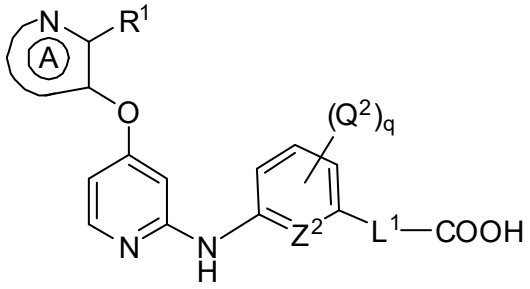
Claims

1. A compound of Formula (II):



(II)

wherein:

Ring A is a 5 or 6 membered heteroaromatic ring optionally containing an additional nitrogen atom as a ring member and optionally fused to a phenyl or pyridinyl ring, and Ring A is optionally substituted by one or two groups independently selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, phenyl, pyridinyl, a 4-6 membered cyclic ether, and C_3-C_6 cycloalkyl;

R^1 is selected from CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, 5-6 membered heterocyclyl containing N, O or S as a ring member, phenyl, and 5-6 membered heteroaryl containing one or two nitrogen atoms as ring members,

wherein said C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, 5-6 membered heterocyclyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with one or two groups selected from Q^1;

Q^1 is independently selected at each occurrence from halo, CN, -OH, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and C_3-C_6 cycloalkyl;

L^1 is a divalent linker selected from $-C(R^9)_2-$, $-(C(R^{10})_2)_{2\text{-}4}-$, $-O-(C(R^{10})_2)_{1\text{-}3}-$, and $-(C(R^{10})_2)_m-X-C(R^{10})_2)_n-$;

each R^9 is independently C_1-C_2 alkyl or halo, or two R^9 can be taken together with the carbon atom to which both are attached to form a 3-6 membered cycloalkyl ring or 3-6 membered cyclic ether;

R^{10} is independently selected at each occurrence from H, F, and C_1-C_4 alkyl; or two R^{10} groups on the same carbon can be taken together with the carbon to which they are attached to form a 3-6 membered cycloalkyl ring or 3-6 membered cyclic ether;

m is 0, 1, or 2;

n is 0, 1 or 2;

X is a pyrazolyl, triazolyl, or tetrazolyl ring;

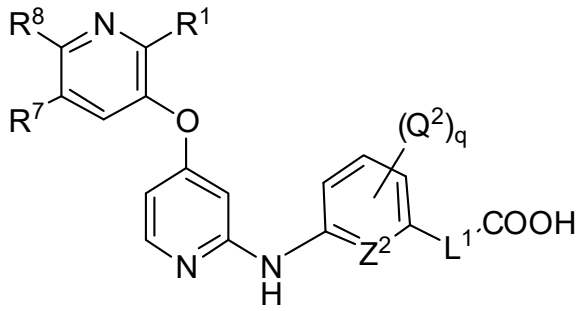
Z^2 is selected from CH, CQ^2, and N; and

q is 0 or 1;

Q^2 is selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein the compound is of Formula (IIa):



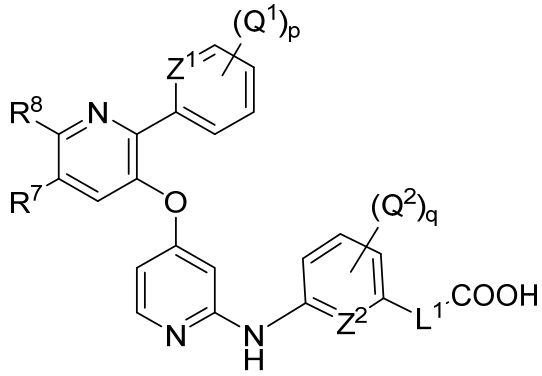
(IIa)

wherein:

R^7 and R^8 are independently selected from H, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, phenyl and pyridinyl; or R^7 and R^8 can be taken together with the carbon atoms to which they are attached to form a phenyl ring fused to the pyridinyl ring to which R^7 and R^8 are attached;

or a pharmaceutically acceptable salt thereof.

3. The compound of claim 1 or 2, wherein the compound is of Formula (IIb):



(IIb),

wherein Z^1 is selected from CH and N;

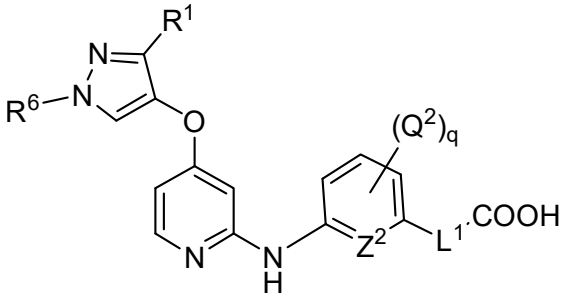
p is 0, 1 or 2; and

each Q^1 is independently selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

or a pharmaceutically acceptable salt thereof.

4. The compound of claim 1 or 2, wherein R^1 is selected from CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_3-C_6 cycloalkyl, and 5-6 membered heterocyclyl containing N, O or S as a ring member; or a pharmaceutically acceptable salt thereof.

5. The compound of claim 1, wherein the compound is of Formula (IIc):



(IIc),

wherein R^6 is selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, and C_3-C_6 cycloalkyl;

or a pharmaceutically acceptable salt thereof.

6. The compound of claim 1 or 2 or 5, wherein L^1 is $C(Me)_2$, -OCH_2-[C], -CH_2CH_2-, -$C(Me)_2CH_2$-[C], -$CH_2C(Me)_2$-[C], or -CF_2CH_2-[C], wherein [C] indicates which end of L is attached to the carboxylic acid in Formula (II) or (IIa) or (IIb);

or a pharmaceutically acceptable salt thereof.

7. The compound of any one of claims 1, 2 and 5, wherein L^1 is –$(CR^{10}{}_2)_m$-X-$(CR^{10}{}_2)_n$-, where m is 1 and n is 1; or a pharmaceutically acceptable salt thereof.

8. The compound of claim 1 or 2, wherein R^7 and R^8 are each independently selected from H, Me and Et; or a pharmaceutically acceptable salt thereof.

9. The compound of claim 1 or 2, wherein Z^2

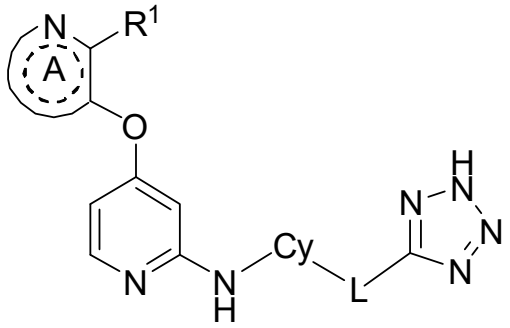
is CH or N; or a pharmaceutically acceptable salt thereof.

10. The compound of claim 9, wherein Z^2 is CH; or a pharmaceutically acceptable salt thereof.

11. The compound of claim 10, wherein R^1 is Me and L^1 is $-C(Me)_2-$, or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1, which is selected from the compounds of Examples 1, 4-7, 10-11, 34-37, 39-41, 43, 66, 68, 70-110, 115-116, 118-174, and 217; or a pharmaceutically acceptable salt thereof.

13. A compound of Formula (I):



(I)

wherein:

Ring A is a 5 or 6 membered heteroaromatic ring optionally containing an additional nitrogen atom as a ring member and is optionally fused to a phenyl or pyridinyl ring, and Ring A is optionally substituted by one or two groups independently selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, phenyl, pyridinyl, a 4-6 membered cyclic ether, and C_3-C_6 cycloalkyl;

R^1 is selected from H, halo, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, 5-6 membered heterocyclyl containing N, O or S as a ring member, phenyl, and 5-6 membered heteroaryl containing one or two nitrogen atoms as ring members,

wherein said C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, phenyl, 5-6 membered heterocyclyl, and 5-6 membered heteroaryl are each optionally substituted with one or two groups selected from R^2;

R^2 is independently selected at each occurrence from halo, CN, -OH, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and C_3-C_6 cycloalkyl;

Cy is a ring selected from C_3-C_6 cycloalkyl, phenyl, and 5-6 membered heteroaryl containing one or two nitrogen atoms as ring members, and is optionally further substituted with one or two groups selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

L is a divalent linker selected from a bond, CR_2, $-(CR_2)_{2\text{-}4}-$, $-O-(CR_2)_{1\text{-}3}-$, and $–(CR_2)_m-X-(CR_2)_n-$,

wherein R is independently selected at each occurrence from H, F, and C_1-C_4 alkyl; or two R groups on the same carbon can be taken together with the carbon to which they are attached to form a 3-6 membered cycloalkyl ring or 3-6 membered cyclic ether;

m is 0, 1, or 2;

n is 0, 1 or 2; and

X is a 5-membered heteroaromatic ring containing one to four heteroatoms selected from N, O and S as ring members;

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13, wherein R^1 is selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, 5-6 membered heterocyclyl containing N, O or S as a ring member, phenyl, and 5-6 membered heteroaryl containing one or two nitrogen atoms as ring members,

wherein said C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_3-C_6 cycloalkyl, 5-6 membered heterocyclyl containing N, O or S as a ring member, phenyl, and 5-6 membered heteroaryl are each optionally substituted with one or two groups selected from R^2;

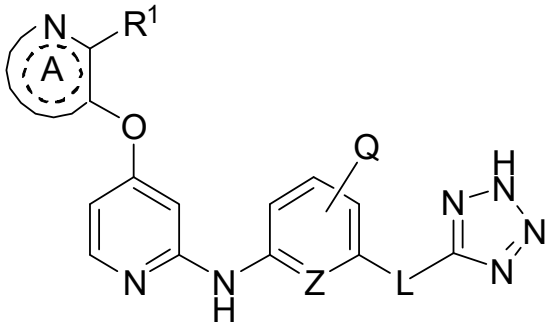
or a pharmaceutically acceptable salt thereof.

15. The compound of claim 13 or 14, wherein R^1 is methyl, phenyl, or 2-pyridinyl; or a pharmaceutically acceptable salt thereof.

16. The compound of claim 13 or 14, wherein Cy is a ring selected from phenyl and pyridinyl, and is optionally further substituted with a group selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

or a pharmaceutically acceptable salt thereof.

17. The compound of claim 16, which is of the formula



wherein Z is CH or N, and Q is selected from H, Me, CF_3, OMe and halo;

or a pharmaceutically acceptable salt thereof.

18. The compound of any one of claims 13, 14 and 17, wherein L is a divalent linker selected from CR_2, -$(CR_2)_{2\text{-}4}$-, -O-$(CR_2)_{1\text{-}3}$-, and –$(CR_2)_m$-X-$(CR_2)_n$-;

or a pharmaceutically acceptable salt thereof.

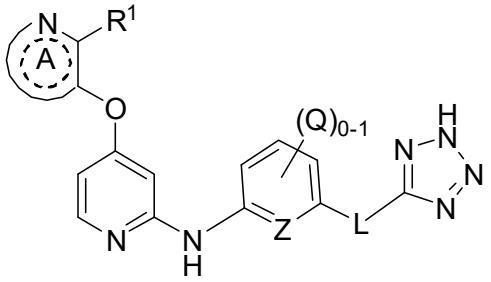
19. The compound of claim 18, wherein R is independently selected at each occurrence from H, F and Me;

or a pharmaceutically acceptable salt thereof.

20. The compound of claim 19, wherein L is selected from CH_2, -CH_2CH_2-, $C(Me)_2$, -CHMe-, -OCH_2-, -CH_2CF_2-, -CF_2CH_2-, -CMe_2CH_2-, and -CH_2CMe_2-;

or a pharmaceutically acceptable salt thereof.

21. The compound of any one of claims 13, 14 and 17, which is a compound of formula (Ia):



(Ia)

wherein Q is independently selected at each occurrence from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, and C_1-C_4 alkoxy; and

Z is CH, CQ or N;

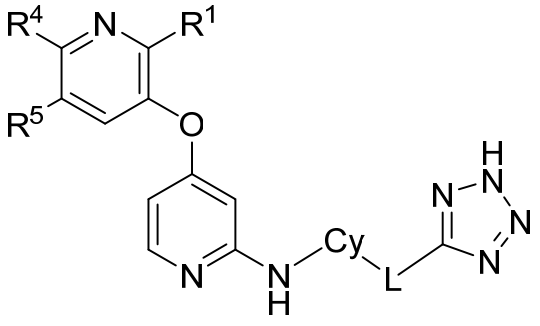
or a pharmaceutically acceptable salt thereof.

22. The compound of any one of claims 13, 14 and 17, wherein Ring A is pyridinyl or pyrazolyl, and is optionally substituted by one or two groups independently selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, and C_3-C_6 cycloalkyl;

or a pharmaceutically acceptable salt thereof.

23. The compound of claim 13, wherein R^1 is pyridinyl, phenyl, tetrahydrofuranyl, or tetrahydropyranyl, and is optionally substituted with one or two groups selected from R^2; or a pharmaceutically acceptable salt thereof.

24. The compound of any one of claims 13, 14, 17, and 23, which is a compound of formula (Ib):

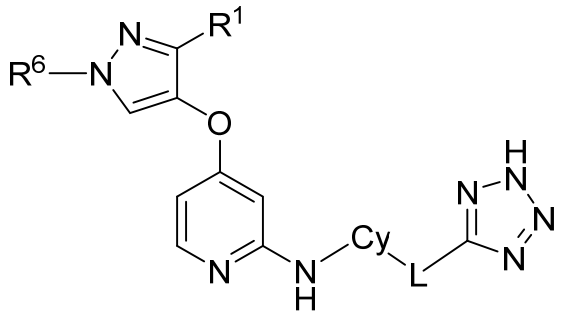


(Ib)

wherein R^4 and R^5 are independently selected from H, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, phenyl and pyridinyl; or R^4 and R^5 can be taken together with the carbon atoms to which they are attached to form a phenyl ring fused to the pyridinyl ring to which R^4 and R^5 are attached;

or a pharmaceutically acceptable salt thereof.

25. The compound of claim 13 or 14, which is a compound of formula (Ic):



(Ic)

wherein R^6 is selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, and C_3-C_6 cycloalkyl;
or a pharmaceutically acceptable salt thereof.

26. The compound of claim 25, wherein R^6 is selected from methyl, ethyl, isopropyl, and cyclopropyl; or a pharmaceutically acceptable salt thereof.

27. The compound of any one of claims 13, 14, 17 and 26, wherein L is [Cy]–$(CR_2)_m$-X-$(CR_2)_n$-, where [Cy] indicates where L is attached to the group Cy;
m is 1 or 2;
n is 0, 1 or 2; and
X is a tetrazolyl ring;
or a pharmaceutically acceptable salt thereof.

28. The compound of any one of claims 13, 14 and 17, wherein L is CH_2, $C(Me)_2$, -OCH_2-[T], -CH_2CH_2-, -$C(Me)_2CH_2$-[T], -$CH_2C(Me)_2$-[T], or -CF_2CH_2-[T], wherein [T] indicates which end of L is attached to the tetrazole ring in Formula (I); or a pharmaceutically acceptable salt thereof.

29. The compound of claim 13, wherein the compound is selected from the compounds of Examples 12-33, 44-65, 67 and 175-216; or a pharmaceutically acceptable salt thereof.

30. A compound selected from the compounds of Examples 1-217;
or a pharmaceutically acceptable salt thereof.

31. A pharmaceutical composition comprising a compound of any one of claims 13, 14, 17, 26, and 29, admixed with at least one pharmaceutically acceptable carrier or excipient.

32. A compound according to any one of claims 1, 2, 13, and 14, for use in therapy.

33. Use of a compound according to any one of claims 1, 2, 13 and 14, for the manufacture of a medicament.

34. A pharmaceutical combination comprising an effective amount of a compound according to any one of claims 1, 2, 13, and 14, and an additional therapeutic agent.

35. A pharmaceutical composition comprising the pharmaceutical combination of claim 34 admixed with at least one pharmaceutically acceptable excipient.