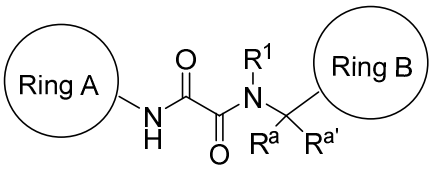
Claims

What is claimed is:

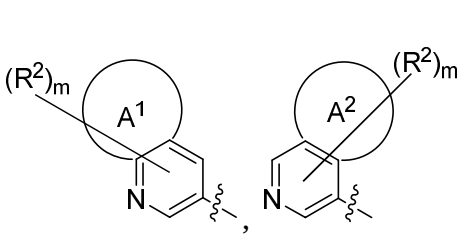
1. A compound of Formula (A) or a pharmaceutically acceptable salt thereof;

wherein:



Formula (A);

Ring A is selected from the group consisting of:



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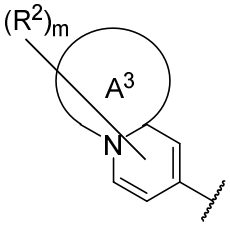
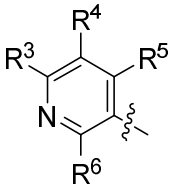
,



, and



;

Ring B is selected from the group consisting of C_6–C_{10} aryl and 5-10 membered heteroaryl, each optionally substituted at any available position;

each of rings A^1 and A^2 is independently 5-6 membered carbocyclyl, 5-6 membered heterocyclyl, 5-6 membered heteroaryl or phenyl;

each ring A^3 is independently a 5-6 membered heterocyclyl or 5-6 membered heteroaryl, wherein the heterocyclyl and heteroaryl contain at least one nitrogen atom;

each R^1 is independently selected from the group consisting of –C_1–C_6 alkyl, –C_2–C_6 heteroalkyl, –C_2–C_6 haloalkyl, –C_3–C_{10} carbocyclyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl and cycloalkylalkyl, each optionally substituted at any available position;

each R^2 is independently selected from the group consisting of –D, halo, =O, –CN, –C_1–C_6 alkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_3–C_9 cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, –OR^{a2}, –$N(R^{a2})_2$, –$C(=O)R^{a2}$, –$C(=O)OR^{a2}$, –$NR^{a2}C(=O)R^{a2}$, –$NR^{a2}C(=O)OR^{a2}$, –$C(=O)N(R^{a2})_2$, –

$C(=O)N(OR^{a2})(R^{a2})$, $–OC(=O)N(R^{a2})_2$, $–S(=O)R^{a2}$, $–S(=O)_2R^{a2}$, $–SR^{a2}$, $–S(=O)(=NR^{a2})R^{a2}$, $–NR^{a2}S(=O)_2R^{a2}$ and $–S(=O)_2N(R^{a2})_2$;

each R^3 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a3}$, $–N(R^{a3})_2$, $–C(=O)R^{a3}$, $–C(=O)OR^{a3}$, $–NR^{a3}C(=O)R^{a3}$, $–NR^{a3}C(=O)OR^{a3}$, $–C(=O)N(R^{a3})_2$, $–OC(=O)N(R^{a3})_2$,$-S(=O)R^{a3}$, $–S(=O)_2R^{a3}$, $–SR^{a3}$, $–S(=O)(=NR^{a3})R^{a3}$, $–NR^{a3}S(=O)_2R^{a3}$ and $–S(=O)_2N(R^{a3})_2$;

each R^4 is independently selected from the group consisting of D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a4}$, $–N(R^{a4})_2$, $–C(=O)R^{a4}$, $–C(=O)OR^{a4}$, $–NR^{a4}C(=O)R^{a4}$, $–NR^{a4}C(=O)OR^{a4}$, $–C(=O)N(R^{a4})_2$, $–OC(=O)N(R^{a4})_2$,$-S(=O)R^{a4}$, $–S(=O)_2R^{a4}$, $–SR^{a4}$, $–S(=O)(=NR^{a4})R^{a4}$, $–NR^{a4}S(=O)_2R^{a4}$ and $–S(=O)_2N(R^{a4})_2$;

each R^5 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a5}$, $–N(R^{a5})_2$, $–C(=O)R^{a5}$, $–C(=O)OR^{a5}$, $–NR^{a5}C(=O)R^{a5}$, $–NR^{a5}C(=O)OR^{a5}$, $–C(=O)N(R^{a5})_2$, $–OC(=O)N(R^{a5})_2$,$-S(=O)R^{a5}$, $–S(=O)_2R^{a5}$, $–SR^{a5}$, $–S(=O)(=NR^{a5})R^{a5}$, $–NR^{a5}S(=O)_2R^{a5}$ and $–S(=O)_2N(R^{a5})_2$;

each R^6 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a6}$, $–N(R^{a6})_2$, $–C(=O)R^{a6}$, $–C(=O)OR^{a6}$, $–NR^{a6}C(=O)R^{a6}$, $–NR^{a6}C(=O)OR^{a6}$, $–C(=O)N(R^{a6})_2$, $–OC(=O)N(R^{a6})_2$, $–S(=O)R^{a6}$, $–S(=O)_2R^{a6}$, $–SR^{a6}$, $–S(=O)(=NR^{a6})R^{a6}$, $–NR^{a6}S(=O)_2R^{a6}$ and $–S(=O)_2N(R^{a6})_2$;

each R^a and $R^{a'}$ are independently selected from H and C_1-C_6 alkyl;

each R^{a2}, R^{a3}, R^{a4}, R^{a5} and R^{a6} is independently selected from the group consisting of H, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl wherein each alkyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position (*e.g.*, substituted with 0, 1, 2 or 3 instances of R^9, wherein each R^9 is

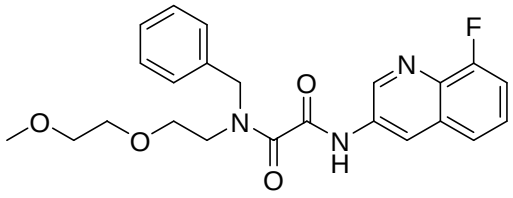
independently selected from the group consisting of =O, halo, –CN, –C_1–C_6 alkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 hydroxyalkyl,–C_1–C_6 haloalkyl, –C_3–C_9 cycloalkyl, 3-10 membered heterocyclyl, C_6–C_{10} aryl, 5-10 membered heteroaryl, cycloalkylalkyl, heterocyclylalkyl, arylalkyl, heteroarylalkyl, –OR^b, –$N(R^b)_2$, –$C(=O)R^b$, –$C(=O)OR^b$, –$NR^bC(=O)R^b$, –$NR^bC(=O)OR^b$, –$C(=O)N(R^b)_2$, –$OC(=O)N(R^b)_2$,-$S(=O)R^b$, –$S(=O)_2R^b$, –SR^b, –$S(=O)(=NR^b)R^b$, –$NR^bS(=O)_2R^b$ and –$S(=O)_2N(R^b)_2$, wherein each R^b is independently selected from the group consisting of H, –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –^{i}Pr,–^{n}Bu, –^{t}Bu, –*sec*-Bu, –*iso*-Bu) and C_3-C_9 cycloalkyl (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl); and

m is 0, 1, 2 or 3; wherein

(i) when R^4 is –CH_3 then R^3 is not H and;

(ii) the compound is not one of compounds a) to k) or a pharmaceutically acceptable salt thereof:

a) N1-benzyl-N2-(8-fluoroquinolin-3-yl)-N1-(2-(2-methoxyethoxy)ethyl)oxalamide:



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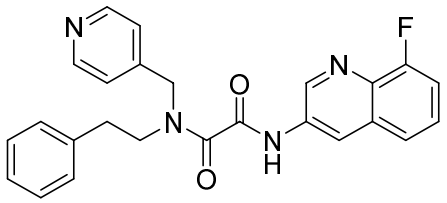
b) N1-(8-fluoroquinolin-3-yl)-N2-phenethyl-N2-(pyridin-4-ylmethyl)oxalamide:



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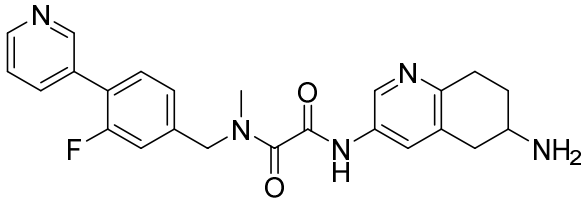
c) N1-(6-amino-5,6,7,8-tetrahydroquinolin-3-yl)-N2-(3-fluoro-4-(pyridin-3-yl)benzyl)-N2-methyloxalamide:



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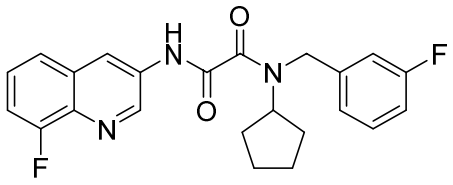
d) N1-cyclopentyl-N1-(3-fluorobenzyl)-N2-(8-fluoroquinolin-3-yl)oxalamide:



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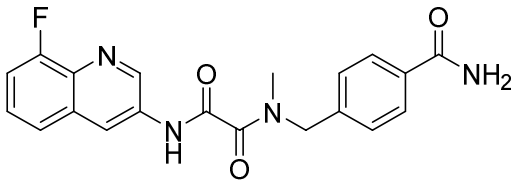
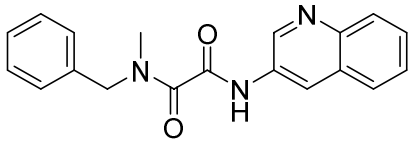
e) N1-(4-carbamoylbenzyl)-N2-(8-fluoroquinolin-3-yl)-N1-methyloxalamide:



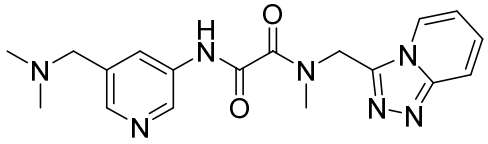
;

f) N1-benzyl-N1-methyl-N2-(quinolin-3-yl)oxalamide:



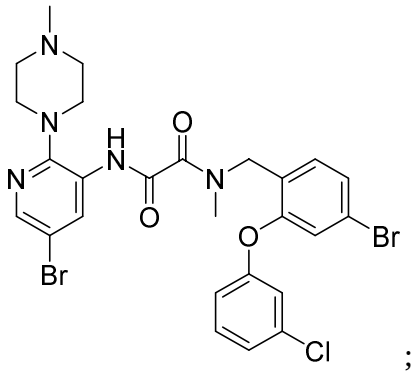
;

g) N1-([1,2,4]triazolo[4,3-a]pyridin-3-ylmethyl)-N2-(5-((dimethylamino)methyl)pyridin-3-yl)-N1-methyloxalamide:



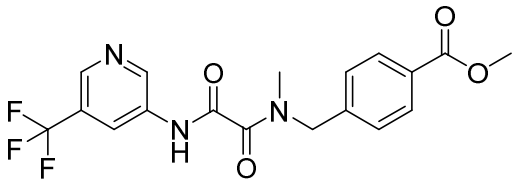
;

h) N1-(4-bromo-2-(3-chlorophenoxy)benzyl)-N2-(5-bromo-2-(4-methylpiperazin-1-yl)pyridin-3-yl)-N1-methyloxalamide:



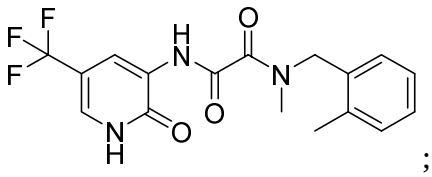
;

i) methyl 4-((N-methyl-2-oxo-2-((5-(trifluoromethyl)pyridin-3-yl)amino)acetamido)methyl)benzoate:



;

j) N1-methyl-N1-(2-methylbenzyl)-N2-(2-oxo-5-(trifluoromethyl)-1,2-dihydropyridin-3-yl)oxalamide:



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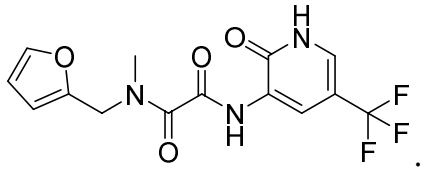
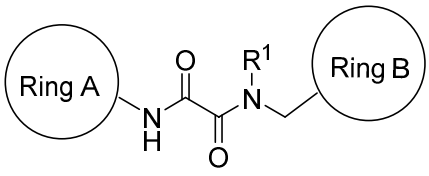
k) N1-(furan-2-ylmethyl)-N1-methyl-N2-(2-oxo-5-(trifluoromethyl)-1,2-dihydropyridin-3-yl)oxalamide:



.

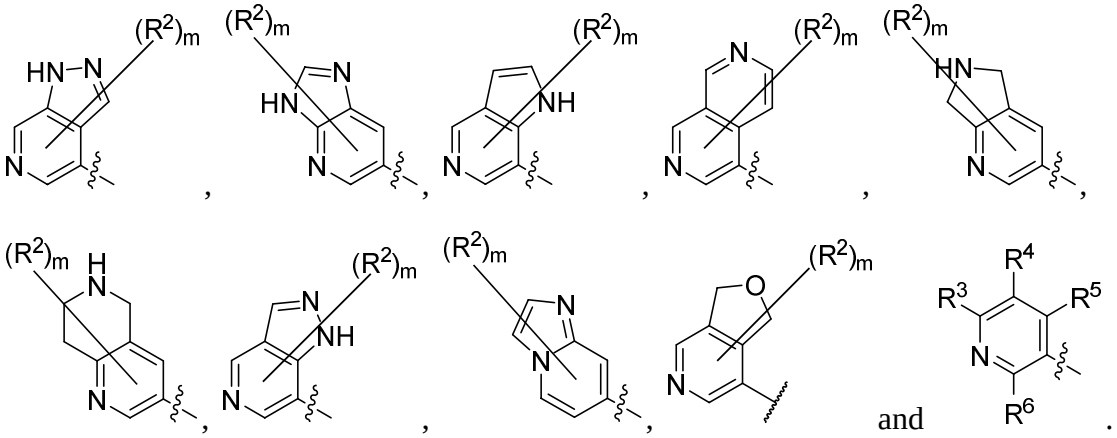
2. The compound of claim 1, wherein R^a and $R^{a'}$ are independently H and Me.

3. The compound of claim 1, wherein the compound is of Formula (I):

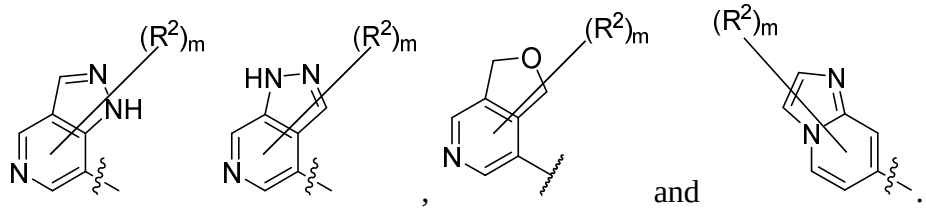


Formula (I).

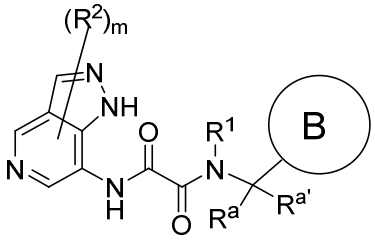
4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:



5. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:

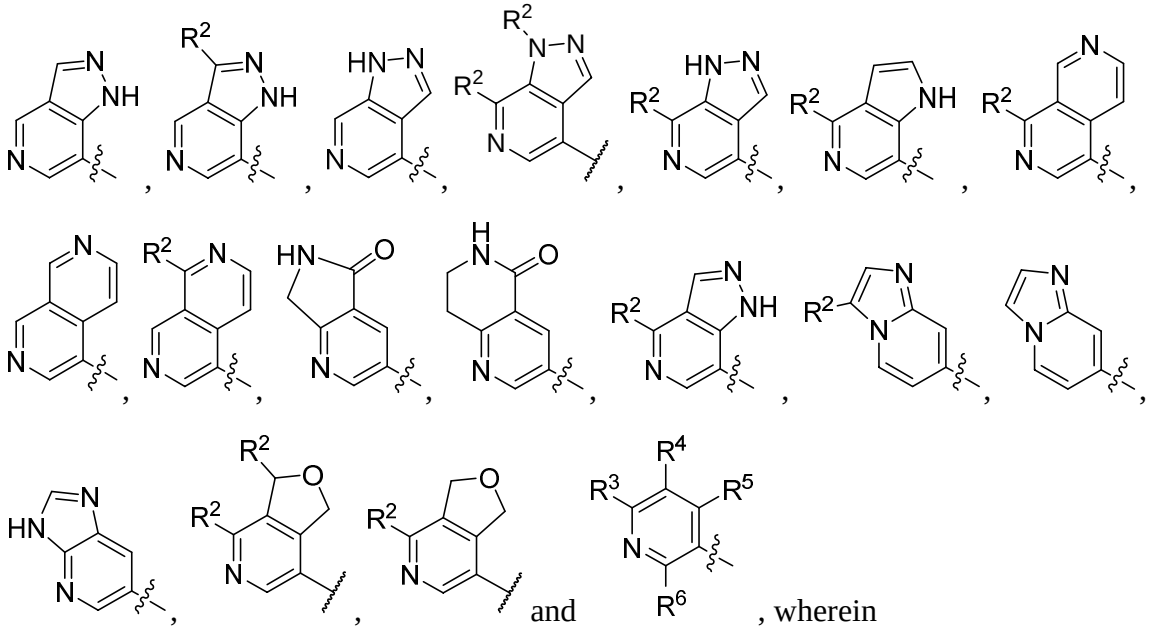


6. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula (A_1):



(A_1).

7. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:



, wherein

each R^2 is independently selected from the group consisting of –D, halo, =O, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a2}$, $–N(R^{a2})_2$, $–C(=O)R^{a2}$, $–C(=O)OR^{a2}$, $–NR^{a2}C(=O)R^{a2}$, $–NR^{a2}C(=O)OR^{a2}$, $–C(=O)N(R^{a2})_2$, $–C(=O)N(OR^{a2})(R^{a2})$, $–OC(=O)N(R^{a2})_2$, $–S(=O)R^{a2}$, $–S(=O)_2R^{a2}$, $–SR^{a2}$, $–S(=O)(=NR^{a2})R^{a2}$, $–NR^{a2}S(=O)_2R^{a2}$ and $–S(=O)_2N(R^{a2})_2$;

each R^3 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a3}$, $–N(R^{a3})_2$, $–C(=O)R^{a3}$, $–C(=O)OR^{a3}$, $–NR^{a3}C(=O)R^{a3}$, $–NR^{a3}C(=O)OR^{a3}$, $–C(=O)N(R^{a3})_2$, $–OC(=O)N(R^{a3})_2$,$-S(=O)R^{a3}$, $–S(=O)_2R^{a3}$, $–SR^{a3}$, $–S(=O)(=NR^{a3})R^{a3}$, $–NR^{a3}S(=O)_2R^{a3}$ and $–S(=O)_2N(R^{a3})_2$;

each R^4 is independently selected from the group consisting of D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a4}$, $–N(R^{a4})_2$, $–C(=O)R^{a4}$, $–C(=O)OR^{a4}$, $–NR^{a4}C(=O)R^{a4}$, $–NR^{a4}C(=O)OR^{a4}$, $–C(=O)N(R^{a4})_2$, $–OC(=O)N(R^{a4})_2$,$-S(=O)R^{a4}$, $–S(=O)_2R^{a4}$, $–SR^{a4}$, $–S(=O)(=NR^{a4})R^{a4}$, $–NR^{a4}S(=O)_2R^{a4}$ and $–S(=O)_2N(R^{a4})_2$;

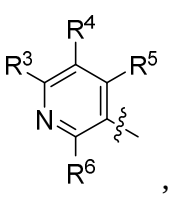
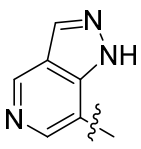
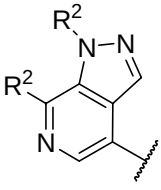
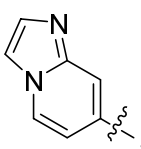
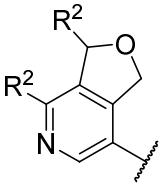
each R^5 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a5}$, $–N(R^{a5})_2$,

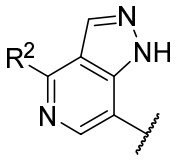
$–C(=O)R^{a5}$, $–C(=O)OR^{a5}$, $–NR^{a5}C(=O)R^{a5}$, $–NR^{a5}C(=O)OR^{a5}$, $–C(=O)N(R^{a5})_2$, $–OC(=O)N(R^{a5})_2$,$-S(=O)R^{a5}$, $–S(=O)_2R^{a5}$, $–SR^{a5}$, $–S(=O)(=NR^{a5})R^{a5}$, $–NR^{a5}S(=O)_2R^{a5}$ and $–S(=O)_2N(R^{a5})_2$;

each R^6 is independently selected from the group consisting of H, D, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl, cycloalkylalkyl, $–OR^{a6}$, $–N(R^{a6})_2$, $–C(=O)R^{a6}$, $–C(=O)OR^{a6}$, $–NR^{a6}C(=O)R^{a6}$, $–NR^{a6}C(=O)OR^{a6}$, $–C(=O)N(R^{a6})_2$, $–OC(=O)N(R^{a6})_2$, $–S(=O)R^{a6}$, $–S(=O)_2R^{a6}$, $–SR^{a6}$, $–S(=O)(=NR^{a6})R^{a6}$, $–NR^{a6}S(=O)_2R^{a6}$ and $–S(=O)_2N(R^{a6})_2$;

each R^{a2}, R^{a3}, R^{a4}, R^{a5} and R^{a6} is independently selected from the group consisting of H, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $C_3–C_9$ cycloalkyl, 3-7 membered heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, 5-6 membered heteroaryl, arylalkyl and heteroarylalkyl wherein each alkyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl is optionally substituted at any available position (*e.g.*, substituted with 0, 1, 2 or 3 instances of R^9, wherein each R^9 is independently selected from the group consisting of =O, halo, –CN, $–C_1–C_6$ alkyl, $–C_1–C_6$ heteroalkyl, $–C_1–C_6$ hydroxyalkyl,$–C_1–C_6$ haloalkyl, $–C_3–C_9$ cycloalkyl, 3-10 membered heterocyclyl, $C_6–C_{10}$ aryl, 5-10 membered heteroaryl, cycloalkylalkyl, heterocyclylalkyl, arylalkyl, heteroarylalkyl, $–OR^b$, $–N(R^b)_2$, $–C(=O)R^b$, $–C(=O)OR^b$, $–NR^bC(=O)R^b$, $–NR^bC(=O)OR^b$, $–C(=O)N(R^b)_2$, $–OC(=O)N(R^b)_2$,$-S(=O)R^b$, $–S(=O)_2R^b$, $–SR^b$, $–S(=O)(=NR^b)R^b$, $–NR^bS(=O)_2R^b$ and $–S(=O)_2N(R^b)_2$, wherein each R^b is independently selected from the group consisting of H, $–C_1–C_6$ alkyl (*e.g.*, –Me, –Et, –Pr, $–^iPr$,$–^nBu$, $–^tBu$, –*sec*-Bu, –*iso*-Bu).and C_3-C_9 cycloalkyl (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl).

8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:

and

.

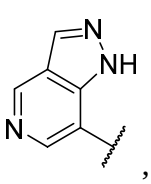
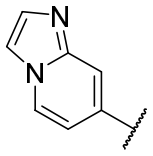
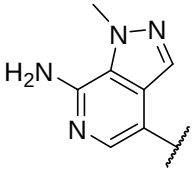
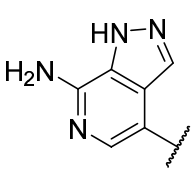
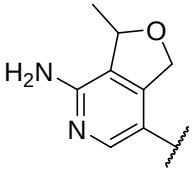
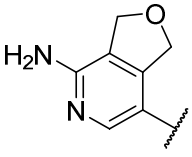
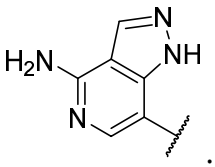
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently selected from the group consisting of –D, =O, $–C_1–C_6$ alkyl and $–N(R^{a2})_2$.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein each R^{a2} is H.

11. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently selected from $–NH_2$ and –Me.

12. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein each R^2 is $–NH_2$.

13. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:







and

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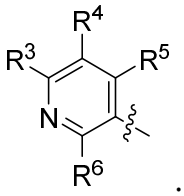
14. The compound of any one of claims 1-4 and 7 to 12 or a pharmaceutically acceptable salt thereof, wherein Ring A is 

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15. The compound of any one of claims 1-4, 7-12 and 14, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from the group consisting of H, halo, –CN, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl and –N(R^{a5})$_2$.

16. The compound of any one of claims 1-4, 7-12 and 14, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from the group consisting of H and –Me.

17. The compound of any one of claims 1-4, 7-12 and 14-16, or a pharmaceutically acceptable salt thereof, wherein R^6 is selected from the group consisting of H, halo, –CN, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl and –N(R^{a6})2.

18. The compound of any one of claims 1-4, 7-12 and 14-16, or a pharmaceutically acceptable salt thereof, wherein R^6 is H.

19. The compound of any one of claims 1-4, 7-12 and 14-18, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from the group consisting of H, –C_1–C_6 alkyl, –C_1–C_6 haloalkyl, –OR^{a3} and –N(R^{a3})$_2$.

20. The compound of any one of claims 1-4, 7-12 and 14-18, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from the group consisting of H, –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –iPr,–nBu, –tBu, –sec-Bu, –iso-Bu), –C_1–C_6 alkyl (*e.g.*, –CF_3, –CHF_2), –OH, –O–(C_1–C_6 alkyl) (*e.g.*, –OCH_3, –OEt), –O–(C_1–C_6 haloalkyl) (*e.g.*, –OCF_3, –$OCHF_2$), –NH_2, –NH–(C_1–C_6 alkyl) (*e.g.*, –$NHCH_3$) and –N–(C_1–C_6 alkyl)$_2$ (e.g, –N(CH_3)$_2$).

21. The compound of any one of claims 1-4, 7-12 and 14-18, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from the group consisting of H, –Me, -CHF_2, –OCH_3 and –NH_2.

22. The compound of any one of claims 1-4, 7-12 and 14-21, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of –C_1–C_6 alkyl, 3-

10 membered heterocyclyl (*e.g.*, oxetanyl), –C_3–C_9 cycloalkyl (*e.g.*, cyclopropyl) and –C(=O)N(R^{a4})$_2$.

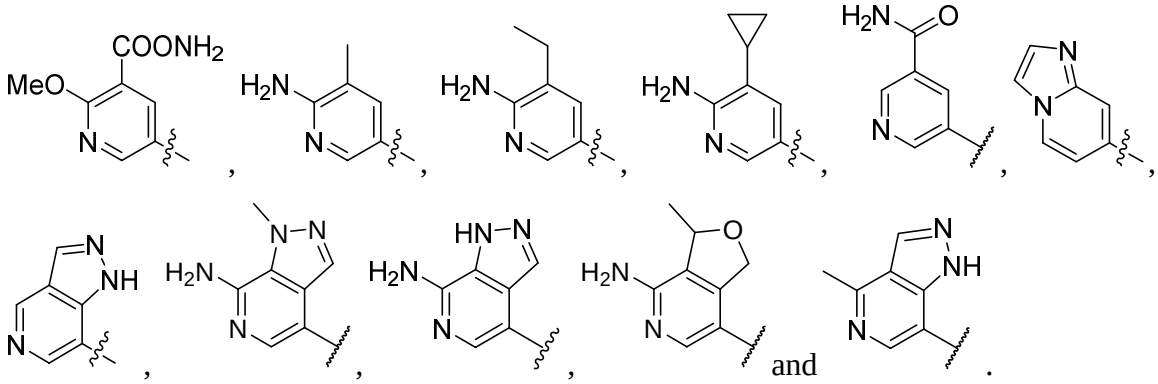
23. The compound of any one of claims 1-4, 7-12 and 14-21, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of –Me, –Et, oxetan-3-yl, cyclopropyl and –C(=O)NH_2.

24. The compound of any one of claims 1-4, 7-12 and 14-21, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from the group consisting of –Me, –Et, cyclopropyl and –C(=O)NH_2.

25. The compound of any one of claims 1-4, 7-12 and 14-18, or a pharmaceutically acceptable salt thereof, wherein R^3 is –OCH_3 and R^4 is –C(=O)NH_2.

26. The compound of any one of claims 1-4, 7-12 and 14-18, or a pharmaceutically acceptable salt thereof, wherein R^3 is –NH_2 and R^4 is selected from the group consisting of –Me, –Et and cyclopropyl.

27. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from the group consisting of:



and .

28. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of C_6–C_{10} aryl (*e.g.*, phenyl, naphthalenyl), 5-6 membered monocyclic heteroaryl, and 8-10 membered bicyclic heteroaryl, each optionally substituted at any available position.

29. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of thiophenyl, oxazolyl, isoxazolyl,

thiazolyl, isothiazolyl, furanyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, phenyl, naphthalenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, benzofuranyl, 1H-indazolyl, 2H-indazolyl, benzo[b]thiophenyl, quinolinyl, 1,5-naphthyridinyl, 1,2-dihydro-1,5-naphthyridinyl, 1,2,3,4-tetrahydro-1,8-naphthyridinyl, imidazo[1,2-a]pyridinyl, imidazo[1,5-a]pyridinyl, isoquinolinyl, benzo[*d*]imidazolyl, benzo[*d*]thiazolyl, benzo[d]isothiazolyl, benzo[*d*]oxazolyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, 1H-pyrazolo[4,3-*b*]pyridinyl, 1H-pyrazolo[3,4-b]pyridinyl, 1H-thieno[2,3-c]pyrazolyl, 1H-thieno[3,2-c]pyrazolyl, thiazolo[5,4-b]pyridinyl, chromanyl and 1,2,3,4-tetrahydro-1,8-naphthyridinyl, each optionally substituted.

30. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of pyridinyl, pyrimidinyl and phenyl, each optionally substituted.

31. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein each Ring B is substituted at any available position with 0, 1, 2 or 3 instances of R^7, wherein:

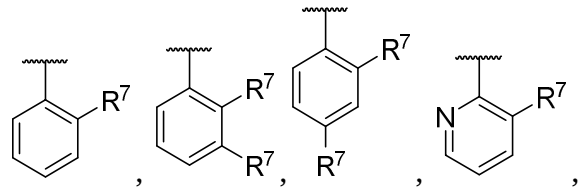
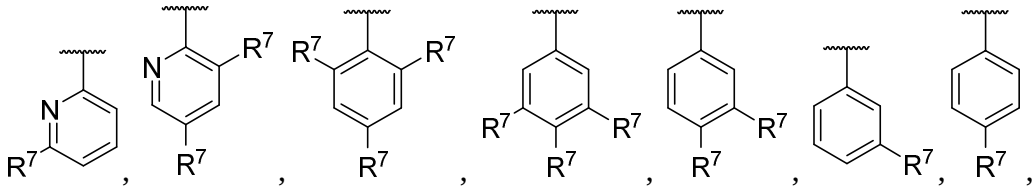
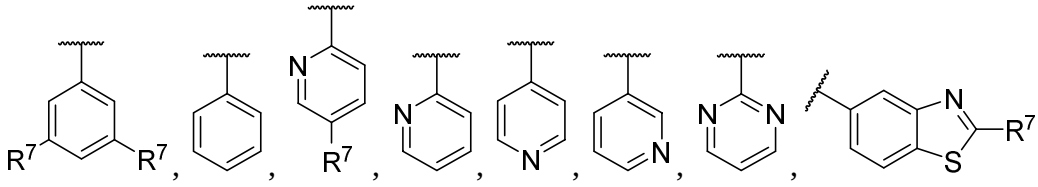
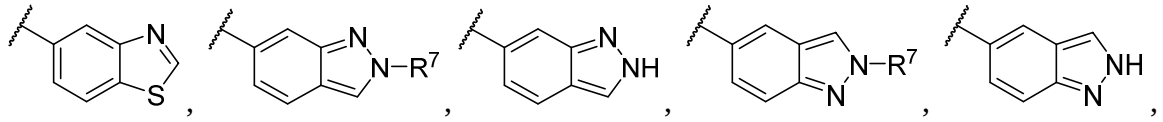
each R^7 is independently selected from the group consisting of –D, =O, –CN, halo, –SF_5, –C_1–C_6 alkyl, –C_1–C_6 heteroalkyl, –C_1–C_6 haloalkyl, –C_3–C_9 cycloalkyl, 3-10 membered heterocyclyl, C_6–C_{10} aryl, 5-10 membered heteroaryl, cycloalkylalkyl, heterocyclylalkyl, arylalkyl, heteroarylalkyl, –OR^{a7}, –$N(R^{a7})_2$, –$C(=O)R^{a7}$, –$C(=O)OR^{a7}$, –$NR^{a7}C(=O)R^{a7}$, –$NR^{a7}C(=O)OR^{a7}$, –$C(=O)N(R^{a7})_2$, –$OC(=O)R^{a7}$, –$OC(=O)N(R^{a7})_2$,-$S(=O)R^{a7}$, –$S(=O)_2R^{a7}$, –SR^{a7}, –$S(=O)(=NR^{a7})R^{a7}$, –$NR^{a7}S(=O)_2R^{a7}$ and –$S(=O)_2N(R^{a7})_2$, wherein each alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, cycloalkylalkyl, heterocyclylalkyl, arylalkyl and heteroarylalkyl of R^7 is optionally substituted (*e.g.*, substituted with 0, 1, 2 or 3 instances of –Me, –OH, –$C(=O)CH_3$, –$C(=O)NHCH_3$, –NH_2, –$NHC(=O)CH_3$ or a combination thereof);

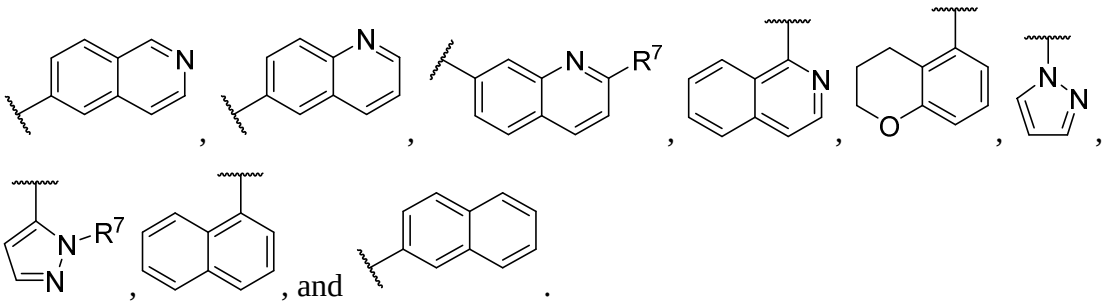
each R^{a7} is independently H; –C_1–C_6 alkyl; –C_1–C_6 haloalkyl; –C_1–C_6 heteroalkyl substituted with 0 or 1 instance of =O; C_3–C_9 cycloalkyl; or 3-10 membered heterocyclyl substituted with 0 or 1 instances of =O, –Me or a combination thereof.

32. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of C_6–C_{10} aryl and 5-6 membered monocyclic heteroaryl wherein the aryl and heteroaryl are substituted at any available position with 0, 1, 2 or 3 instances of R^7.

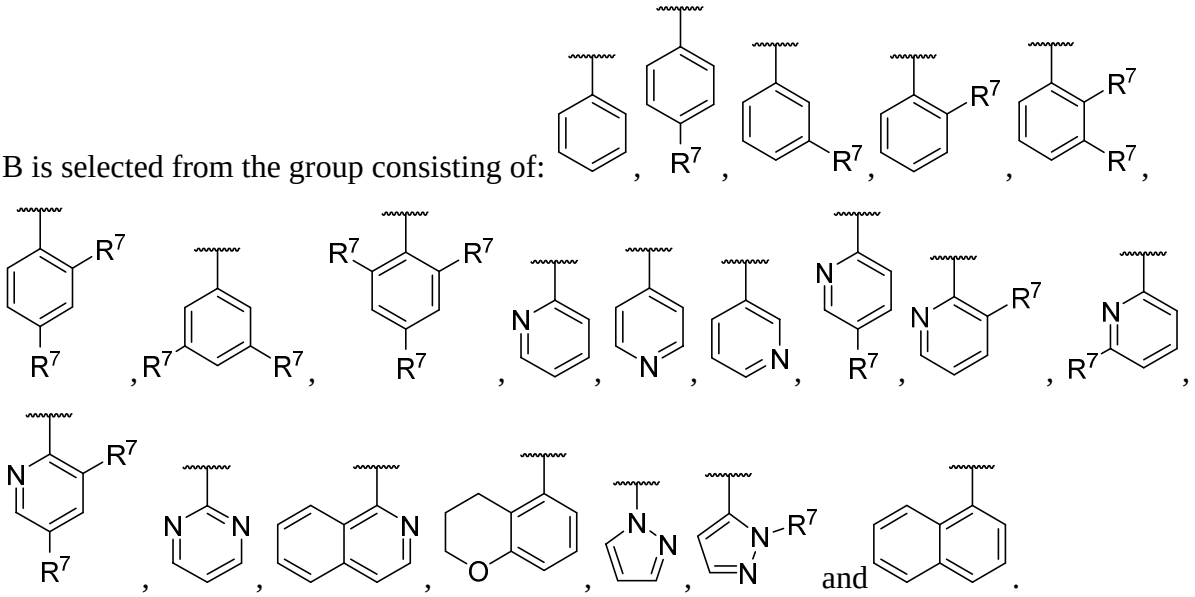
33. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of thiophenyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, furanyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, phenyl, naphthalenyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, indolyl, benzofuranyl, 1H-indazolyl, 2H-indazolyl, benzo[b]thiophenyl, quinolinyl, 1,5-naphthyridinyl, 1,2-dihydro-1,5-naphthyridinyl, 1,2,3,4-tetrahydro-1,8-naphthyridinyl, imidazo[1,2-a]pyridinyl, imidazo[1,5-a]pyridinyl, isoquinolinyl, benzo[*d*]imidazolyl, benzo[*d*]thiazolyl, benzo[d]isothiazolyl, benzo[*d*]oxazolyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, 1H-pyrazolo[4,3-*b*]pyridinyl, 1H-pyrazolo[3,4-b]pyridinyl, 1H-thieno[2,3-c]pyrazolyl, 1H-thieno[3,2-c]pyrazolyl, thiazolo[5,4-b]pyridinyl, chromanyl and 1,2,3,4-tetrahydro-1,8-naphthyridinyl, each substituted at any available position with 0, 1, 2 or 3 instances of R^7.

34. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of pyridinyl, pyrimidinyl and phenyl, each substituted at any available position with 0, 1, 2 or 3 instances of R^7.

35. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of:  ,  ,  ,  .



36. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein Ring B is selected from the group consisting of:



37. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein each R^7 is independently selected from the group consisting of –D, =O, –SF_5, halo (*e.g.*, –F, –Cl, –Br), –CN, –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*–Bu, –^{t}Bu), –C_1–C_6 heteroalkyl (*e.g.*, –CH_2OH, –$CH(OH)(CH_3)$, –$C(OH)(CH_3)_2$, –CH_2NH_2), –C_1–C_6 haloalkyl (*e.g.*, –CHF_2, –CH_2CF_3, –CF_3, –CF_2CF_3), –C_3–C_9 cycloalkyl (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl), 3-10 membered heterocyclyl (*e.g.*, oxetanyl, pyrolidinyl, piperidinyl, piperazinyl), phenyl, 5-10 membered heteroaryl (*e.g.*, pyrazolyl, thiazolyl, thiophenyl, pyridinyl), cycloalkylalkyl (*e.g.* –CH_2-cyclopropyl), heterocyclylalkyl (*e.g.*, –CH_2-morpholinyl), heteroarylalkyl (*e.g.*, –CH_2-triazolyl, –CH_2-imidazolyl, –CH_2-pyrazolyl), –OR^{a7} (*e.g.*, –OH, –OCH_3, –O-tetrahydrofuranyl, –O-tetrahydropyran-4-yl, –OCF_3, –$OCHF_2$), –$N(R^{a7})_2$, (*e.g.*, –NH_2, –NHR^{a7}, –$NHCH_3$, –$N(CH_3)_2$), –$NR^{a7}C(=O)R^{a7}$ (*e.g.*, –$NHC(=O)CH_3$), –$C(=O)N(R^{a7})_2$, (*e.g.*, –$C(=O)NH_2$, –$C(=O)NHCH_3$), –$OC(=O)R^{a7}$ (*e.g.*, –$OC(=O)CH_3$), –$S(=O)R^{a7}$ (*e.g.*, –SO_2CH_3), –$NR^{a7}S(=O)_2R^{a7}$ (*e.g.*, –$NHSO_2CH_3$) and –$S(=O)_2N(R^{a7})_2$ (*e.g.*, –SO_2NH_2, –SO_2NHCH_3), wherein each alkyl, cycloalkyl, heterocyclyl,

phenyl, heteroaryl, cycloalkylalkyl, heterocyclylalkyl, arylalkyl and heteroarylalkyl is optionally substituted (*e.g.*, substituted with 0, 1, 2 or 3 instances of –Me, –OH, –C(=O)CH_3, –NHC(=O)CH_3 or a combination thereof); and

each R^{a7} is independently selected from the group consisting of H, –C_1–C_6 alkyl, (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu), –C_1–C_6 haloalkyl (*e.g.*, –CF_3, –CHF_2, –CF_2CF_3, –CH_2CF_3), –C_1–C_6 heteroalkyl substituted with 0 or 1 instances of =O (*e.g.*, –$CH_2CH_2N(CH_3)_2$, –$CH_2C(=O)N(CH_3)_2$, –$CH(CH_3)CH_2N(CH_3)_2$, –$CH(CH_3)C(=O)N(CH_3)_2$), C_3–C_9 cycloalkyl and 3-10 membered heterocyclyl substituted with 0 or 1 instances of =O, –Me or a combination thereof (*e.g.* tetrahydrofuran-3-yl, tetrahydropyran-4-yl, oxetan-3-yl, N-CH_3-2-oxo-pyrrolidin-3-yl).

38. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein each R^7 is independently selected from the group consisting of –D, halo (*e.g.*, –F, –Cl, Br), –SF_5, –CN, –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*–Bu, –^{t}Bu), –C_1–C_6 haloalkyl (*e.g.*, –CHF_2, –CH_2CF_3, –CF_3), –$N(R^{a7})_2$, (*e.g.*, –NH_2, –NHR^{a7}, –$NHCH_3$, –$N(CH_3)_2$), –$NR^{a7}C(=O)R^{a7}$ (*e.g.*, –NHC(=O)CH_3) and –C(=O)$N(R^{a7})_2$, (*e.g.*, –C(=O)NH_2, –C(=O)$NHCH_3$), wherein each R^{a7} is independently selected from the group consisting of H and –C_1–C_6 alkyl, (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu).

39. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein each R^7 is independently selected from the group consisting of halo (*e.g.*, –F, –Cl, Br) and –C_1–C_6 haloalkyl (*e.g.*, –CHF_2, –CH_2CF_3, –CF_2CF_3, –CF_3).

40. The compound of any one of claims 31-39, or a pharmaceutically acceptable salt thereof, wherein each R^{a7} is independently selected from the group consisting of H and –Me.

41. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein each R^7 is independently selected from the group consisting of –D, –F, –Cl, Br, –CN, –SF_5, –Me, –Et, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu, –CHF_2, –CH_2CF_3, –CF_2CF_3, –CF_3, –CH_2OH, –CH(OH)(CH_3), –$C(OH)(CH_3)_2$, –CH_2NH_2, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyrrolidin-1-yl, piperidin-4-yl, piperazin-4-yl, pyridin-4-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thiazol-2-yl, thiazol-5-yl, thiophen-2-yl, –CH_2-cyclopropyl, –CH_2-morpholin-4-yl, –CH_2-1,2,4-triazol-1-yl, –CH_2-imidazol-1-yl, –CH_2-pyrazol-1-yl, –OH, –OCH_3, –OCF_3, –$OCHF_2$, –O-tetrahydrofuran-3-yl, –O-tetrahydropyran-4-yl, –O-(N-CH_3-2-oxo-pyrrolidin-3-yl), –OCF_3, –$OCHF_2$, –NH_2, –$NHCH_3$, –$NHCH_2CF_3$, –

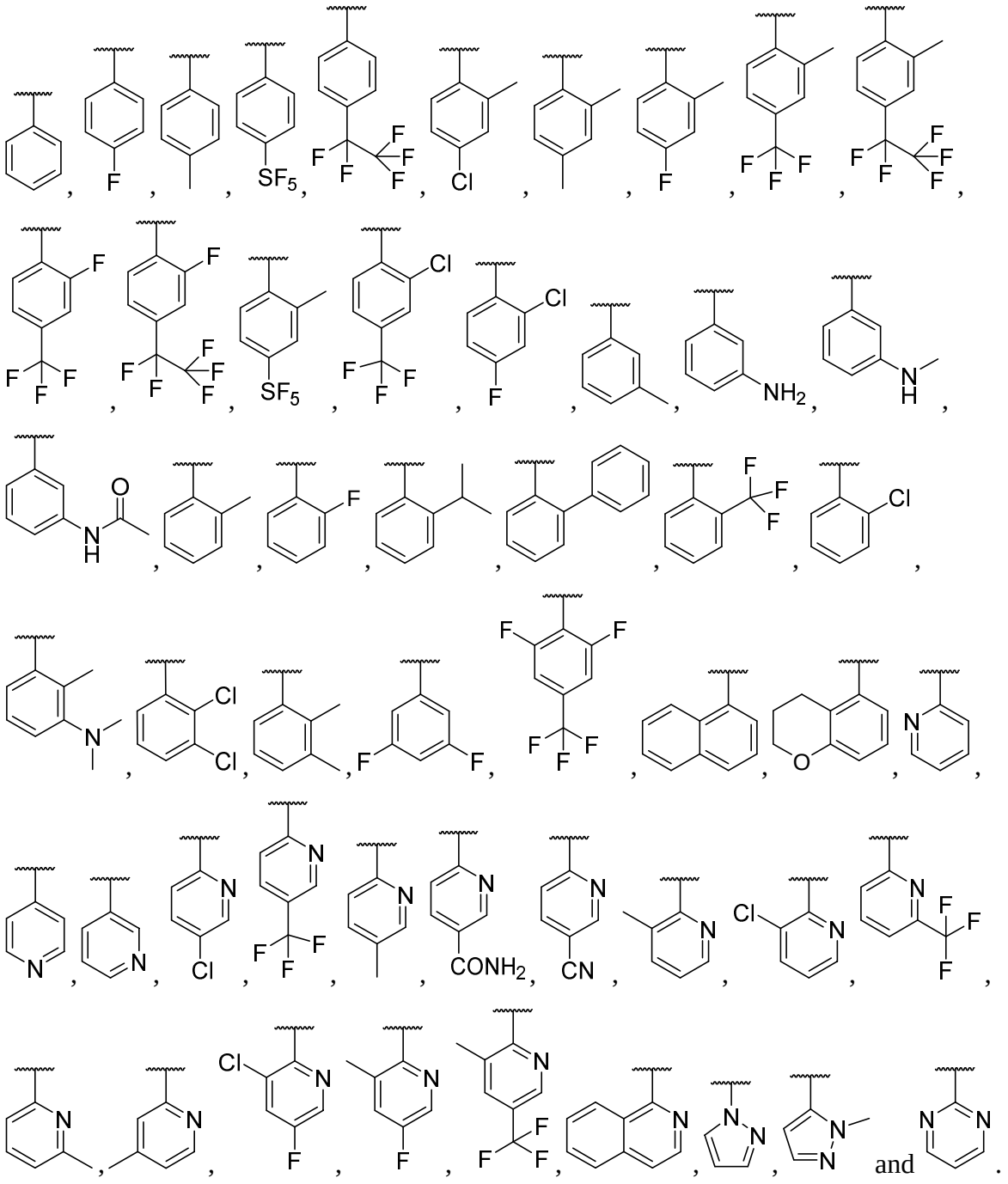
NH-oxetan-3-yl, –NH-(N-CH_3-2-oxo-pyrrolidin-3-yl), –$N(CH_3)_2$, –$NHC(=O)CH_3$, –$NHCH_2C(=O)N(CH_3)_2$, –$NHCH(CH_3)C(=O)N(CH_3)_2$, –$C(=O)NH_2$, –$C(=O)NHCH_3$, –$OC(=O)CH_3$, –SO_2CH_3, –$NHSO_2CH_3$,– SO_2NH_2 and –SO_2NHCH_3, wherein each cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyrrolidin-1-yl, piperidin-4-yl, piperazin-4-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thiazol-2-yl, thiophen-2-yl, –CH_2-cyclopropyl, –CH_2-morpholin-4-yl, –CH_2-1,2,4-triazol-1-yl, –CH_2-imidazol-1-yl and –CH_2-pyrazol-1-yl, can be independently substituted with 0, 1, 2 or 3 instances of –Me, –OH, –$C(=O)CH_3$, –$NHC(=O)CH_3$ or a combination thereof.

42. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof wherein each R^7 is independently selected from the group consisting of –D, =O, –F, –Cl, –Me, –^{i}Pr, –CHF_2,–CF_2CF_3, –CF_3, –CN, –SF_5, cyclopropyl, piperidin-4-yl, piperazin-4-yl, phenyl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, –OH, –OCH_3, –OCF_3, –$OCHF_2$, –NH_2, –$NHCH_3$, –$N(CH_3)_2$, –$NHC(O)CH_3$, –$CONH_2$, wherein each cyclopropyl, phenyl, piperazin-4-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl and pyrazol-5-yl, can be independently substituted with 0, 1, 2 or 3 instances of –Me, –OH, –$C(=O)CH_3$, –$NHC(=O)CH_3$ or a combination thereof.

43. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof wherein each R^7 is independently selected from the group consisting of –F, –Cl, –Me, –^{i}Pr, –CF_2CF_3, –CF_3, –CN, –SF_5, phenyl, –NH_2, –$NHCH_3$, –$N(CH_3)_2$, –$NHC(O)CH_3$ and –$CONH_2$.

44. The compound of any one of claims 31-36, or a pharmaceutically acceptable salt thereof wherein each R^7 is independently selected from the group consisting of –F, –Cl, –Me, –CF_2CF_3 and –CF_3.

45. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof wherein Ring B is selected from :



46. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –C_1–C_6 alkyl, –C_2–C_6 heteroalkyl, –C_2–C_6 haloalkyl, –C_3–C_{10} carbocyclyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, 3-10 membered heterocyclyl, heterocyclylalkyl, heteroarylalkyl, arylalkyl and cycloalkylalkyl, each substituted at any available position with 0, 1, 2 or 3 instances of R^8 wherein each R^8 is independently selected from the group consisting of halo, =O, –CN, –OH, –NH_2, –C_1-C_6 alkyl, –C_1-C_6 haloalkyl, –O(C_1-C_6 alkyl), –O(C_1-C_6 haloalkyl), –NH(C_1-C_6

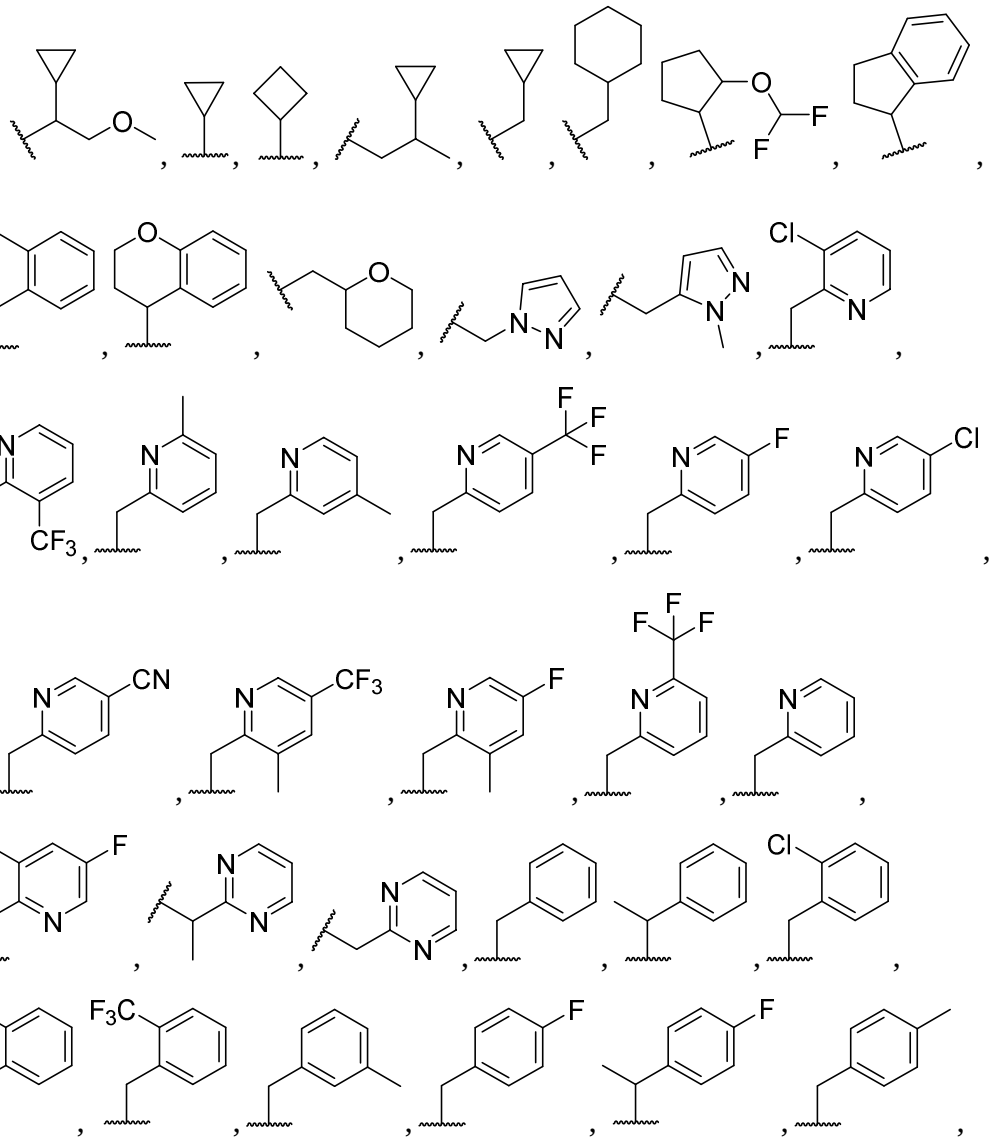
alkyl), –NH(C_1-C_6 haloalkyl), –N(C_1-C_6 alkyl)$_2$, –N(C_1-C_6 haloalkyl)$_2$, –C(O)NH_2, –NHC(O)(C_1-C_6 alkyl), C_3-C_9 cycloalkyl and C_1-C_6 heteroalkyl.

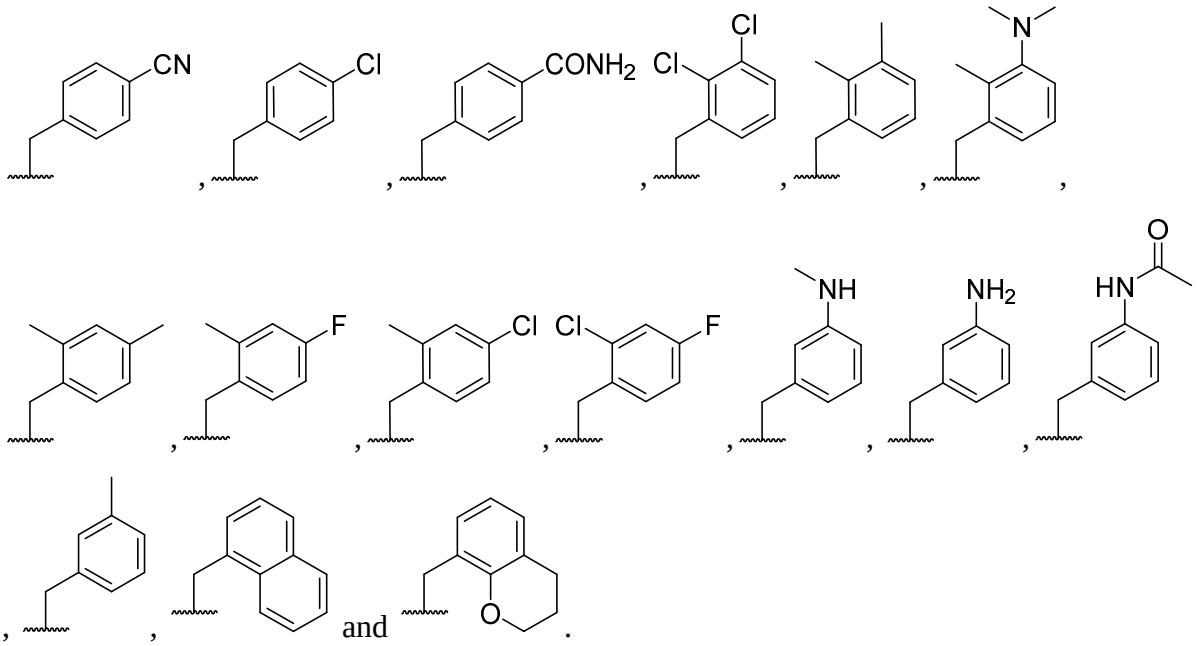
47. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu, –$CH(CH_3)CH(CH_3)_2$, –$CH_2CH(CH_3)_2$, –$CH_2CH(CH_3)CH_2CH_3$), –C_2–C_6 heteroalkyl (*e.g.*, –$CH_2CH_2OCH_3$), –C_2–C_6 haloalkyl (*e.g.*, –$CH_2CH_2CF_3$), –C_3–C_{10} carbocyclyl (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 2,3-dihydro-1H-indenyl, 1,2,3,4 tetrahydronaphthalenyl), 3-10 membered heterocyclyl (*e.g.*, chromanyl), heteroarylalkyl (*e.g.*, –CH_2-pyridinyl, –$CH(CH_3)$-pyridinyl, –CH_2-pyrimidinyl, –$CH(CH_3)$-pyrimidinyl, –CH_2-pyrazolyl), arylalkyl (*e.g.*, benzyl, –$CH(CH_3)$phenyl, –CH_2-naphthalenyl, –CH_2-chromanyl, –CH_2CH_2-phenyl), heterocyclylalkyl (*e.g.*, CH_2-tetrahydropyranyl) and cycloalkylalkyl (*e.g.*, –CH_2-cyclopropyl, –CH_2-cyclobutyl, –CH_2-cyclopentyl, –CH_2-cyclohexyl, –$CH(CH_3)$cyclopropyl, –CH_2CH_2-cyclopropyl), each substituted at any available position with 0, 1, 2 or 3 instances of R^8 wherein each R^8 is independently selected from the group consisting of halo (*e.g.*, –F, –Cl), =O, –CN, –OH, –NH_2, –C_1-C_6 alkyl (*e.g.*, –Me, –Et–, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu), –C_1-C_6 haloalkyl (*e.g.*, –CF_3), –O(C_1-C_6 alkyl) (*e.g.*, –OCH_3, –OCH_2CH_3, –$OCH(CH_3)_2$), –O(C_1-C_6 haloalkyl) (*e.g.*, –OCF_3, –$OCHF_2$, –OCH_2CF_3), C_3-C_9 cycloalkyl (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl) and C_1-C_6 heteroalkyl (*e.g.*, –CH_2OCH_3, –$CH_2CH_2OCH_3$, –CH_2NHCH_3, –$CH_2CH_2NHCH_3$, –$CH_2N(CH_3)_2$, –$CH_2CH_2N(CH_3)_2$).

48. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –C_1–C_6 alkyl (*e.g.*, –Me, –Et, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu, –$CH(CH_3)CH(CH_3)_2$, –$CH_2CH(CH_3)_2$, –$CH_2CH(CH_3)CH_2CH_3$), –C_2–C_6 heteroalkyl (*e.g.*, –$CH_2CH_2OCH_3$) and arylalkyl (*e.g.*, benzyl, –$CH(CH_3)$phenyl, –CH_2-naphthalenyl, –CH_2-chromanyl), each substituted at any available position with 0, 1 or 2 instances of R^8 wherein each R^8 is independently selected from the group consisting of halo (*e.g.*, –F, –Cl) and –C_1-C_6 alkyl (*e.g.*, –Me, –Et–, –Pr, –^{i}Pr, –*sec*-Bu, –^{t}Bu).

49. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –Me, –Et, –^{i}Pr, –$CH(CH_3)CH(CH_3)_2$, –$CH_2CH(CH_3)_2$, –$CH_2CH(CH_3)CH_2CH_3$, –$CH_2CH_2OCH_3$, –$CH_2CH_2CF_3$, cyclopropyl, cyclobutyl, cyclopentyl, 2,3-dihydro-1H-indenyl, 1,2,3,4

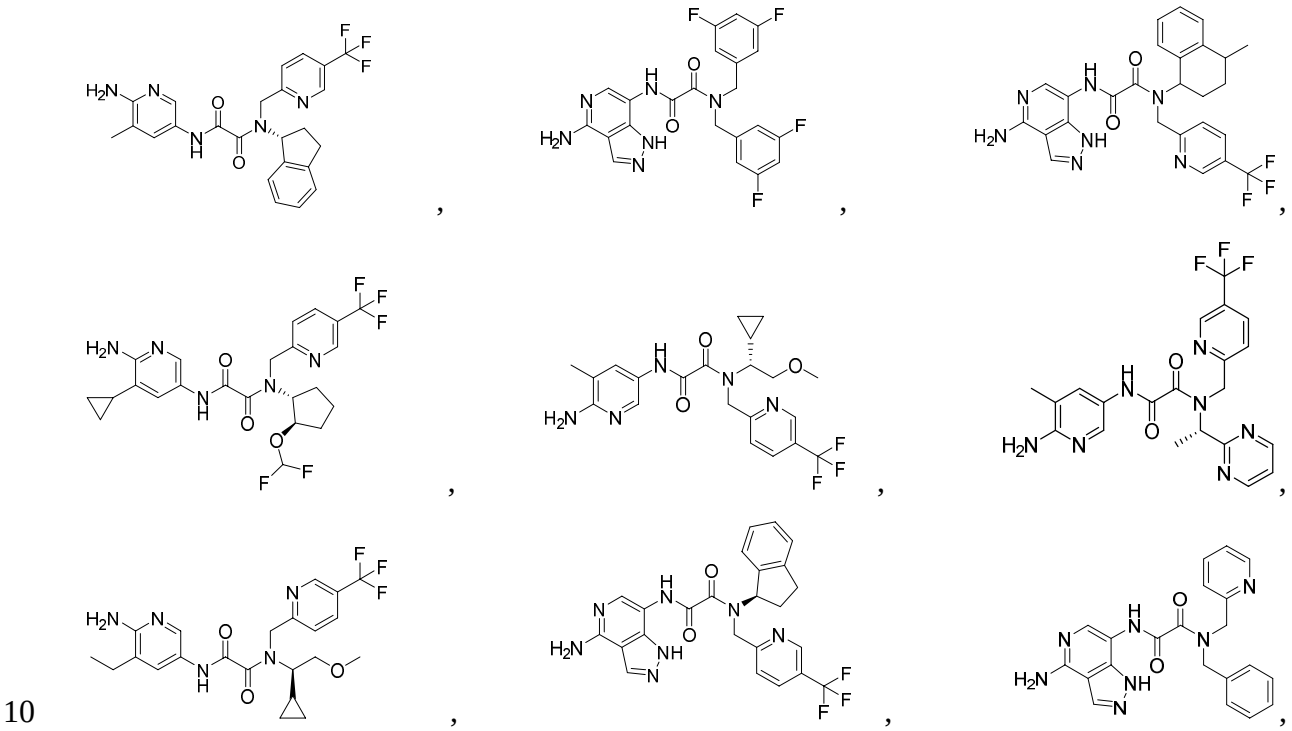
tetrahydronaphthalenyl, chromanyl, –CH_2-cyclohexyl, –CH_2CH_2-cyclopropyl, –CH_2-tetrahydropyranyl, –CH_2-pyridinyl, –CH_2-pyrimidinyl, –CH_2-pyrazolyl, –benzyl CH_2-chromanyl, –CH2-naphthyl, and –CH_2-cyclopropyl, each substituted at any available position with 0, 1 or 2 instances of R^8 wherein each R^8 is independently selected from the group consisting of –F, –Cl, –Me, –NH_2, –$NHCH_3$, –$N(CH_3)_2$, –$NHC(O)CH_3$, –$C(O)NH_2$, –CF_3, –$OCHF_2$, –cyclopropyl, and –CH_2OCH_3.

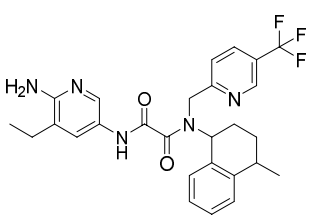
50. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –Me, –Et, –^{i}Pr, –$CH(CH_3)CH(CH_3)_2$, –$CH_2CH(CH_3)_2$, –$CH_2CH(CH_3)CH_2CH_3$, –$CH_2CH_2CF_3$, –$CH_2CH_2OCH_3$, 



51. The compound of any one of claims 1 to 45, or a pharmaceutically acceptable salt thereof wherein each R^1 is independently selected from the group consisting of –Me and –Et.

52. The compound of any one of claims 1 to 51 wherein the compound is selected from the group consisting of:

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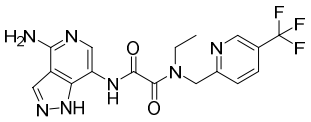
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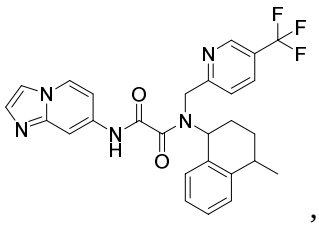
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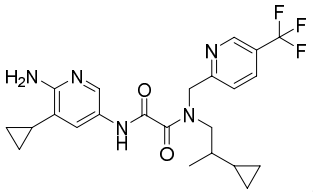
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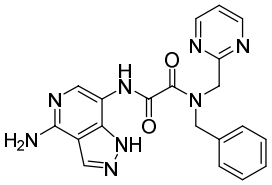
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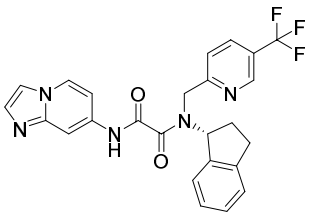
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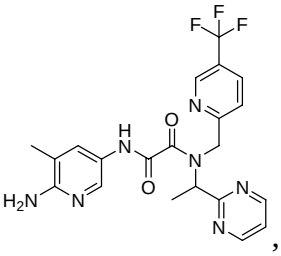
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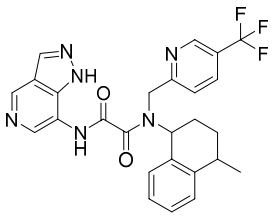
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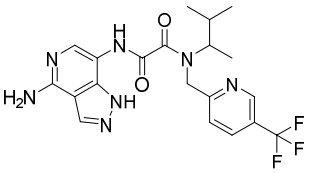
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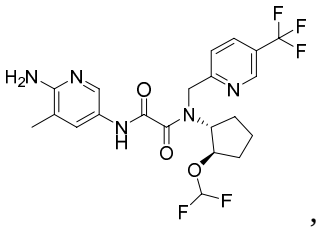
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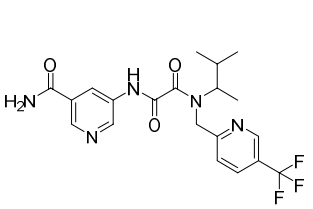
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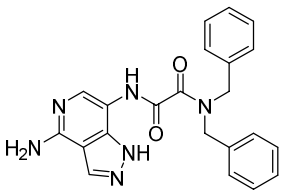
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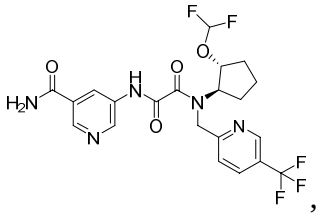
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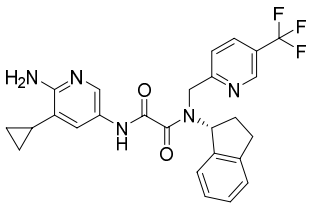
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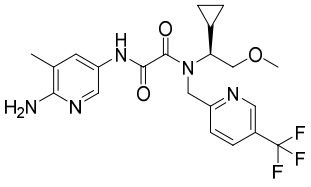
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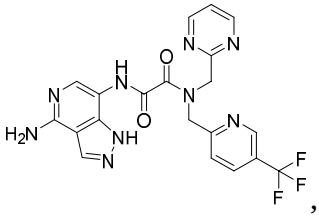
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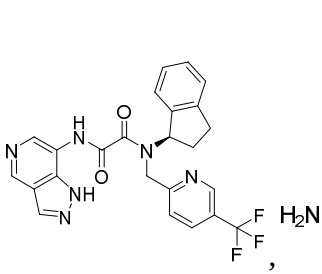
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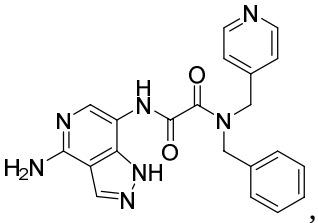
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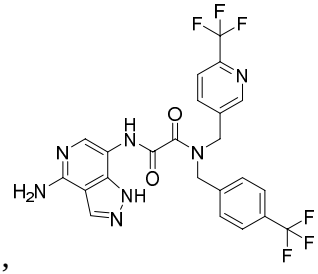
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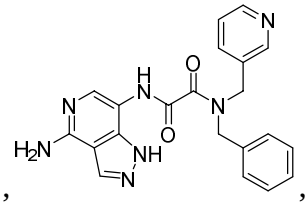
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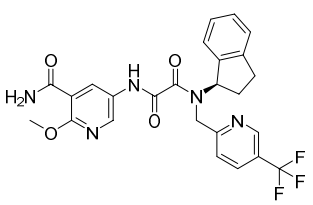
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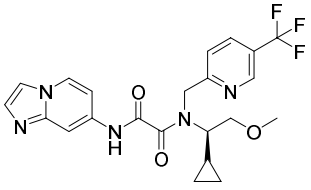
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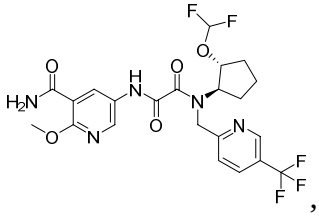
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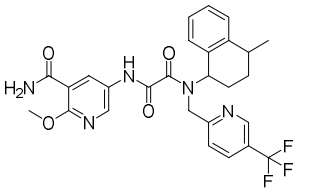
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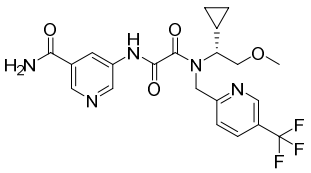
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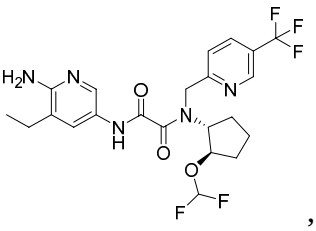
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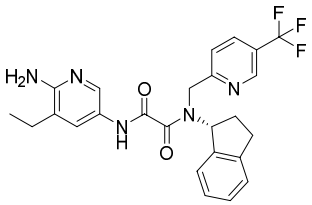
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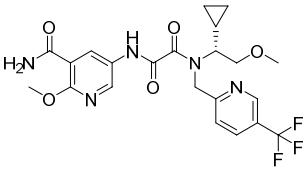
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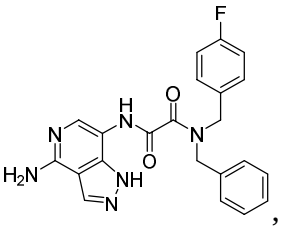
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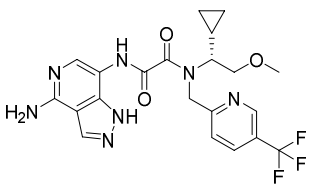
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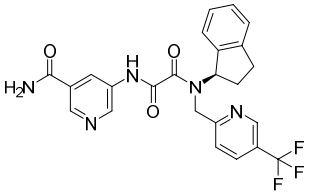
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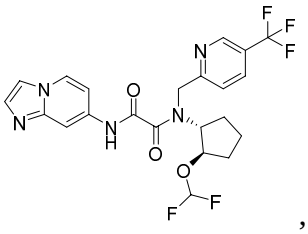
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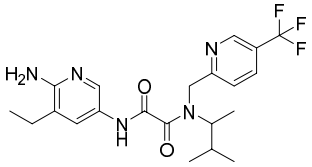
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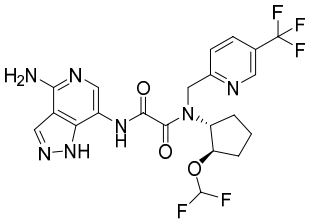
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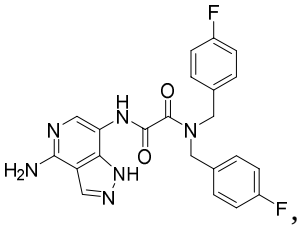
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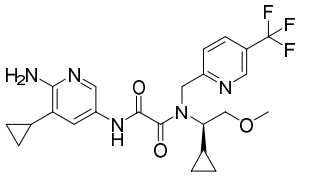
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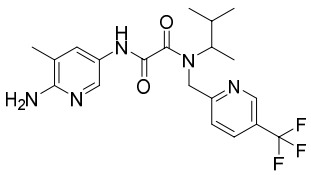
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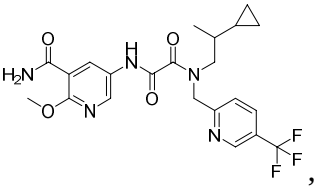
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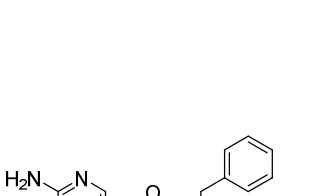
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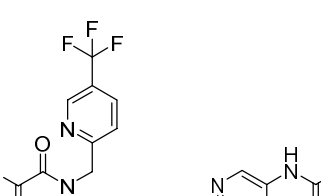
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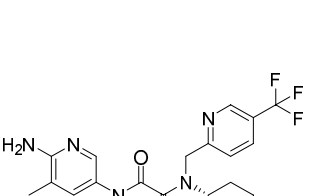
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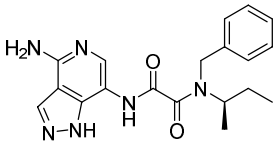
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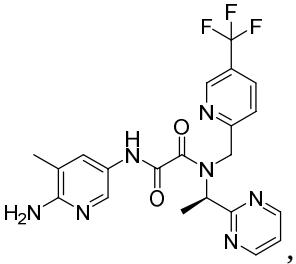
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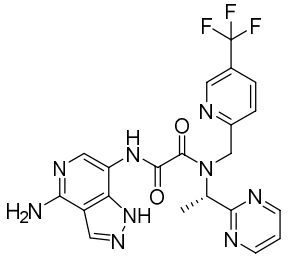
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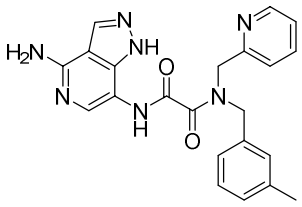
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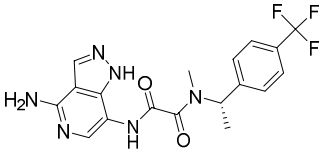
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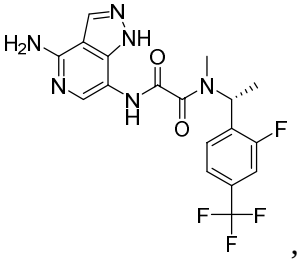
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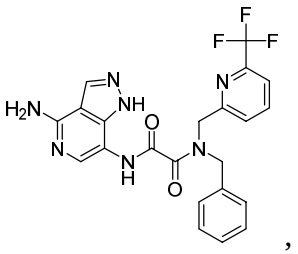
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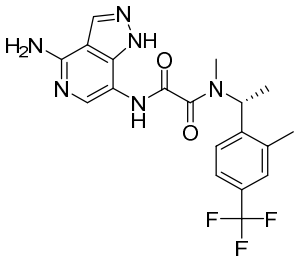
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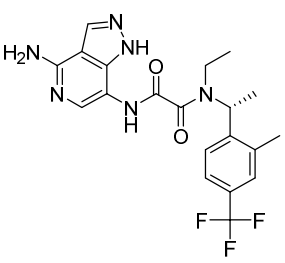
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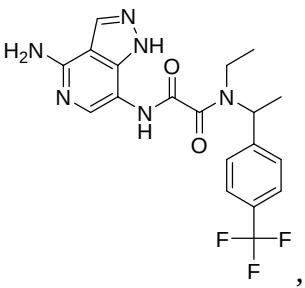
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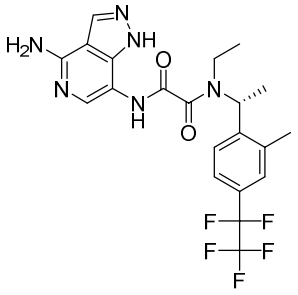
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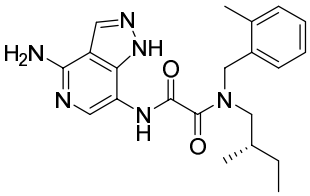
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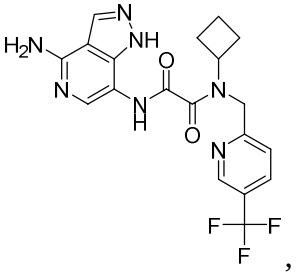
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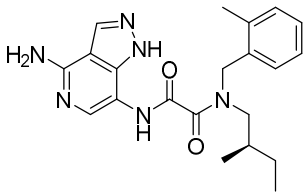
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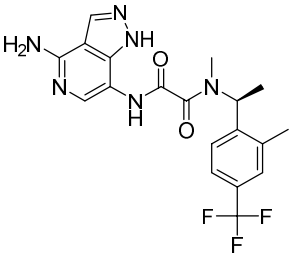
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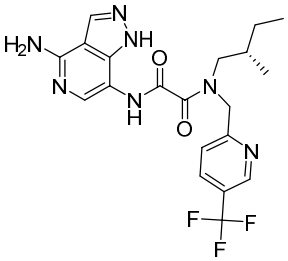
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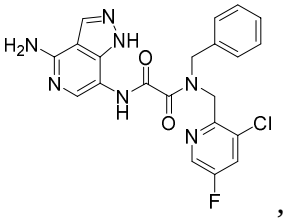
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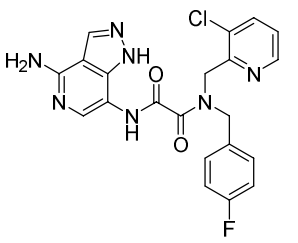
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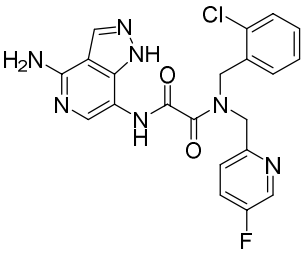
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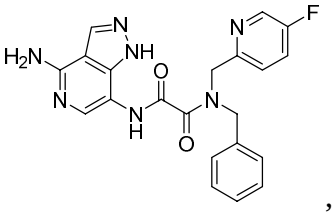
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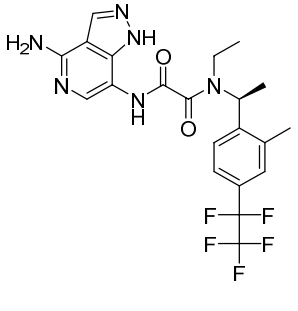
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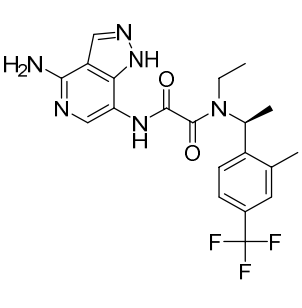
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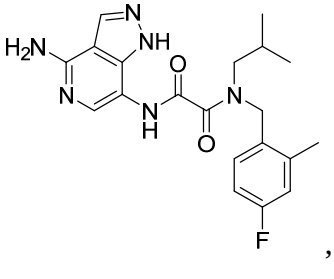
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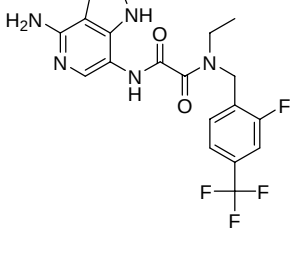
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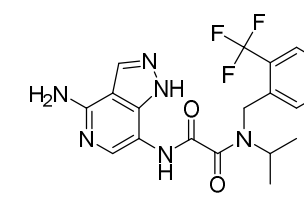
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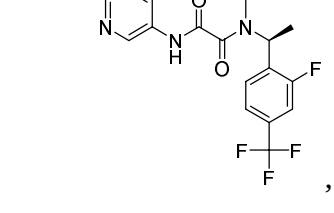
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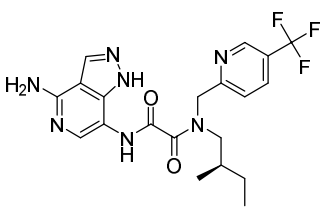
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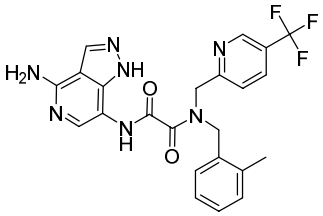
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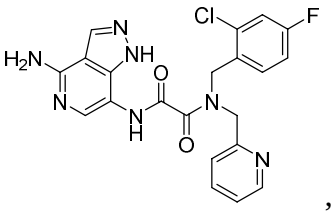
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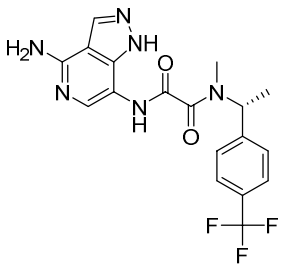
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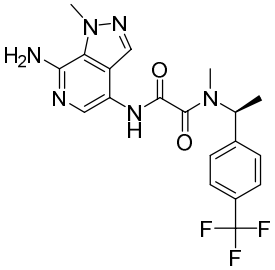
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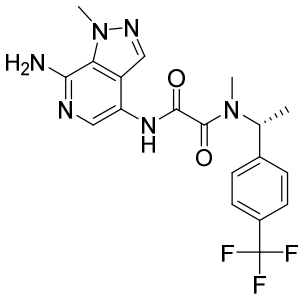
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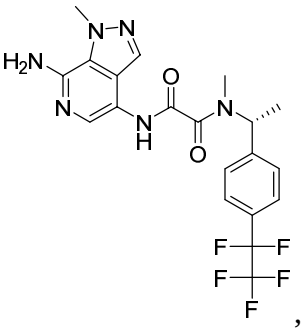
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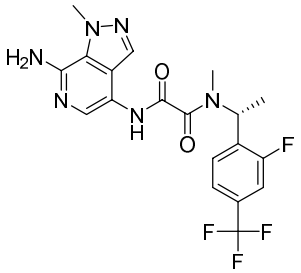
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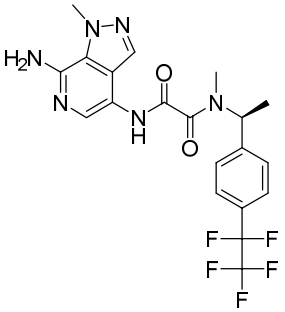
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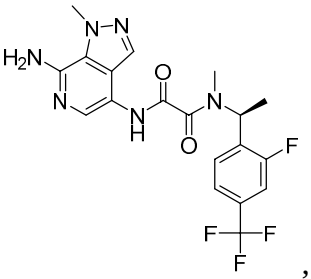
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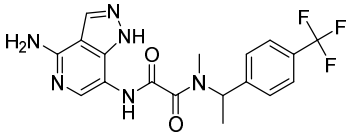
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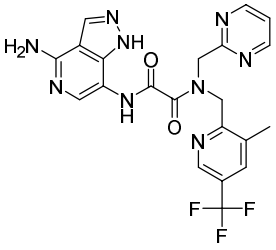
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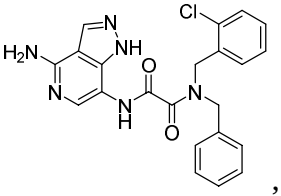
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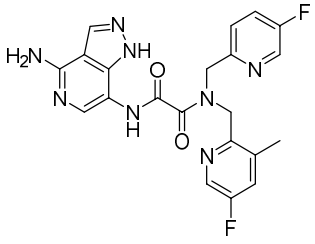
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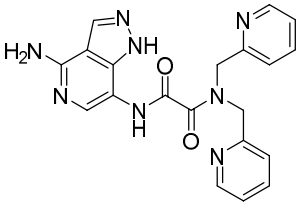
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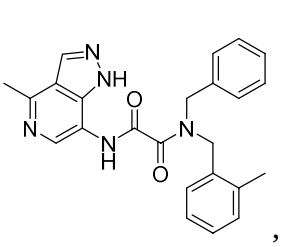
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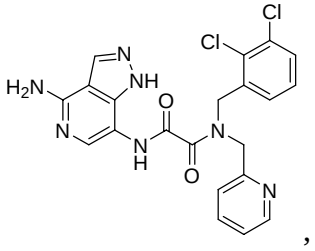
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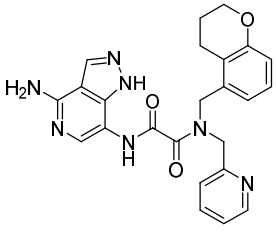
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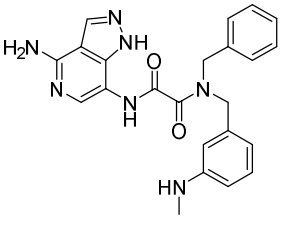
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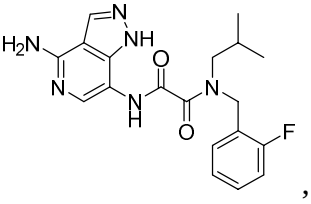
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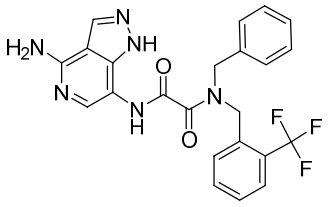
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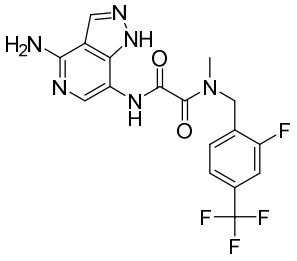
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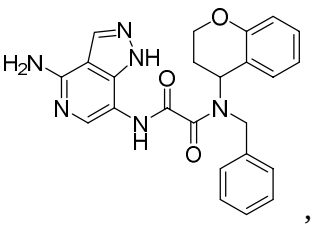
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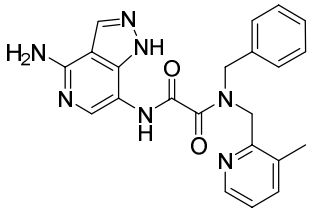
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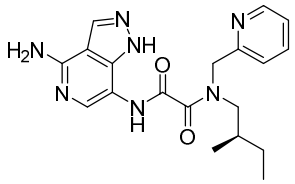
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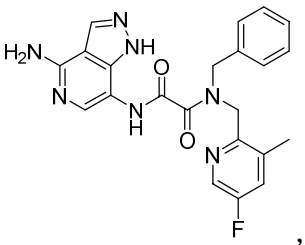
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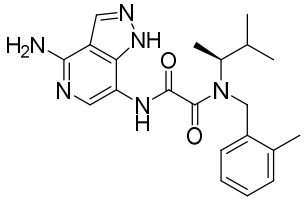
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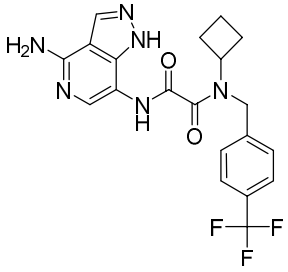
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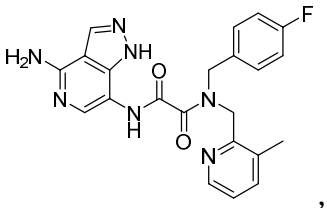
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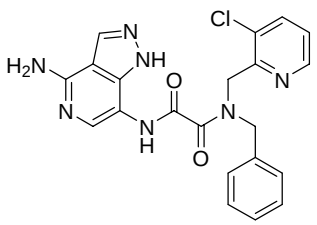
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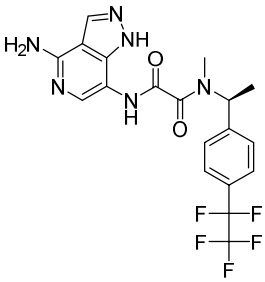
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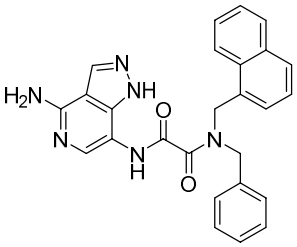
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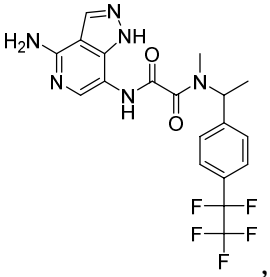
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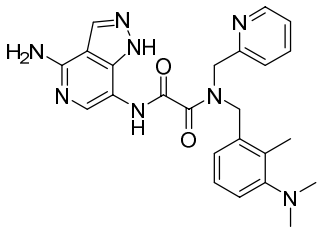
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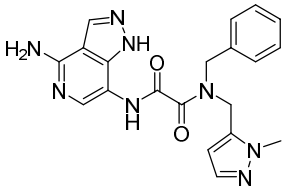
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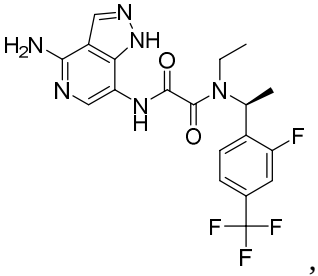
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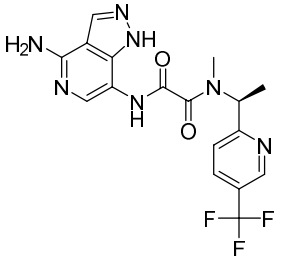
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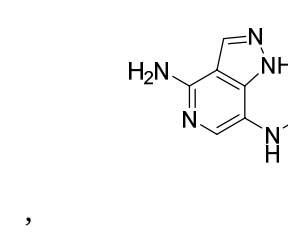
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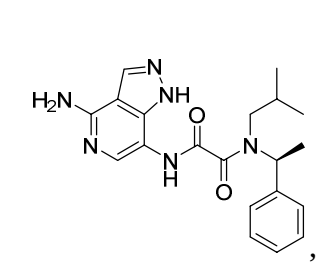
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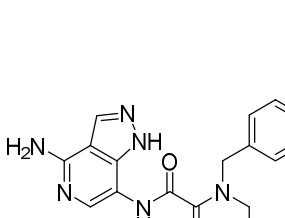
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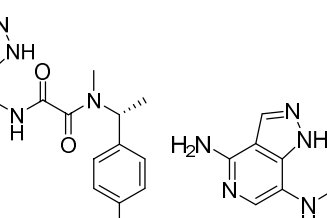
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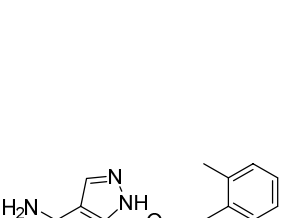
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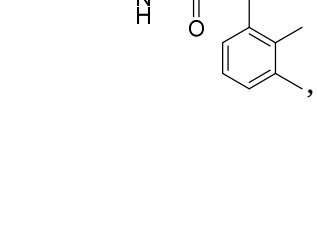
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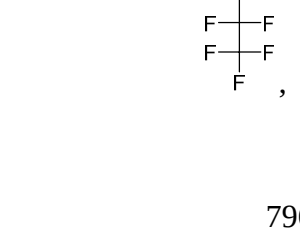
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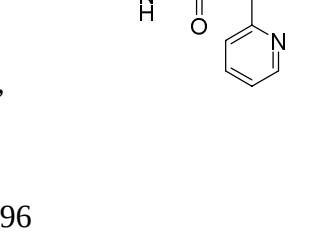
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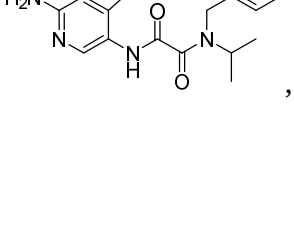
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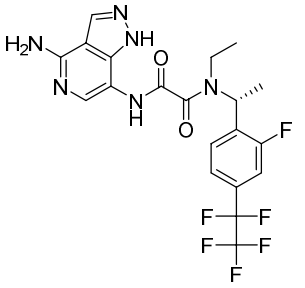
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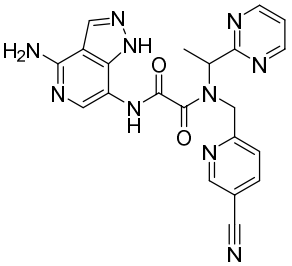
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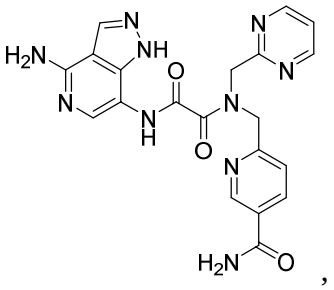
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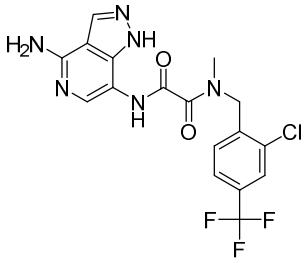
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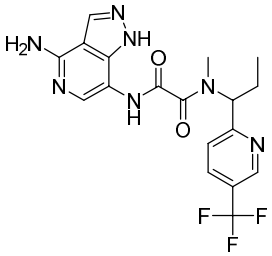
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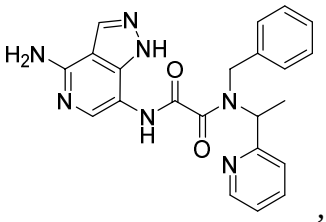
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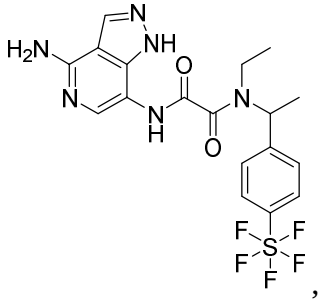
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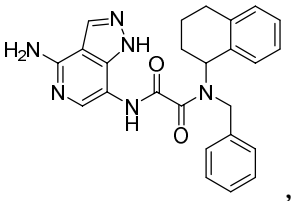
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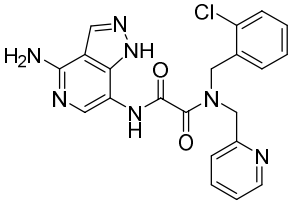
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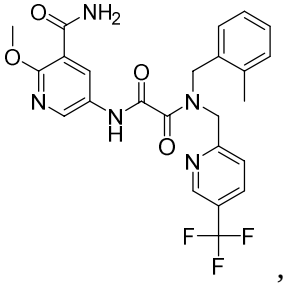
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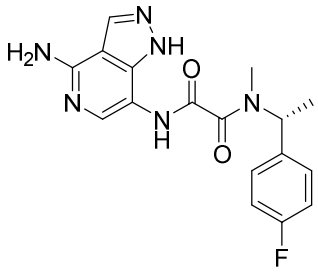
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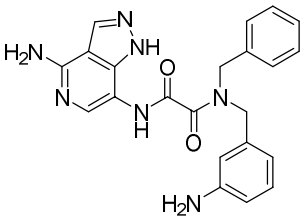
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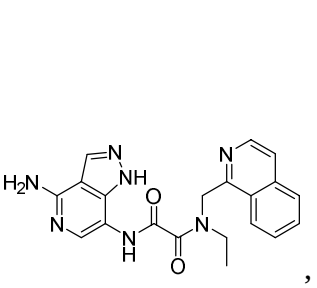
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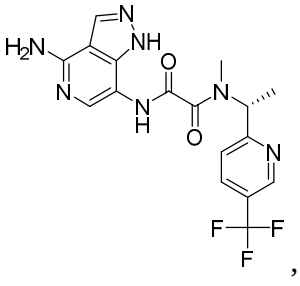
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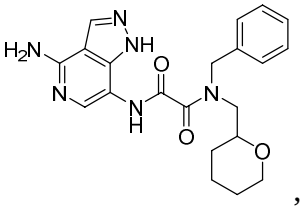
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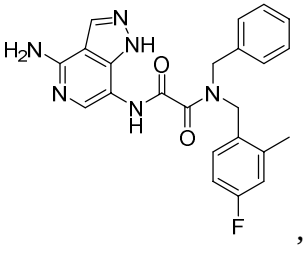
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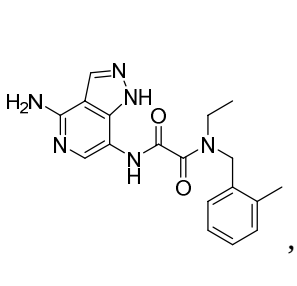
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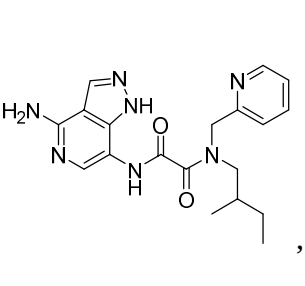
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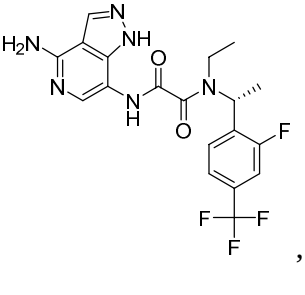
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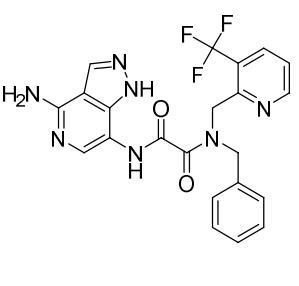
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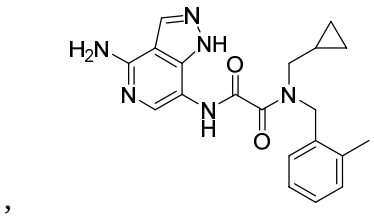
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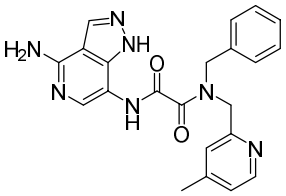
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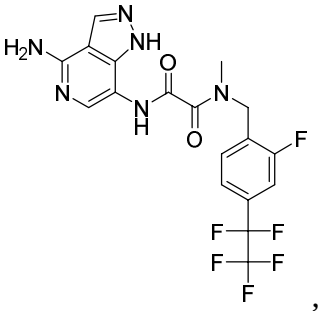
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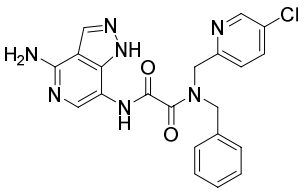
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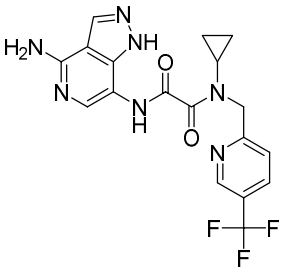
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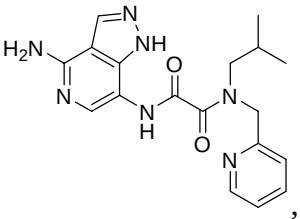
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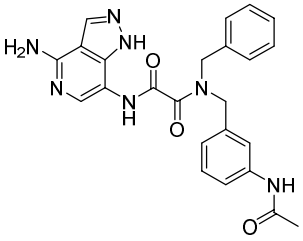
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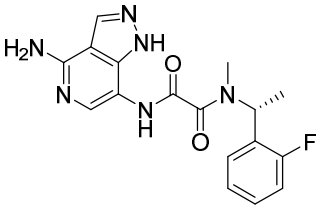
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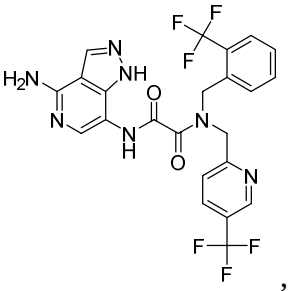
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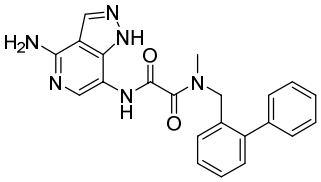
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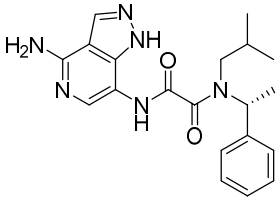
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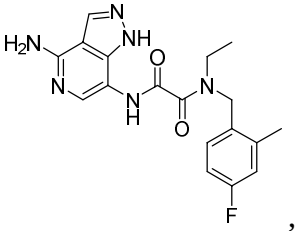
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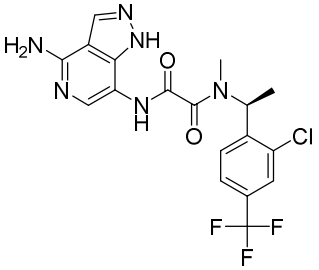
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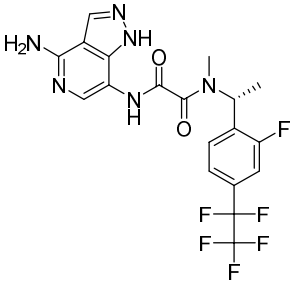
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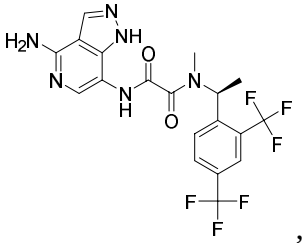
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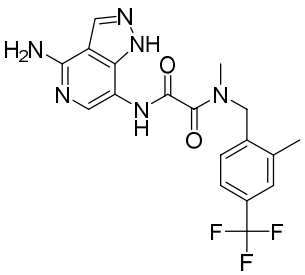
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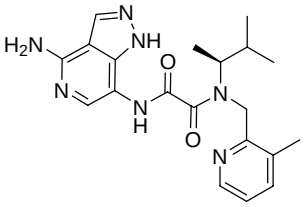
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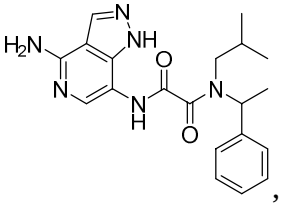
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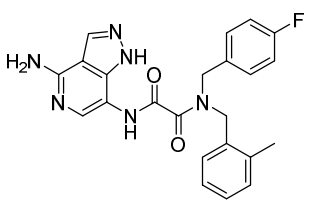
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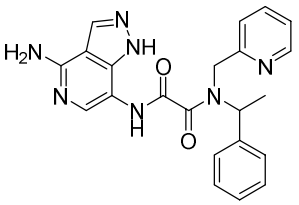
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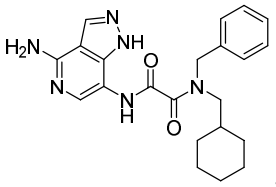
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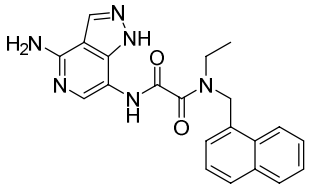
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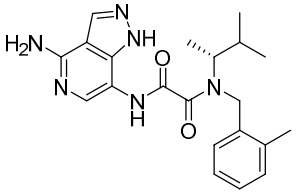
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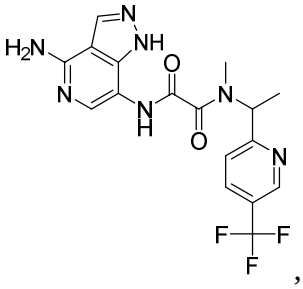
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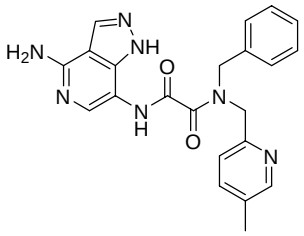
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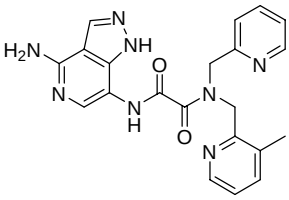
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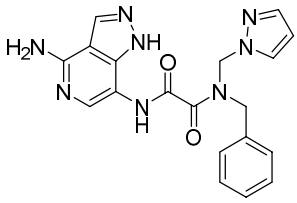
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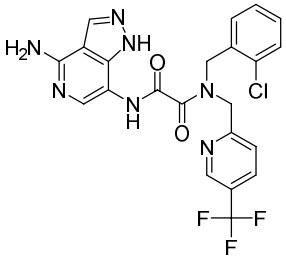
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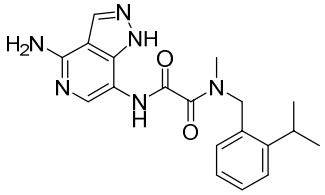
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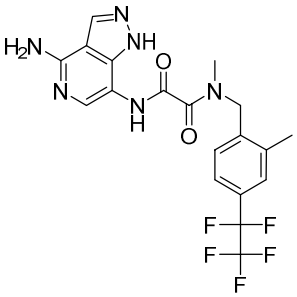
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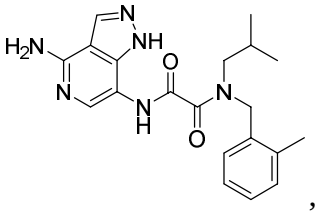
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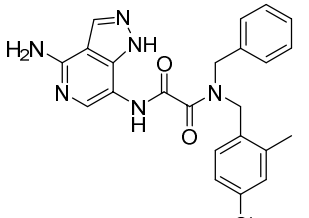
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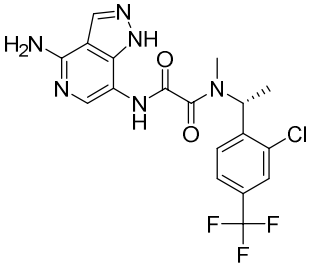
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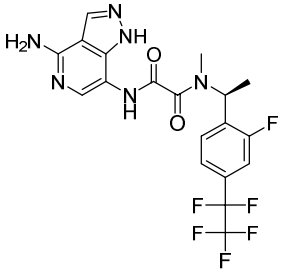
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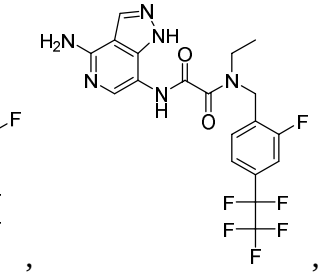
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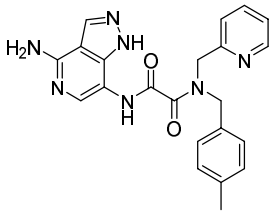
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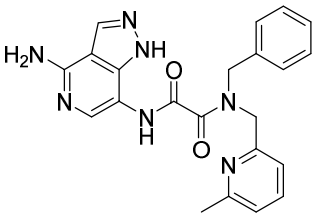
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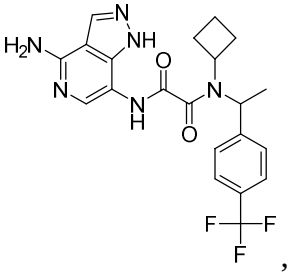
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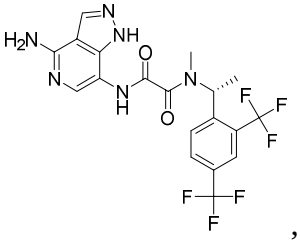
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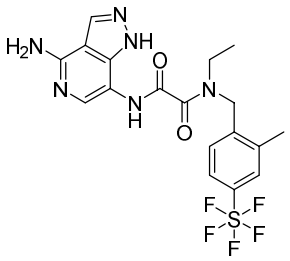
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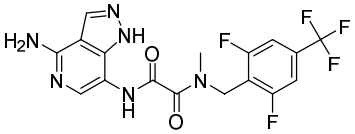
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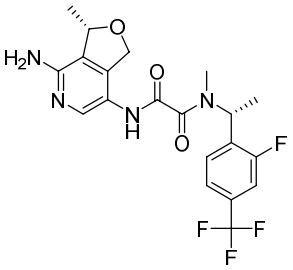
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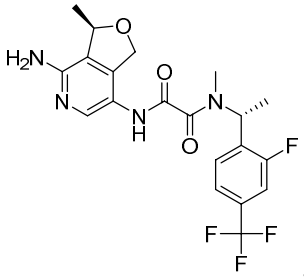
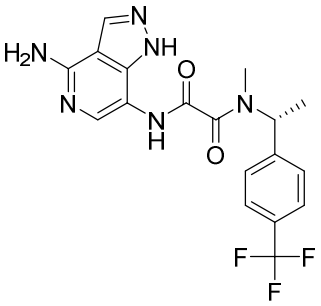
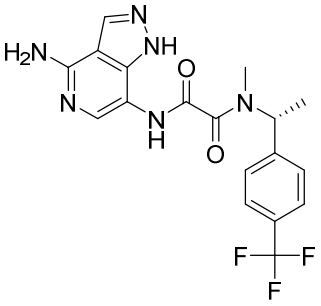
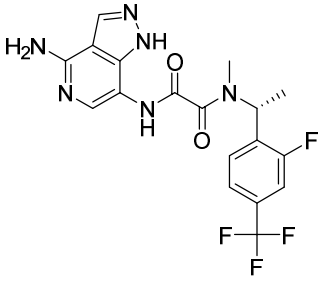

, or a pharmaceutical acceptable salt thereof.



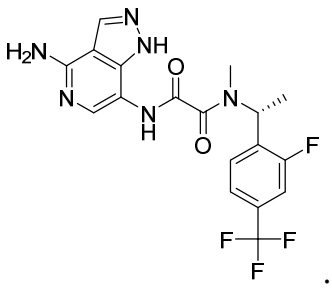
53. A compound of Formula , or a pharmaceutically acceptable salt thereof.



54. A compound of Formula .



55. A compound of Formula , or a pharmaceutically acceptable salt thereof.

56. A compound of Formula  .

57. A composition comprising a compound of any one of claims 1 to 56, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

58. The composition of claim 57, further comprising a second therapeutic agent.

59. Use of a compound of any one of claims 1 to 56, or a pharmaceutically acceptable salt thereof, or of a composition of claim 57, in the manufacture of a medicament for treating an MTAP-deficient and/or an MTA-accumulating disease in a subject in need thereof.

60. The use of claim 59 wherein the compound, or a pharmaceutically acceptable salt thereof, or composition is configured to be administered in combination with a second therapeutic agent.

61. Use of a composition of claim 58, in the manufacture of a medicament for treating an MTAP-deficient and/or an MTA-accumulating disease in a subject in need thereof.

62. The use of any one of claims 59 to 61 wherein the disease is a proliferating disease.

63. The use of claim 62 wherein the disease is an MTAP-deficient and/or MTA-accumulating cancer.

64. The use of claim 63 wherein the cancer is glioma, glioblastoma, malignant peripheral nerve sheath tumors (MPNST), esophageal cancer (*e.g.*, esophageal squamous cell carcinoma or esophageal adenocarcinoma), bladder cancer (*e.g.*, bladder urothelial carcinoma), pancreatic cancer (*e.g.*, pancreatic adenocarcinoma), mesothelioma, melanoma, non-small cell lung cancer (NSCLC; *e.g.*, lung squamous or lung adenocarcinoma), astrocytoma, undifferentiated pleiomorphic sarcoma, diffuse large B-cell lymphoma (DLBCL), leukemia, head and neck cancer, stomach adenocarcinoma, myxofibrosarcoma, cholangiosarcoma, cancer of the brain, stomach, kidney, breast, endometrium, urinary tract, liver, soft tissue, pleura and large intestine or sarcoma.