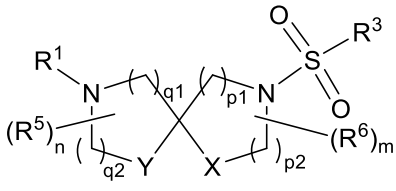
remyelination, as its inhibition leads to an increase of these 8-9 sterol starting materials (Theodoropoulous *et al*, 2020, *J. Am. Chem. Soc.*, 142, (13), 6128-6138).

In addition to its role in remyeliniation, EBP has also been shown to be a key enzyme in certain colorectal cancers due to the reduction in essential lipids such as cholesterol (Theodoropoulous *et al*, 2020, *J. Am. Chem. Soc.*, 142, (13), 6128-6138).

Thus, there is a need for EBP inhibitors as potential therapeutic agents for treating diseases or disorders that are responsive to EBP inhibition.

SUMMARY

The present disclosure provides compounds that are EBP inhibitors. In a first aspect, the present disclosure relates to compounds having the Formula I:



(I),

or a pharmaceutically acceptable salt thereof, wherein:

X is CH_2 or O;

Y is CH_2 or O;

provided only one of X and Y is O;

q1 is 1 or 2;

q2 is 0 or 1 when Y is CH_2, or q2 is 2 when Y is O;

p1 is 1 or 2;

p2 is 0 or 1 when X is CH_2, or p2 is 2 when X is O;

R^1 is C_{2-6}alkyl, Het, or –Z-Het, wherein the C_{2-6}alkyl is optionally substituted with one or more R^A and Het is optionally substituted with one or more R^2;

Z is C_{1-4}alkyl optionally substituted with one or more halo or C_{1-3}alkoxy;

Het is C_{3-6}cycloalkyl, a 4 to 6 membered monocyclic heterocyclyl, or a 6 to 8-membered bicyclic heterocyclyl, each of which is optionally substituted with R^2;

R^A, for each occurrence, is independently OR^{2a}, SR^{2a}, or $C(O)OR^{2a}$;

R^2, for each occurrence, is independently C_{1-6}alkyl, halo, -CN or OR^{2a}, wherein the C_{1-6}alkyl is optionally substituted with one or more halo or C_{1-3}alkoxy;

R^{2a} is H C_{1-6}alkyl, or C_{3-6}cycloalkyl wherein the C_{1-6}alkyl is optionally substituted with one or more halo or C_{1-3}alkoxy;

R^3 is C_{1-4}alkyl-phenyl, phenyl, 5 or 6-membered monocyclic heteroaryl, or 9 to 10-membered bicyclic heteroaryl, wherein the phenyl, 5 or 6-membered monocyclic heteroaryl and 9 to 10-membered bicyclic heteroaryl are each optionally substituted with one or more substituent R^4;

R^4, for each occurrence, is independently halo, -OR^{4a}, -CN, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{2-6}alkenyl, phenyl, or 5 or 6-membered monocyclic heteroaryl, wherein the C_{1-6}alkyl or C_{3-6}cycloalkyl are each optionally substituted with one or more C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or halo, and wherein the or 5 or 6-membered monocyclic heteroaryl is optionally substituted with one or more C_{1-6}alkyl; or

two R^4 together with their intervening atoms form a 5 to 7-membered heterocyclyl;

R^{4a} is H or C_{1-6}alkyl, wherein the C_{1-6}alkyl is optionally substituted with one or more halo;

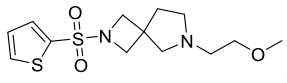
n is 1 or 2;

m is 1 or 2;

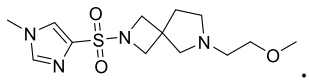
R^5, for each occurrence, is independently H, halo, C_{1-3}alkyl, or C_{1-3}haloalkyl; or two R^5 together form a C_{1-3}alkylene;

R^6, for each occurrence, is independently H, halo, C_{1-3}alkyl, or C_{1-3}haloalkyl; or two R^6 together form a C_{1-3}alkylene;

provided that the compound is not:



, or



.

The disclosure also relates to pharmaceutical compositions comprising compounds of Formula (I) or pharmaceutically acceptable salts thereof, and a pharmaceutical carrier. Another aspect of the disclosure relates to a pharmaceutical composition comprising a compound as defined herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

The present disclosure also provides a method of treating a disease or disorder that is responsive to inhibition of EBP in a subject comprising administering to said subject an effective amount of at least one compound described herein or a pharmaceutically acceptable salt thereof. In some examples, the present

disclosure provides a method for treating multiple sclerosis. In some examples, the present disclosure provides a method for promoting myelination in a subject with a myelin-related disorder.

The present disclosure also relates to the use of at least one compound described herein or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a disease or disorder responsive to inhibition of EBP. Also provided is a compound described herein or a pharmaceutically acceptable salt thereof for use in treating a disease or disorder responsive to inhibition of EBP.

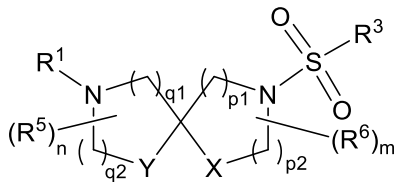
Another aspect of the present disclosure relates to a compound as defined herein, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as defined herein for use in: (i) treating a disease mediated by Emopamil-Binding Protein; or (ii) treating an autoimmune disease in a subject, optionally, the autoimmune disease is multiple sclerosis.

DETAILED DESCRIPTION OF THE INVENTION

The present disclosure provides compounds and pharmaceutical compositions thereof that may be useful in the treatment of diseases or disorders through mediation of EBP function/activity, such as multiple sclerosis or other myelin-related disorders. In some embodiments, the compounds of present disclosure are EBP inhibitors.

COMPOUNDS AND COMPOSITIONS

In a first embodiment, the present disclosure provides a compound of Formula (I):



(I);

or a pharmaceutically acceptable salt thereof, wherein the variables in Formula (I) are as defined in the first embodiment above. In another embodioment, for the compounds of Formula (I):

X is CH_2 or O;

Y is CH_2 or O;

provided only one of X and Y is O;

q1 is 1 or 2;

q2 is 0 or 1 when Y is CH_2, or q2 is 2 when Y is O;

p1 is 1 or 2;

p2 is 0 or 1 when X is CH_2, or p2 is 2 when X is O;

R^1 is $C_{2\text{-}6}$alkyl, Het, or –Z-Het, wherein the $C_{2\text{-}6}$alkyl is substituted with one or more OR^{2a} and Het is optionally substituted with one or more R^2;

Z is C_{1-4}alkyl optionally substituted with one or more halo;

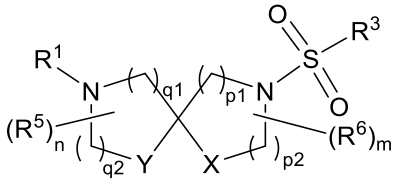
Het is a 4 to 6 membered monocyclic heterocyclyl, or a 6 to 8-membered bicyclic heterocyclyl, each of which is optionally substituted with R^2;

R^2, for each occurrence, is independently C_{1-6}alkyl or OR^{2a};

CLAIMS

What is claimed is:

1. A compound represented by Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

X is CH_2 or O;

Y is CH_2 or O;

provided only one of X and Y is O;

q1 is 1 or 2;

q2 is 0 or 1 when Y is CH_2, or q2 is 2 when Y is O;

p1 is 1 or 2;

p2 is 0 or 1 when X is CH_2, or p2 is 2 when X is O;

R^1 is C_{2-6}alkyl, Het, or –Z-Het, wherein the C_{2-6}alkyl is optionally substituted with one or more R^A and Het is optionally substituted with one or more R^2;

Z is C_{1-4}alkyl optionally substituted with one or more halo or C_{1-3}alkoxy;

Het is C_{3-6}cycloalkyl, a 4 to 6 membered monocyclic heterocyclyl, or a 6 to 8-membered bicyclic heterocyclyl, each of which is optionally substituted with R^2;

R^A, for each occurrence, is independently OR^{2a}, SR^{2a}, or $C(O)OR^{2a}$;

R^2, for each occurrence, is independently C_{1-6}alkyl, halo, -CN or OR^{2a}, wherein the C_{1-6}alkyl is optionally substituted with one or more halo or C_{1-3}alkoxy;

R^{2a} is H C_{1-6}alkyl, or C_{3-6}cycloalkyl wherein the C_{1-6}alkyl is optionally substituted with one or more halo or C_{1-3}alkoxy;

R^3 is C_{1-4}alkyl-phenyl, phenyl, 5 or 6-membered monocyclic heteroaryl, or 9 to 10-membered bicyclic heteroaryl, wherein the phenyl, 5 or 6-membered monocyclic heteroaryl and 9 to 10-membered bicyclic heteroaryl are each optionally substituted with one or more substituent R^4;

R^4, for each occurrence, is independently halo, $-OR^{4a}$, -CN, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{2-6}alkenyl, phenyl, or 5 or 6-membered monocyclic heteroaryl, wherein the C_{1-6}alkyl or C_{3-6}cycloalkyl are each optionally substituted with one or more C_{1-}

$_{6}$alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, or halo, and wherein the or 5 or 6-membered monocyclic heteroaryl is optionally substituted with one or more C_{1-6}alkyl; or

two R^4 together with their intervening atoms form a 5 to 7-membered heterocyclyl;

R^{4a} is H or C_{1-6}alkyl, wherein the C_{1-6}alkyl is optionally substituted with one or more halo;

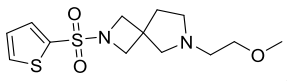
n is 1 or 2;

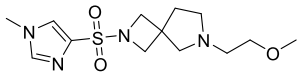
m is 1 or 2;

R^5, for each occurrence, is independently H, halo, C_{1-3}alkyl, or C_{1-3}haloalkyl; or two R^5 together form a C_{1-3}alkylene;

R^6, for each occurrence, is independently H, halo, C_{1-3}alkyl, or C_{1-3}haloalkyl; or two R^6 together form a C_{1-3}alkylene;

provided that the compound is not:


, or


.

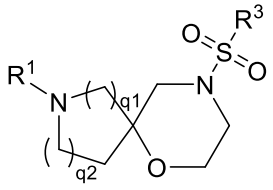
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Het is:

(i) a 4 to 6 membered oxygen-containing monocyclic saturated heterocyclyl, or a 6 to 8-membered oxygen-containing bicyclic saturated heterocyclyl;

(ii) C_{3-6}cycloalkyl, a 4 to 6 membered oxygen-containing monocyclic saturated heterocyclyl, or a 6 to 8-membered oxygen-containing bicyclic saturated heterocyclyl, each of which is optionally substituted with one to three R^2; or

(iii) cyclohexyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, dioxolanyl, dioxanyl, 2-oxaspiro[3.3]heptanyl, 2-oxaspiro[3.3]heptanyl, 2-oxabicyclo[2.1.1]hexanyl, 6-oxabicyclo[3.2.1]octanyl, or 2-oxabicyclo[3.1.1]heptanyl, each of which is optionally substituted with one to three R^2.

3. The compound of claim 1 or 2, wherein the compound is represented by Formula II:

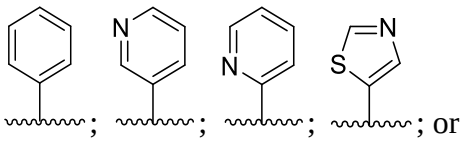
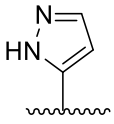

(II);

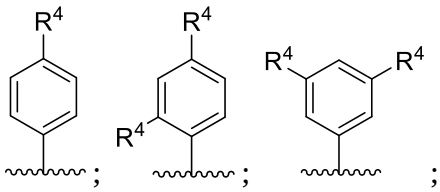
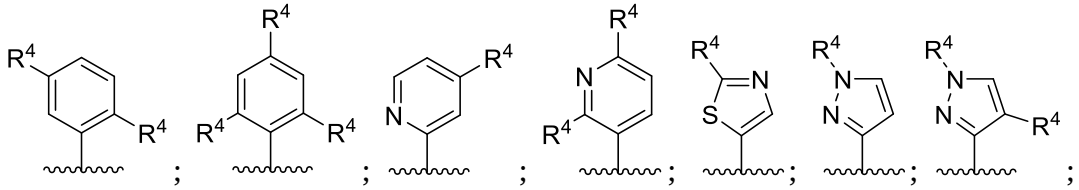
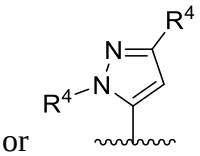
or a pharmaceutically acceptable salt thereof.

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

(a) R^3 is:

(i) selected from the group consisting of phenyl, pyridyl, thiazoyl, and pyrazolyl, each of which is optionally substituted with one to three R^4;

(ii) represented by the following formula: ; or ; wherein each of the formula depicted above is optionally substituted with one to three R^4; or

(iii) represented by the following formula: ; ; ; or ; and/or

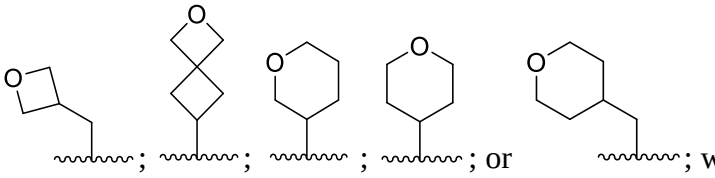
(b) R^4, for each occurrence, is independently selected from:

(i) halo, -CN, -OR^{4a}, C_{1-4}alkyl, C_{1-4}haloalkyl, C_{3-6}cycloalkyl and 5 or 6-membered heteroaryl optionally substituted with C_{1-3}alkyl; and R^{4a} is C_{1-3}alkyl or C_{1-3}haloalkyl; or

(ii) -CH_3, -CF_3, -$OCHF_2$, -OCH_3, -CN, -F, -Cl, isopropyl, cyclopropyl, and 4-methylpyridin-2-yl; and/or

(c) R^1 is:

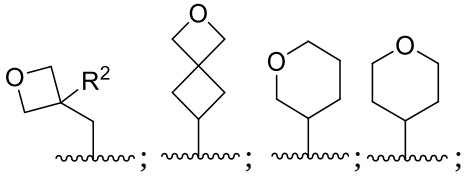
(i) $C_{2\text{-}4}$alkyl substituted with OR^{2a} or is represented by the following formula:

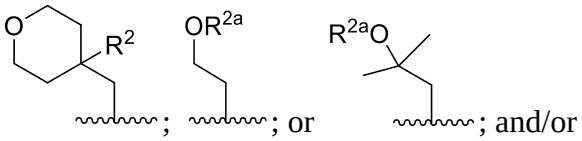


; wherein each of the formula depicted above is optionally substituted with one to three R^2;

wherein R^2, for each occurrence, is independently $C_{1\text{-}3}$alkyl or $–OR^{2a}$; and R^{2a}, for each occurrence, is independently H or $C_{1\text{-}3}$alkyl;

(ii) represented by the following formula:



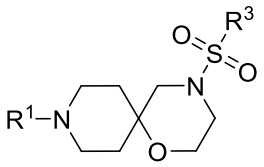


; and/or

(d) R^2, for each occurrence, is independently selected from $–CH_3$ and –OH; and R^{2a}, for each occurrence, is independently H or $–CH_3$.

5. The compound of any one of claims 1 to 4, wherein the compound is represented by

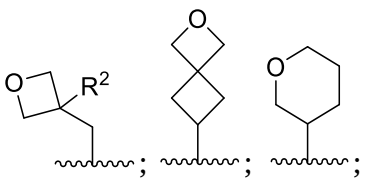
(i) Formula III:

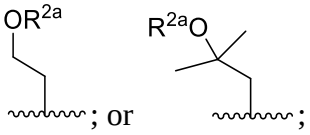


(III);

or a pharmaceutically acceptable salt thereof, optionally wherein:

R^1 is represented by the following formula:

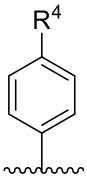
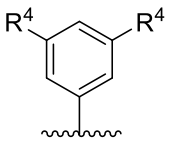
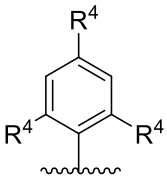
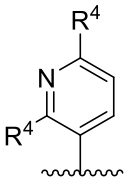
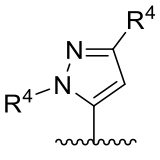




; or

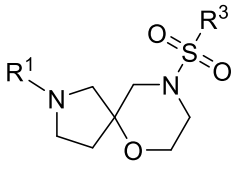
R^2, for each occurrence, is independently selected from $–CH_3$ and OH;

R^{2a}, for each occurrence, is independently selected from H or $–CH_3$;

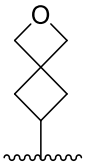
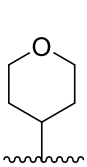
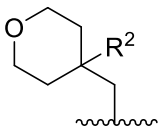
R^3 is represented by the following formula:  ;  ;  ;  ; or  ; and

R^4, for each occurrence, is independently selected from $–CH_3$,$-CF_3$, $-OCHF_2$, $-OCH_3$, and –F;

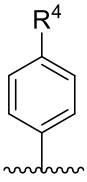
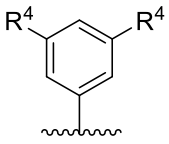
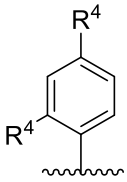
(ii) Formula IV:

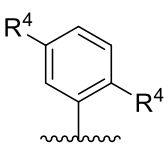
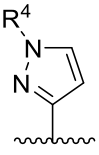
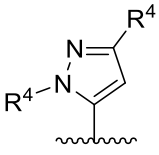
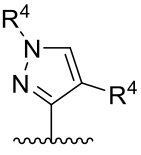
 (IV);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula:  ;  ; or  ;

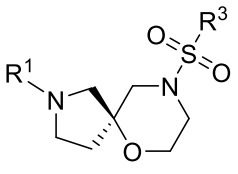
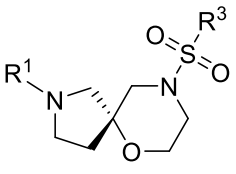
R^2 is OH;

R^3 is represented by the following formula:  ;  ;  ;

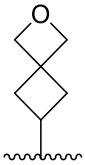
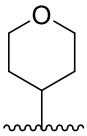
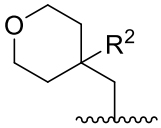
 ;  ;  ; or  ; and

R^4, for each occurrence, is independently selected from $–CH_3$, $-CF_3$, $-OCH_3$, $–OCHF_2$, -CN, isopropyl, –F, -Cl, and 4-methylpyridin-2-yl;

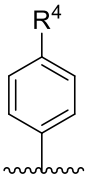
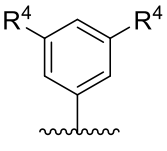
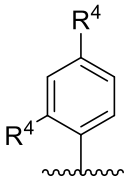
(iii) Formulas (IVA) or (IVB):

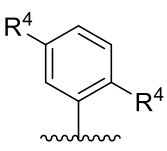
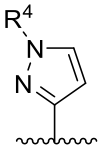
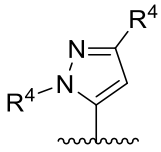
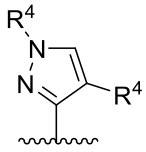

(IVA);

(IVB);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula: ; ; or ;

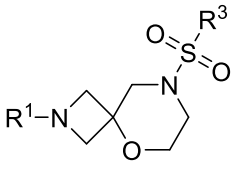
R^2 is OH;

R^3 is represented by the following formula: ; ; ;

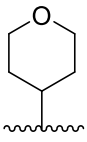
; ; ; or ; and

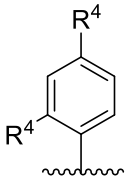
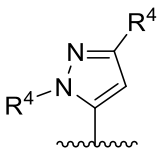
R^4, for each occurrence, is independently selected from $–CH_3$, $-CF_3$, $-OCH_3$, $–OCHF_2$, -CN, isopropyl, –F, -Cl, and 4-methylpyridin-2-yl; or

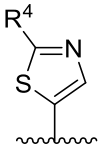
(iv) Formula V:


(V);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula: ;

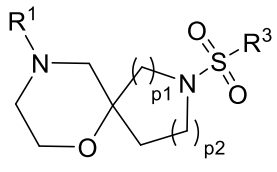
R^3 is represented by the following formula: ; ; or

; and

R^4, for each occurrence, is independently selected from $–CH_3$, -F, and cyclopropyl.

6. The compound of claim 1, wherein the compound is represented by:

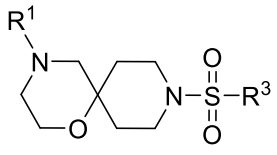
(i) Formula VI:



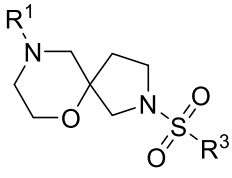
(VI);

or a pharmaceutically acceptable salt thereof; or

(ii) Formula VII or VIII:



(VII), or



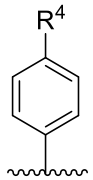
(VIII);

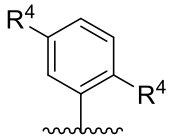
or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein

(a) R^3 is:

(i) phenyl optionally substituted with one to three R^4; or

(ii) represented by the following formula: 

; or 

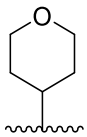
; and/or

(b) R^4, for each occurrence, is independently selected from:

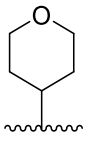
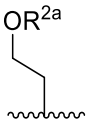
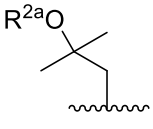
(i) halo, CN, and OR^{4a}; and R^{4a} is $C_{1\text{-}3}$alkyl or $C_{1\text{-}3}$haloalkyl; or

(ii) $–OCHF_2$, -F, and –CN; and/or

(c) R^1 is:

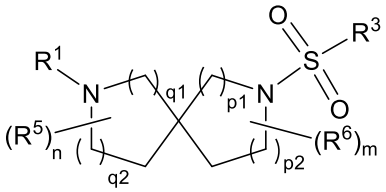
(i) $C_{2\text{-}4}$allkyl substituted with $–OR^{2a}$ or is represented by the following formula: 

; optionally substituted with one to three R^2; or

(ii) represented by the following formula: ; ; or ; and/or

(d) R^2, for each occurrence, is independently selected from $–CH_3$ and –OH; and R^{2a}, for each occurrence, is independently selected from H and $–CH_3$.

8. The compound of claim 1, wherein the compound is represented by Formula IX:


(IX);

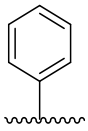
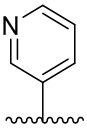
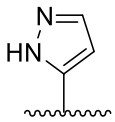
or a pharmaceutically acceptable salt thereof, wherein R^5 is H, or two R^5 together form a C_{1-3}alkylene; and R^6 is H, or two R^6 together form a C_{1-3}alkylene, optionally, wherein p1 is 1 and p2 is 0; or p1 is 1 and p2 is 1; or p1 is 2 and p2 is 1.

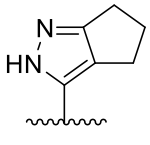
9. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein

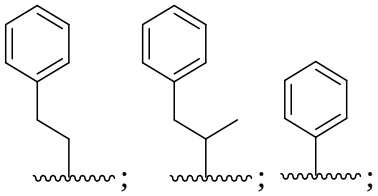
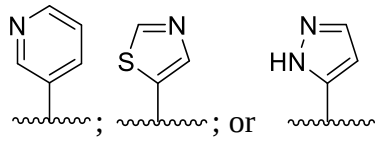
(i) R^3 is:

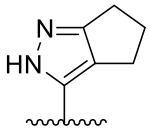
(i) selected from the group consisting of phenyl, pyridyl, and pyrazolyl, each of which is optionally substituted with one to three R^4;

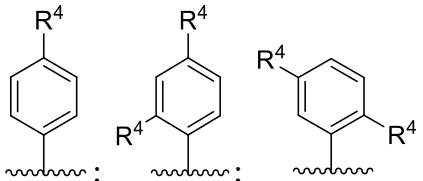
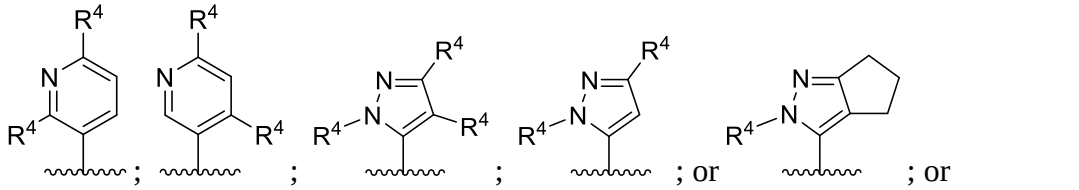
(ii) selected from the group consisting of C_{1-4}alkyl-phenyl, phenyl, pyridyl, thiazoyl, and pyrazolyl, each of which is optionally substituted with one to three R^4;

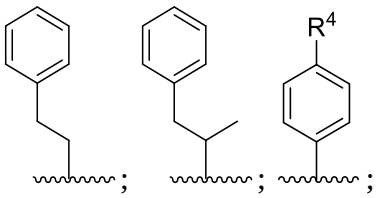
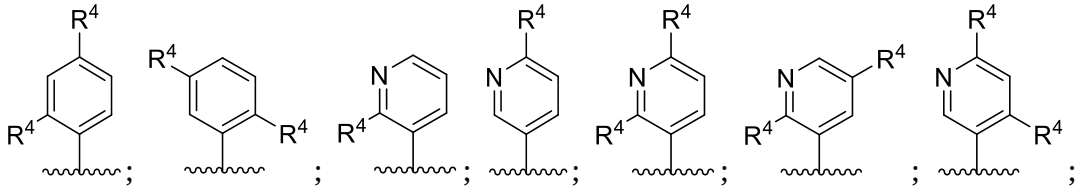
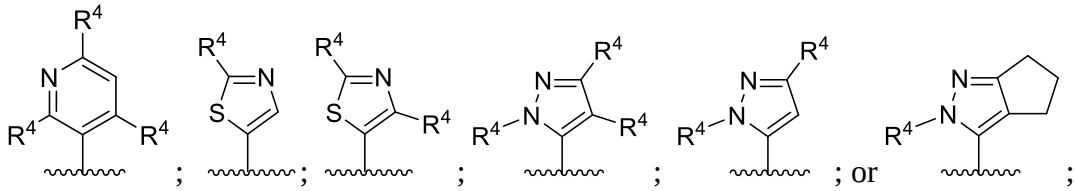
(iii) represented by the following formula: ; ; or ; each of which is optionally substituted with one to three R^4;

or R^3 is represented by the following formula: , optionally substituted with one or two R^4;

(iv) represented by the following formula: ; ; or ; each of which is optionally substituted with one to three R^4;

or R^3 is represented by the following formula: , optionally substituted with one or two R^4;

(v) represented by the following formula: ; ; or ; or

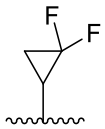
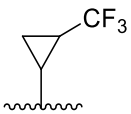
(vi) represented by the following formula: ; ; ; or ;

and/or

(b) R^4, for each occurrence, is independently selected from:

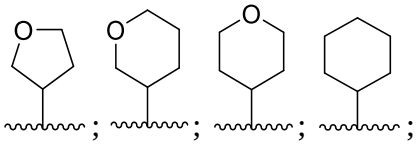
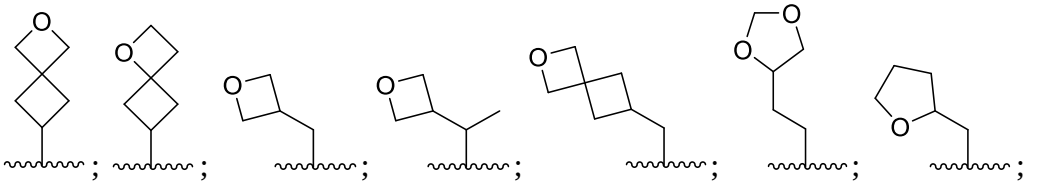
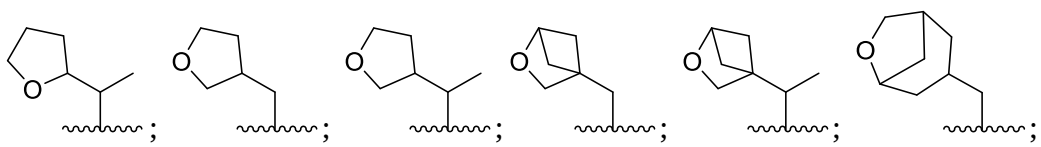
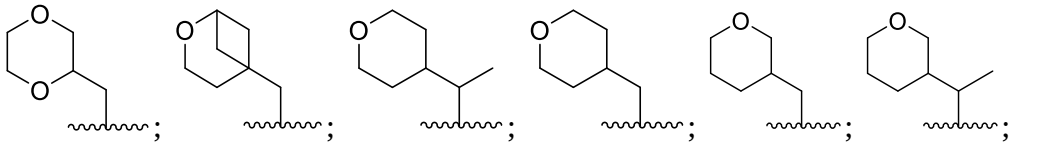
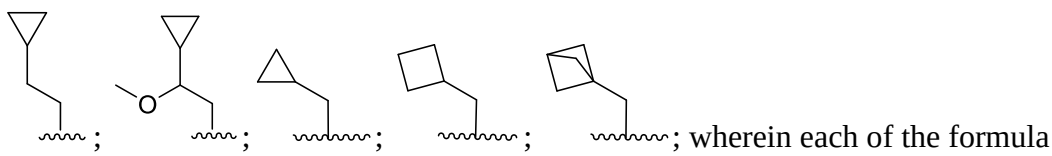
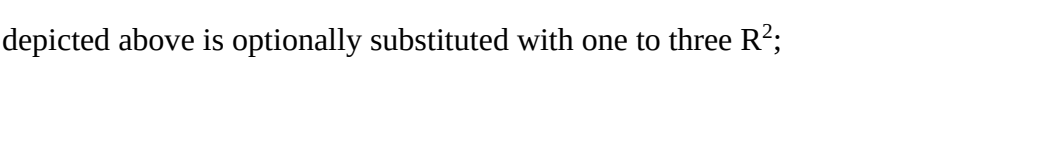
(i) halo, CN, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{2-4}alkenyl, C_{3-6}cycloalkyl, phenyl, and $–OR^{4a}$; wherein the C_{3-6}cycloalkyl is optionally substituted with one to three halo or C_{1-4}haloalkyl and the C_{1-3}alkyl is optionally substituted with one or two C_{3-4}cycloalkyl; and R^{4a} is C_{1-3}alkyl or C_{1-3}haloalkyl;

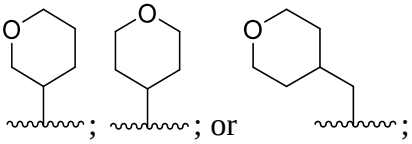
(ii) halo, CN, C_{1-3}alkyl, C_{1-3}haloalkyl, C_{3-6}cycloalkyl, and $–OR^{4a}$; and R^{4a} is C_{1-3}alkyl or C_{1-3}haloalkyl;

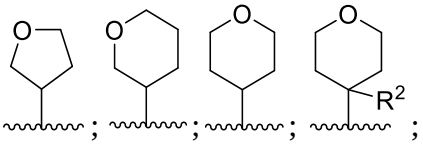
(iii) $–CH_3$, $-CH_2CH_3$, $-CF_2CH_3$, $-CF(CH_3)_2$, $-CH=CH_2$, $-CHF_2$, $-CH(CH_3)_2$, $-CF_3$, $-OCH_3$, $-OCHF_2$, $-OCF_3$, cyclopropyl, , , $-CH_2$-cyclopropyl, cyclobutyl, phenyl, -CN, -Cl, -Br, and –F; or

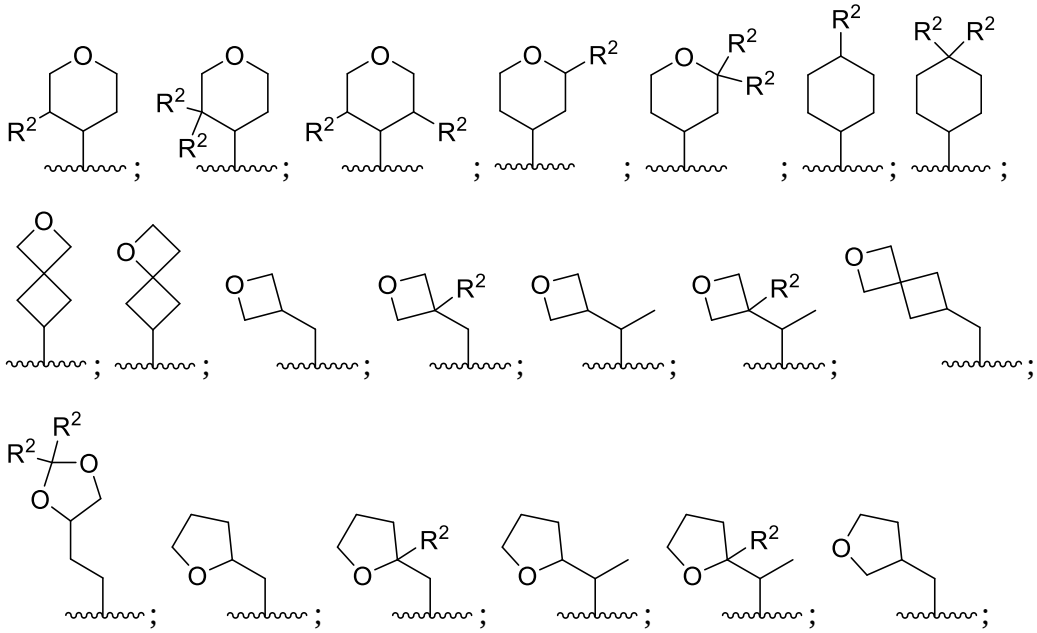
(iv) $–CH_3$, $-CHF_2$, $-CF_3$, $-OCH_3$, $-OCHF_2$, $-OCF_3$, cyclopropyl, -CN, and –F; and/or

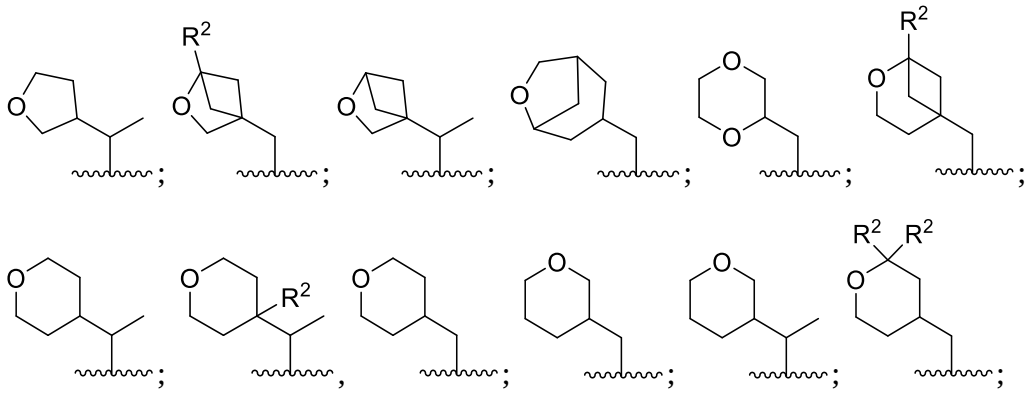
(c) R^1 is:

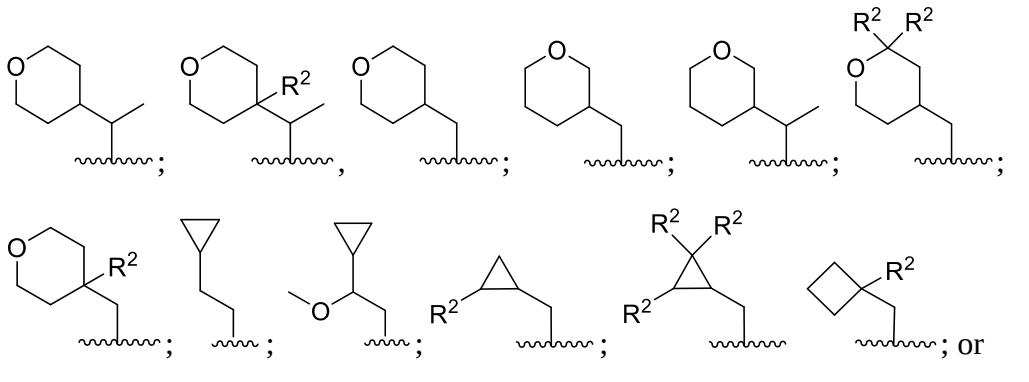
(i) represented by the following formula: ; ; ; ; ; ; wherein each of the formula depicted above is optionally substituted with one to three R^2;

(ii) represented by the following formula: ; wherein each of the formula depicted above is optionally substituted with one to three R^2;

(iii) represented by the following formula: ;

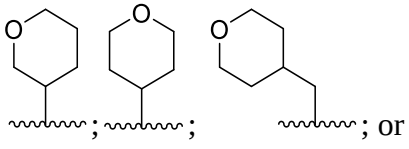


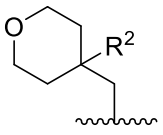




; or

; or

(iv) represented by the following formula: ; or

; and/or

(d) R^2 is :

(i)–CH_3, -F, -OCH_3 –CN, -$CH_2CH_2OCH_3$ or -OH; or

(ii) -OH.

10. The compound of claim 8 or 9, or a pharmaceutically acceptable salt thereof, wherein:

(i) R^1 is $C_{2\text{-}6}$alkyl optionally substituted with one or two R^A;

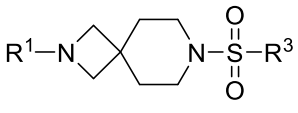
R^A, for each occurrence, is independently OR^{2a}, SR^{2a}, or $C(O)OR^{2a}$; and

R^{2a} is H, $C_{1\text{-}4}$alkyl, or $C_{3\text{-}6}$cycloalkyl wherein the $C_{1\text{-}4}$alkyl is optionally substituted with one or two $C_{1\text{-}3}$alkoxy; or

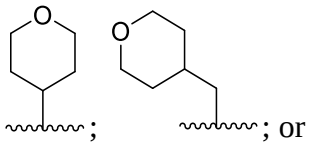
(ii) R^1 is –CH_2CH_3, –$CH_2CH_2CH_2SCH_2CH_3$, -$CH_2CH_2CH_2O$-cyclopentyl, -$CH_2CH_2CH_2CH_2CH_2OCH_3$, -$CH_2CH_2OC(CH_3)_3$, -$CH_2CH_2CH_2CH(CH_3)OCH_3$, -$CH_2CH(CH_3)CH_2CH_2C(O)OCH_3$, -$CH_2CH_2C(CH_3)_2C(O)OCH_3$, or -$CH_2CH_2CH_2OCH_2CH_2OCH_3$.

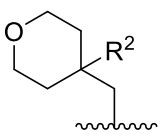
11. The compound of claim 8, wherein the compound is represented by:

(i) Formula X:

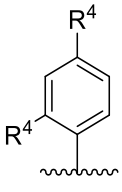
 (X);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula: ; or

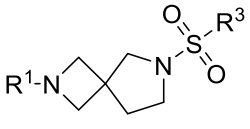
;

R^2 is OH;

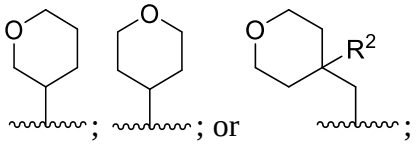
R^3 is represented by the following formula: ; and

R^4 is $–CH_3$;

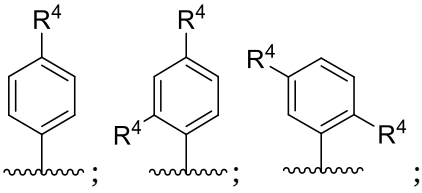
(ii) Formula XI:

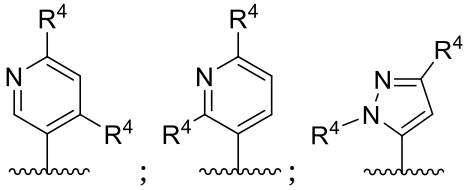

(XI);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula: ;

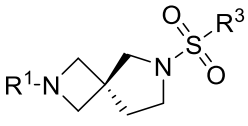
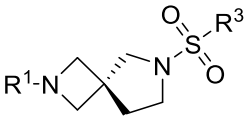
R^2 is OH;

R^3 is represented by the following formula: ;

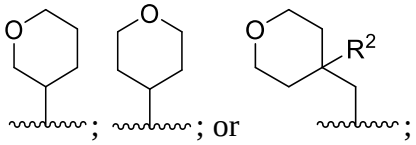
; and

R^4, for each occurrence, is independently selected from $–CH_3$, $-CF_3$, $-OCH_3$, $-OCHF_2$, $-OCF_3$, –CN, -F, and cyclopropyl;

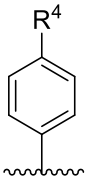
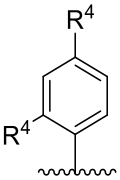
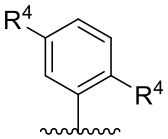
(iii) Formulas (XIA) or (XIB):

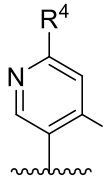
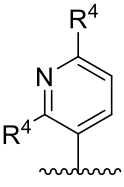
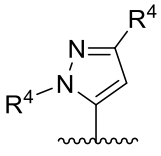

(XIA); 
(XIB);

or a pharmaceutically acceptable salt thereof, optionally, wherein:

R^1 is represented by the following formula: ;

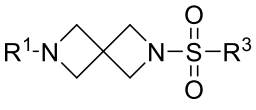
R^2 is OH;

R^3 is represented by the following formula: ; ; ;

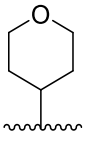
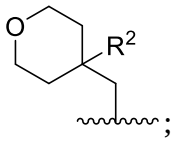
; ; ; and

R^4, for each occurrence, is independently selected from $–CH_3$, $-CF_3$, $-OCH_3$, $-OCHF_2$, $-OCF_3$, –CN, -F, and cyclopropyl; or

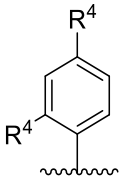
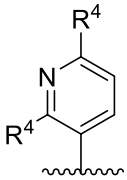
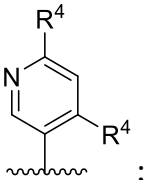
(iv) Formula XII:

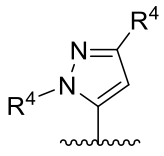
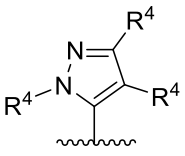
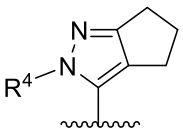
 (XII);

or a pharmaceutically acceptable salt thereof, optionally, wherein,

R^1 is represented by the following formula: ; or ;

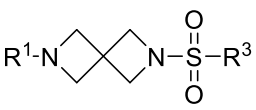
R^2 is OH;

R^3 is represented by the following formula: ; ; ;

; ; ; and

R^4, for each occurrence, is independently selected from $–CH_3$, $-CHF_2$, $-CF_3$, $-OCH_3$, $-OCHF_2$, and $–OCF_3$.

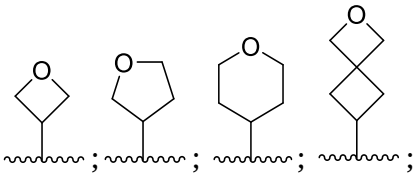
12. The compound of claim 8, wherein the compound is represented by Formula XII:

 (XII);

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is Het or Z-Het;

Z is CH_2;

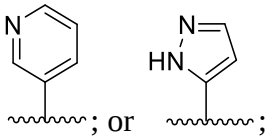
Het is represented by the following formula: ; wherein each of the formula depicted above is optionally substituted with one to two R^2;

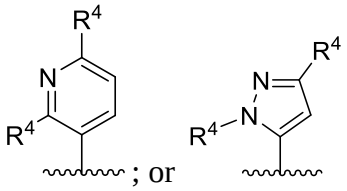
R^2, for each occurrence, is independently $C_{1\text{-}4}$alkyl, -OH, or halo;

R^3 is pyridinyl or pyrazolyl, each of which is optionally substituted with one to two R^4;

R^4, for each occurrence, is independently $C_{1\text{-}4}$alkyl or $C_{1\text{-}4}$haloalkyl.

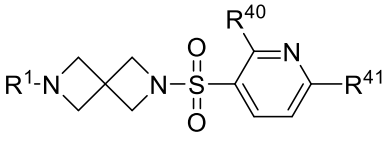
13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein:
(a) R^3 is:

(i) represented by the following formula: ; each of which is optionally substituted with one to two R^4;

(ii) represented by the following formula: ; and/or

(b) R^4, for each occurrence, is independently $–CH_3$, $-CF_3$, or $-CF_2CH_3$.

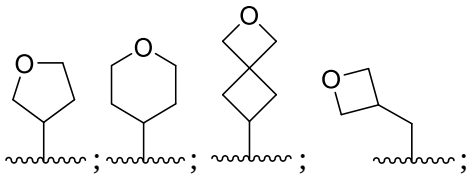
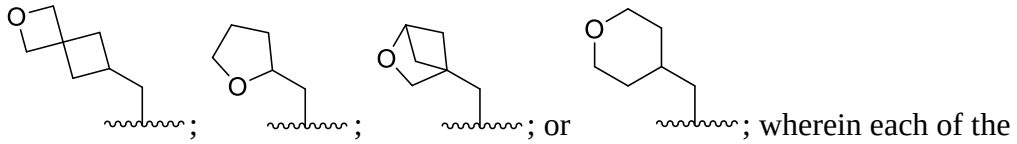
14. The compound of claim 13, wherein the compound is represented by Formula XIIA:

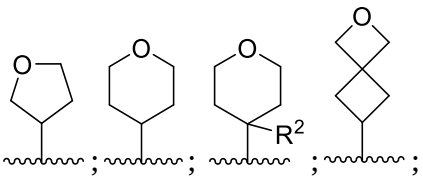
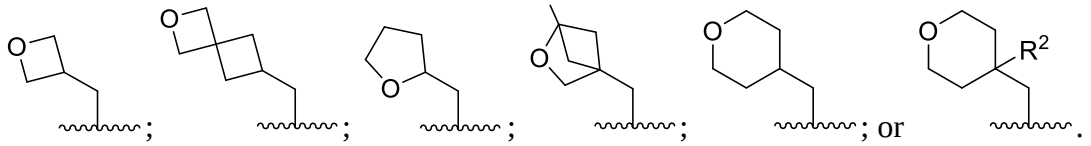
 (XIIA),

or a pharmaceutically acceptable salt thereof, wherein R^{40} is $C_{1\text{-}3}$alkyl and R^{41} is $C_{1\text{-}3}$haloalkyl.

15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein R^{40} is $-CH_3$ and R^{41} is $-CF_3$ or $-CF_2CH_3$.

16. The compound of any one of claims 12 to 15, or a pharmaceutically acceptably salt thereof, wherein R^1 is:

(i) represented by the following formula: ; ; or ; wherein each of the formula depicted above is optionally substituted with one to two R^2; or

(ii) represented by the following formula: ; ; or .

17. The compound of any one of claims 12 to 16, or a pharmaceutically acceptably salt thereof, wherein R^2, for each occurrence, is independently $-CH_3$, OH, or –F.

18. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from:

8-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-5-oxa-2,8-diazaspiro[3.5]nonane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*S*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*R*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-(tetrahydro-2*H*-pyran-4-yl)-1-oxa-4,9-diazaspiro[5.5]undecane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-(tetrahydrofuran-3-yl)-1-oxa-4,9-diazaspiro[5.5]undecane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-(2-methoxyethyl)-1-oxa-4,9-diazaspiro[5.5]undecane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-((*S*)-tetrahydro-2*H*-pyran-3-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(±)-(*R*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-((*S*)-tetrahydro-2*H*-pyran-3-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(±)-(*R*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-((*R*)-tetrahydro-2*H*-pyran-3-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

1-(4-((4-(Difluoromethoxy)phenyl)sulfonyl)-1-oxa-4,9-diazaspiro[5.5]undecan-9-yl)-2-methylpropan-2-ol;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-(2-methoxy-2-methylpropyl)-1-oxa-4,9-diazaspiro[5.5]undecane;

9-((2,4-Difluorophenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((3,5-Difluorophenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*S*)-9-((3,5-Difluorophenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*R*)-9-((3,5-Difluorophenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((2-Methoxy-5-methylpyridin-3-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(oxetan-3-ylmethyl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-((tetrahydro-2*H*-pyran-4-yl)methyl)-6-oxa-2,9-diazaspiro[4.5]decane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-((tetrahydro-2*H*-pyran-4-yl)methyl)-1-oxa-4,9-diazaspiro[5.5]undecane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-((3-methyloxetan-3-yl)methyl)-1-oxa-4,9-diazaspiro[5.5]undecane;

4-((4-(Difluoromethoxy)phenyl)sulfonyl)-9-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-1-oxa-4,9-diazaspiro[5.5]undecane;

8-((2-Cyclopropylthiazol-5-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-5-oxa-2,8-diazaspiro[3.5]nonane;

9-((2-Cyclopropylthiazol-5-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((2-Cyclopropylthiazol-5-yl)sulfonyl)-2-(2-oxaspiro[3.3]heptan-6-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(2-oxaspiro[3.3]heptan-6-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*R*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(2-oxaspiro[3.3]heptan-6-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

(*S*)-9-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(2-oxaspiro[3.3]heptan-6-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

9-((3,5-Difluorophenyl)sulfonyl)-2-(2-oxaspiro[3.3]heptan-6-yl)-6-oxa-2,9-diazaspiro[4.5]decane;

4-((3,5-Difluorophenyl)sulfonyl)-9-((3-methyloxetan-3-yl)methyl)-1-oxa-4,9-diazaspiro[5.5]undecane;

9-((4-(Difluoromethoxy)phenyl)sulfonyl)-4-(tetrahydro-2*H*-pyran-4-yl)-1-oxa-4,9-diazaspiro[5.5]undecane;

7-((2,4-Dimethylphenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,7-diazaspiro[3.5]nonane;

7-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,7-diazaspiro[3.5]nonane;

7-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,7-diazaspiro[3.5]nonane;

1-((7-((2,4-Dimethylphenyl)sulfonyl)-2,7-diazaspiro[3.5]nonan-2-yl)methyl)tetrahydro-2H-pyran-4-ol;

7-((2,4-Dimethylphenyl)sulfonyl)-2-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,7-diazaspiro[3.5]nonane;

8-((2-Chloro-4-methylphenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((1,3-Dimethyl-1*H*-pyrazol-5-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((4-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((4-(Difluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((1-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((2-Methyl-4-(trifluoromethoxy)phenyl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((2-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

8-((6-Methoxy-2-methylpyridin-3-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,8-diazaspiro[4.5]decane;

2-((2,4-Dimethylphenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

4-((6-((2,4-Dimethylphenyl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)methyl)tetrahydro-2*H*-pyran-4-ol;

2-((1-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-Methoxy-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((4-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((4-(Difluoromethyl)-1,3-dimethyl-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-Methyl-4-(trifluoromethoxy)phenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-Dimethylphenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((4,6-Dimethylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((4-(Difluoromethoxy)phenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((1-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((2-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((4-Methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((2-Methyl-4-(trifluoromethoxy)phenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

2-((3-Cyclopropyl-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

6-((1-methyl-3-(Trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-2-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.4]octane;

(1'*R*,5'*S*)-8'-((4-(Difluoromethoxy)phenyl)sulfonyl)-1-(tetrahydro-2*H*-pyran-4-yl)-8'-azaspiro[azetidine-3,3'-bicyclo[3.2.1]octane];

1-((1'*R*,5'*S*)-1-((2,4-Dimethylphenyl)sulfonyl)-8'-azaspiro[azetidine-3,3'-bicyclo[3.2.1]octan]-8'-yl)-2-methylpropan-2-ol;

(1'*R*,5'*S*)-8'-((4-(Difluoromethoxy)phenyl)sulfonyl)-1-(2-methoxy-2-methylpropyl)-8'-azaspiro[azetidine-3,3'-bicyclo[3.2.1]octane];

(1'*R*,5'*S*)-1-((4-(Difluoromethoxy)phenyl)sulfonyl)-8'-(2-methoxy-2-methylpropyl)-8'-azaspiro[azetidine-3,3'-bicyclo[3.2.1]octane];

2-((1-(cyclopropylmethyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((1-(cyclopropylmethyl)-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((6-bromo-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(1-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-((4-methyltetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((1-methyl-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((1-methyl-2-oxabicyclo[3.1.1]heptan-5-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)-1,6-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

4-((6-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)methyl)tetrahydro-2*H*-pyran-4-ol;

2-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(4-methyltetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(4-methyltetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-3-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methyl-3,4-dihydropyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(1-(tetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-((4-methyltetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydrofuran-3-yl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-((S)-1-((S)-tetrahydrofuran-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(1-(oxetan-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-6-((3-methyloxetan-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethyl)-2-methylpyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(2-fluoropropan-2-yl)-2-methyl-1,4-dihydropyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(2-fluoropropan-2-yl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethoxy)-2-methyl-3,4-dihydropyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethoxy)-2-methylpyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((5-(difluoromethyl)-2-methyl-1*H*-2l4-pyrazol-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((3-methoxy-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-chloro-6-methoxypyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((5-chloro-2-methoxypyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-dimethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-dimethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-dimethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2,4-dimethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-dimethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

2-((6-methyl-2-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-methyl-2-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((6-cyclopropyl-2-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-cyclopropyl-2-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2,6-bis(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,6-bis(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((2,6-bis(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2,6-bis(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

2-((2-oxaspiro[3.3]heptan-6-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2-oxaspiro[3.3]heptan-6-yl)methyl)-6-((6-(1,1-difluoroethyl)-2-methylpyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2-oxaspiro[3.3]heptan-6-yl)methyl)-6-((2-methyl-5-(trifluoromethyl)-2,5-dihydro-1*H*-pyrazol-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(difluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(difluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-((1s,4s)-4-methoxycyclohexyl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(difluoromethyl)pyridin-3-yl)sulfonyl)-6-(4-methoxycyclohexyl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(difluoromethyl)pyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((1-cyclopropyl-3-(difluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((4-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((4-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(1r,4r)-4-(6-((4-cyclopropyl-6-(trifluoromethyl)-2,3-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

4-(6-((4-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

2-((4-ethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

2-((4-ethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(1r,4r)-4-(6-((4-ethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

(1s,4s)-4-(6-((4-ethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((4-methyltetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-((1R)-1-(tetrahydrofuran-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(1-(4-methyltetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(3-methyloxetan-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((2-methyltetrahydrofuran-2-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((S)-1-((S)-2-methyltetrahydrofuran-2-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((S)-1-((S)-tetrahydro-2*H*-pyran-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((R)-1-((S)-tetrahydrofuran-2-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-2-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydrofuran-3-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((3-methyloxetan-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-(3,3-dimethyltetrahydro-2*H*-pyran-4-yl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((2S,4S)-2-methyltetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((2S,4R)-2-methyltetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((3R,4R)-3-methyltetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((3R,4R)-3-fluorotetrahydro-2*H*-pyran-4-yl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((3R,4S)-3-fluorotetrahydro-2*H*-pyran-4-yl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((3R,5R)-3,5-dimethyltetrahydro-2*H*-pyran-4-yl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((3R,5S)-3,5-dimethyltetrahydro-2*H*-pyran-4-yl)-6-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-(4,4-difluorocyclohexyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-3-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(1-(tetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(oxetan-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(tetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(tetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(oxetan-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(1-(oxetan-3-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-(tetrahydro-2*H*-pyran-4-yl)-6-((2-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((6-(2,2-difluorocyclopropyl)-2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-chloro-5-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((3-(1,1-difluoroethyl)-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-(1-(1-methyl-2-oxabicyclo[2.1.1]hexan-4-yl)ethyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((6-methoxy-4-methylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-methyl-3-((6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-2,4,5,6-tetrahydrocyclopenta[c]pyrazole;

2-ethyl-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)methyl)cyclopropane-1-carbonitrile;

2-(3-(2-methoxyethoxy)propyl)-6-((2-methyl-6-(trifluoromethyl)-1,2-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-(2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(1R,3R)-2,2-dimethyl-3-((6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)methyl)cyclopropane-1-carbonitrile;

2-(((1S,2R,5S)-6-oxabicyclo[3.2.1]octan-2-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-(3-(cyclopentyloxy)propyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

methyl 2,2-dimethyl-4-(6-((2-methyl-6-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)butanoate;

2-(2-cyclopropyl-2-methoxyethyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane ;

2-(5-methoxypentyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-(4-methoxypentyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((1-(2-methoxyethyl)cyclobutyl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

methyl 4-methyl-5-(6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)pentanoate;

2-(3-(ethylthio)propyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-(2-cyclopropylethyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-(2-(tert-butoxy)ethyl)-6-((2-methyl-6-(trifluoromethyl)-1,2-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

4-((6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)methyl)tetrahydro-2*H*-pyran-4-ol;

2-((4-fluorotetrahydro-2*H*-pyran-4-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((3-isopropyl-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-6-(1-(trifluoromethyl)cyclopropyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-chloro-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-methyl-4-(trifluoromethyl)phenyl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(1s,4s)-4-(6-((2-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

(1s,4s)-4-(6-((2-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

2-((2-methyl-5-(trifluoromethyl)-2,5-dihydro-1*H*-pyrazol-3-yl)sulfonyl)-6-(((R)-tetrahydrofuran-3-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)-6-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)-6-((2-methyl-5-(trifluoromethyl)-1*H*-2l4-pyrazol-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(S)-2-((2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methyl)-6-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((tetrahydro-2*H*-pyran-4-yl)methyl)-6-((2-(trifluoromethyl)-3,4-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-(tetrahydro-2*H*-pyran-4-yl)-6-((6-(trifluoromethyl)-2-vinylpyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((2-ethyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethyl)-2-ethylpyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-(difluoromethyl)-2-ethylpyridin-3-yl)sulfonyl)-6-(2-oxaspiro[3.3]heptan-6-yl)-2,6-diazaspiro[3.3]heptane;

(1r,4r)-4-(6-((6-(difluoromethyl)-2-ethylpyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

(1s,4s)-4-(6-((6-(difluoromethyl)-2-ethylpyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)-1-methylcyclohexan-1-ol;

2-((2-cyclopropyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

2-((3-(1,1-difluoroethyl)-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2,4-bis(trifluoromethyl)phenyl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(1-(tetrahydro-2*H*-pyran-4-yl)ethyl)-2,6-diazaspiro[3.3]heptane;

2-((6-chloro-2-(trifluoromethyl)-1,4-dihydropyridin-3-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((2-fluoro-4-(trifluoromethoxy)phenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((1,4-dioxan-2-yl)methyl)-6-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

(R)-2-((1,4-dioxan-2-yl)methyl)-6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

2-((4-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)sulfonyl)-6-(oxetan-3-ylmethyl)-2,6-diazaspiro[3.3]heptane;

2-((3-cyclopropyl-1-methyl-1*H*-pyrazol-5-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((2-fluoro-4-(trifluoromethoxy)phenyl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((3-methyl-5-(trifluoromethyl)pyridin-2-yl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

(1s,4s)-1-methyl-4-(6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)cyclohexan-1-ol;

(1s,4s)-1-methyl-4-(6-((2-methyl-6-(trifluoromethyl)pyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptan-2-yl)cyclohexan-1-ol;

2-((3-methyl-5-(trifluoromethyl)pyridin-2-yl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((4-(difluoromethoxy)-2,6-difluorophenyl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((4-(difluoromethoxy)-2-fluorophenyl)sulfonyl)-6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptane;

2-((4-(difluoromethoxy)-2-fluorophenyl)sulfonyl)-6-(tetrahydro-2*H*-pyran-4-yl)-2,6-diazaspiro[3.3]heptane;

2-((6-((tetrahydro-2*H*-pyran-4-yl)methyl)-2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5-(trifluoromethyl)benzonitrile; and

2-((tetrahydro-2*H*-pyran-4-yl)methyl)-6-((6-(trifluoromethyl)-2,3-dihydropyridin-3-yl)sulfonyl)-2,6-diazaspiro[3.3]heptane;

or a pharmaceutically acceptable salt thereof.

19. A pharmaceutical composition comprising a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

20. A compound of any one of claims 1–18, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 19 for use in:

(i) treating a disease mediated by Emopamil-Binding Protein; or

(ii) treating an autoimmune disease in a subject, optionally, the autoimmune disease is multiple sclerosis.