of a compound from Table 1 or a pharmaceutically acceptable salt, stereoisomer, tautomer, or prodrug thereof to a subject in need thereof~~.