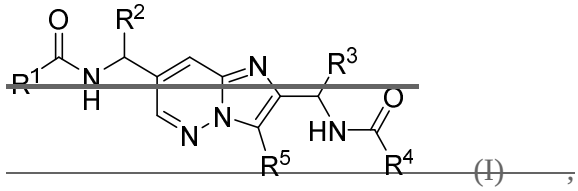
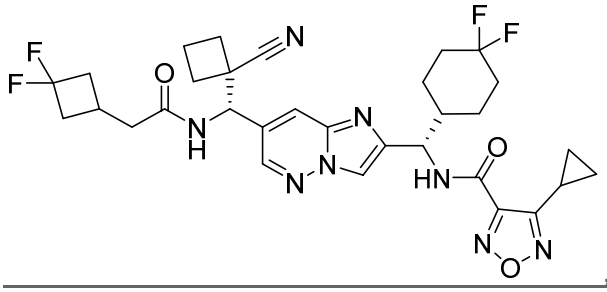
We Claim

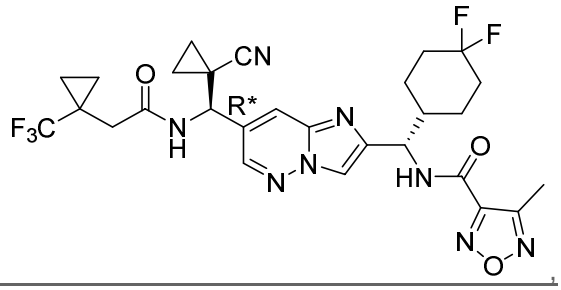
1. A compound ~~of Formula I~~selected from the group consisting of:



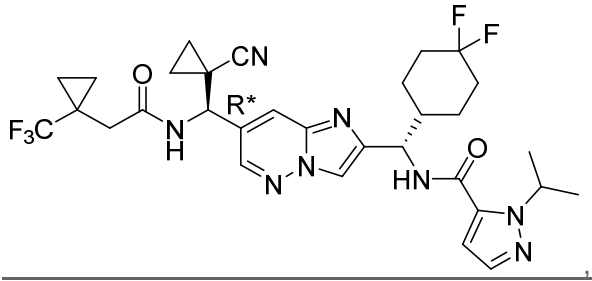
~~(I)~~ ,



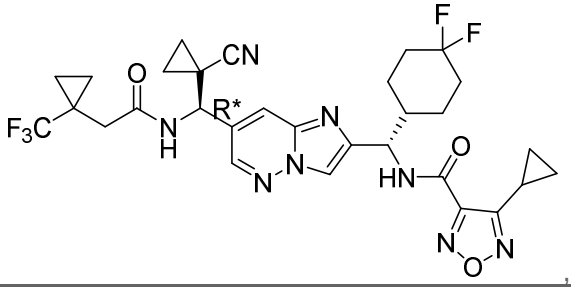
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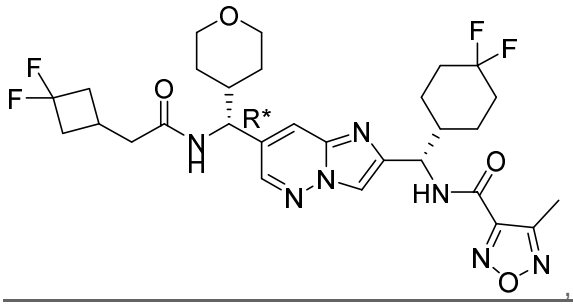
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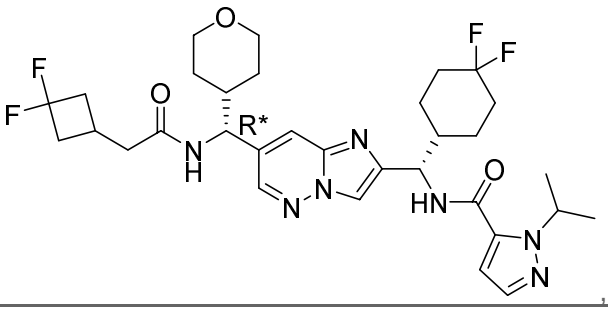
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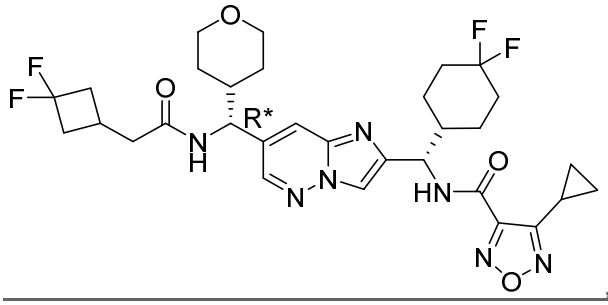
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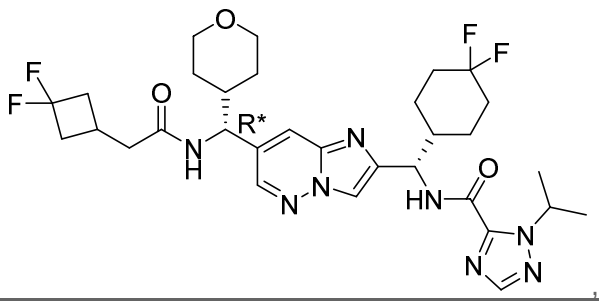
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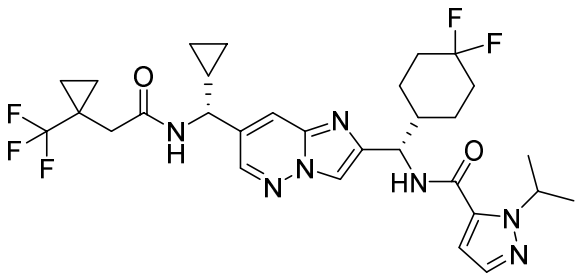
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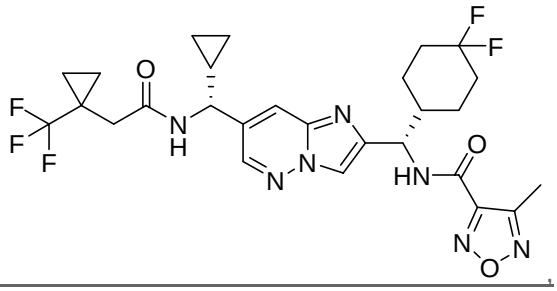


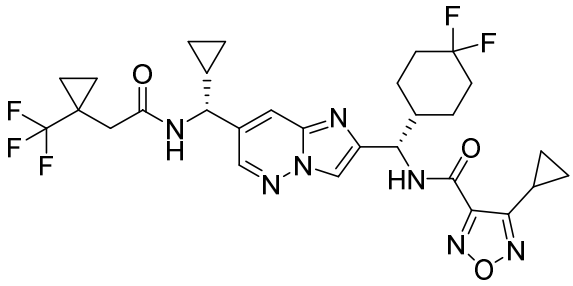
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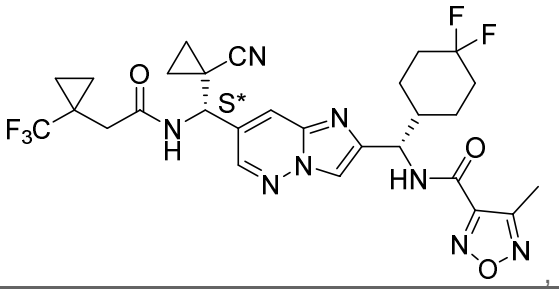


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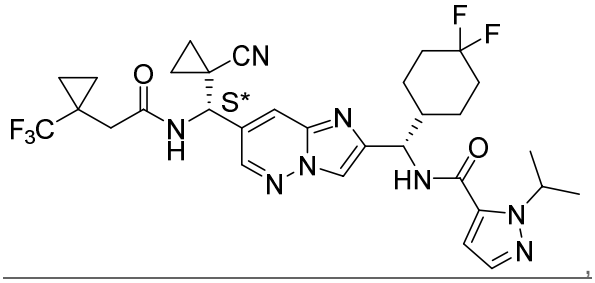


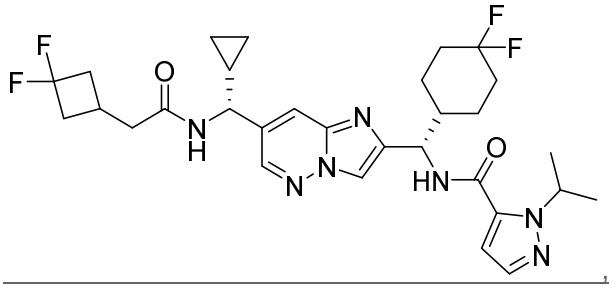


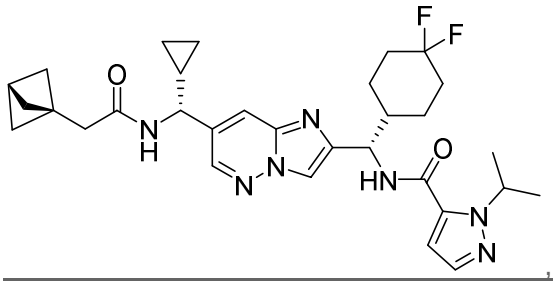


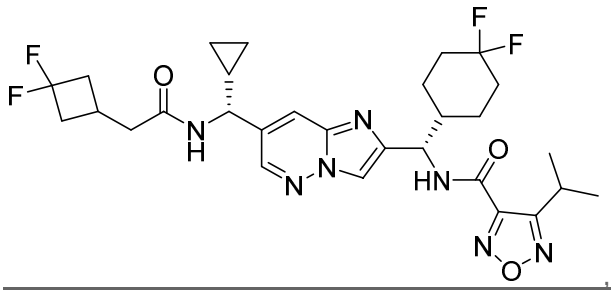


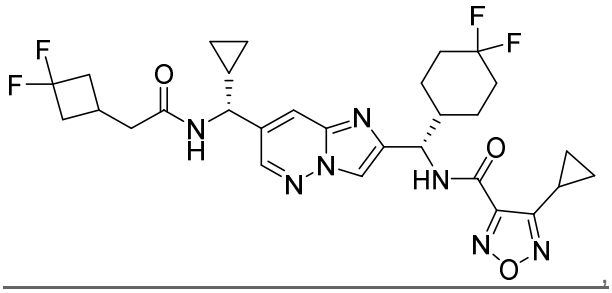
and

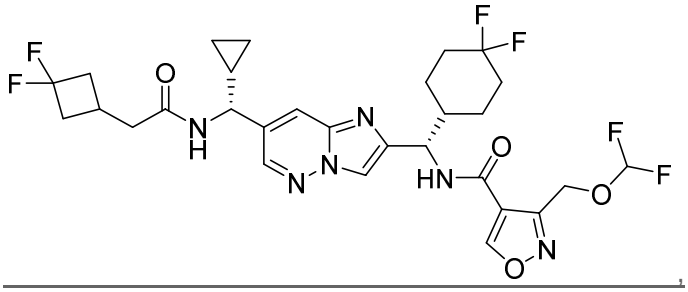


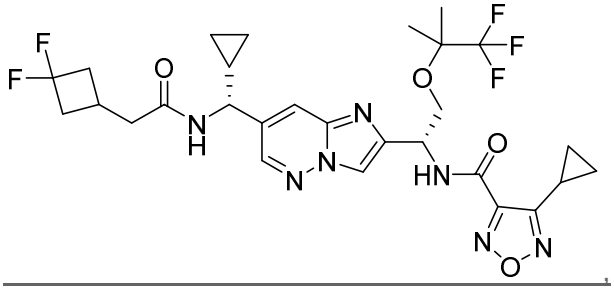


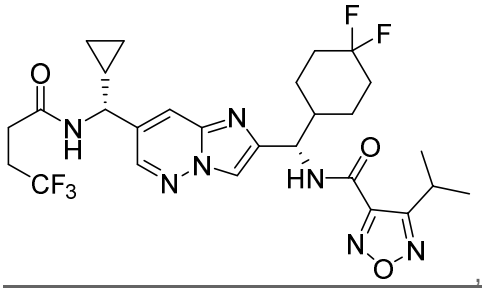


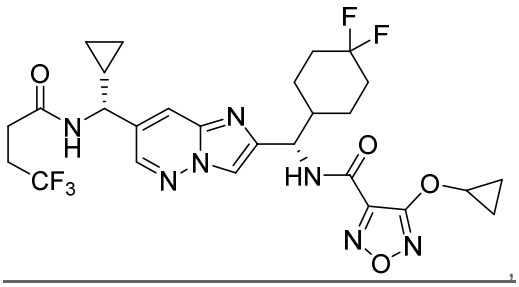


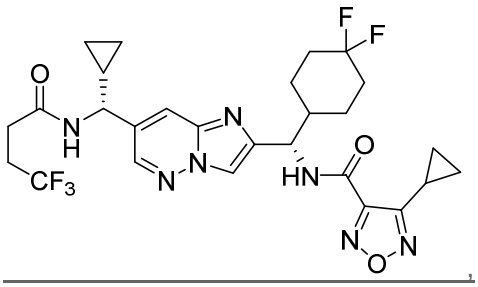


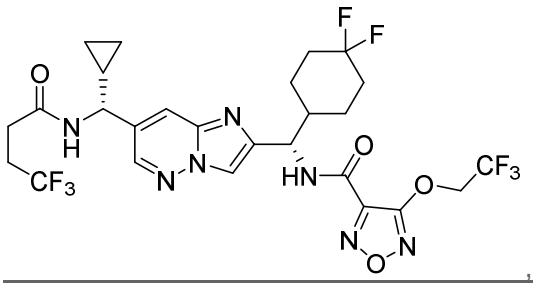


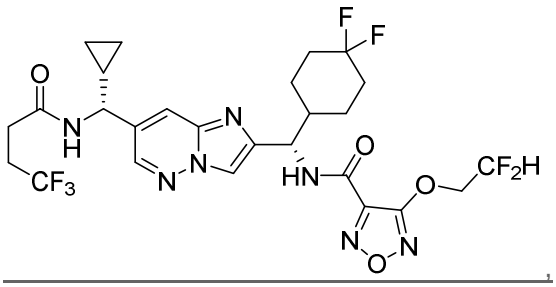


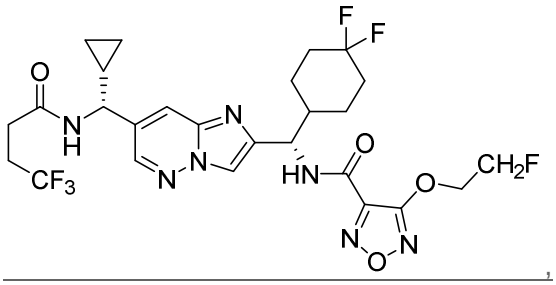


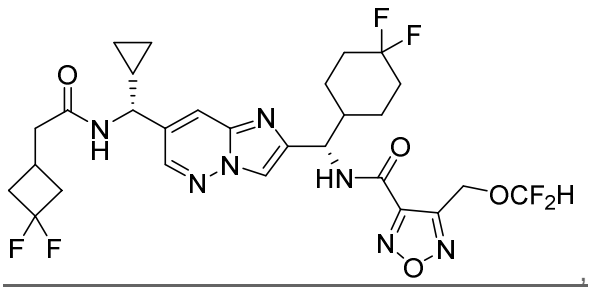




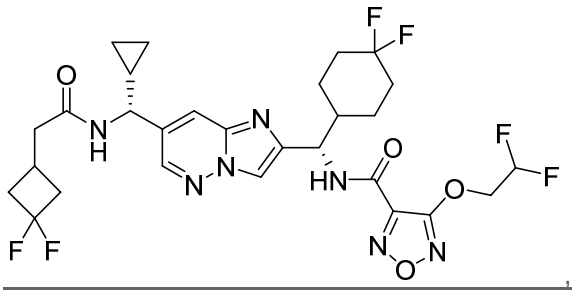




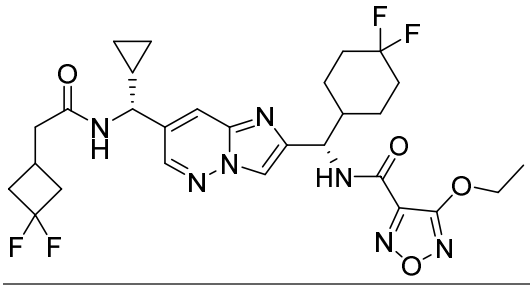




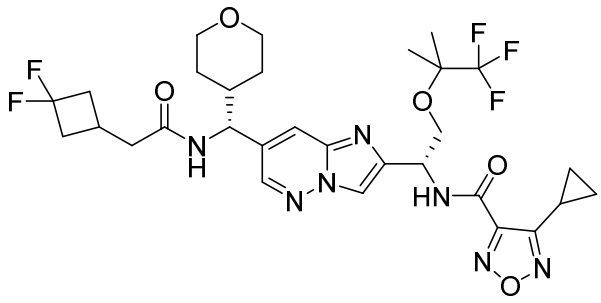
,



,



, and



,

or a pharmaceutically acceptable salt thereof~~, wherein: .~~

~~R^1 is $C_{(1-6)}$alkyl, $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, or a 5- to 6-membered heterocyclyl having 1 to 2 nitrogen atoms;~~

~~wherein the $C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;~~

~~wherein the $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to six R^{1b} groups; and~~

wherein the 5 to 6-membered heterocyclyl is unsubstituted or substituted with one to three R^{1c} groups;

R^2 is H, $-C_{(3-5)}$cycloalkyl, or $-C_{(1-4)}$alkyl; wherein the $-C_{(1-4)}$alkyl is unsubstituted or substituted with one to six R^{2a} groups;

R^{1a}, R^{1b} and R^{2a} are each independently fluorine, $-C_{(3-5)}$cycloalkyl, $-CN$, $-OH$, $-OC_{(1-3)}$alkyl or $-OC_{(3-4)}$cycloalkyl, wherein the $-OC_{(1-3)}$alkyl and $-OC_{(3-4)}$cycloalkyl groups are unsubstituted or substituted with one to three fluorine atoms;

each R^{1c} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, or $-C_{(1-4)}$alkyl that is unsubstituted or substituted with one to six fluorine atoms;

R^3 is $-C_{(0-1)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(3-6)}$alkyl or $-C_{(1-2)}$alkyl-O-$C_{(1-3)}$alkyl, wherein the $-C_{(0-1)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(3-6)}$alkyl and $-C_{(1-2)}$alkyl-O-$C_{(1-3)}$alkyl are unsubstituted or substituted with one to five R^{3a} groups each independently selected from fluorine, $-CH_3$, $-CHF_2$, $-CF_3$, OH and $=O$;

R^4 is $-C_{(3-6)}$cycloalkyl, phenyl, or a 5 to 6-membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S;

wherein the $C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to three R^{4a} groups each independently selected from halogen, $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl wherein the $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms;

alternatively, two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a $C_{(3-6)}$cycloalkyl;

wherein the phenyl is unsubstituted or substituted with one to three R^{4b} groups each independently selected from halogen, $-CN$, $-C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(1-3)}$alkyl, $-C_{(1-4)}$alkyl and a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-OC_{(1-3)}$alkyl, $-C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;

wherein the 5 to 6-membered heteroaryl is unsubstituted or substituted with one or two R^{4c} groups;

each R^{4c} is independently halogen, -CN, -OH, $-N(R^{4c1})(R^{4c2})$, $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl, or a 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;

alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;

each R^{4d} is independently fluorine, -CN, -OH, oxo, $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl, $-OC_{(3-4)}$cycloalkyl, $-C_{(0-2)}$alkyl-$N(R^{4d1})(R^{4d2})$, $-C_{(0-2)}$alkyl-$N(C_{(1-4)}$alkyl$)C(O)(C_{(1-4)}$alkyl) or a 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl, $-OC_{(3-4)}$cycloalkyl and heterocyclyl groups are unsubstituted or substituted with one to three fluorine atoms;

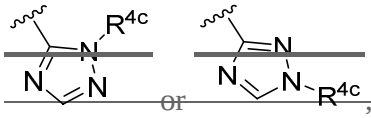
R^{4c1}, R^{4c2}, R^{4d1} and R^{4d2} are each independently H or $-C_{(1-3)}$alkyl, wherein the $-C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;

alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3 to 6 membered heterocyclyl having 1 to 3 heteroatoms selected from N, O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms; and

R^5 is hydrogen or halogen;

wherein

when R^4 is 1,2,4-triazolyl, then R^4 is

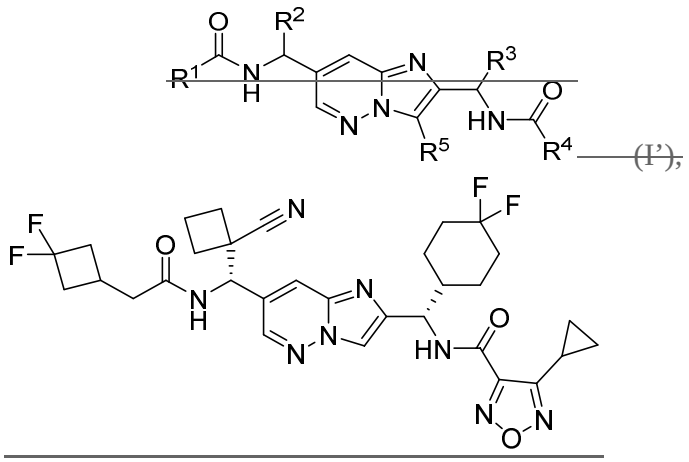


, and

when R^4 is a substituted 6-membered heteroaryl, the substituted heteroaryl is unsubstituted at the para-position.

A

2. The compound of Formula I: claim 1, having the following structure:



(I'),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is $C_{(1-6)}$alkyl, $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $C_{(0-2)}$alkyl-cyclopropyl-$C_{(1-3)}$perfluoroalkyl, or a 5- to 6-membered heterocyclyl having 1 to 2 nitrogen atoms;

wherein the $C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

wherein the $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to six R^{1b} groups; and

wherein the 5- to 6-membered heterocyclyl is unsubstituted or substituted with one to three R^{1c} groups;

R^2 is H, $C_{(3-5)}$cycloalkyl, $C_{(1-4)}$alkyl, or a 6-membered heterocycle having 1 to 2 oxygen atoms; wherein the $C_{(1-4)}$alkyl is unsubstituted or substituted with one to six R^{2a} groups; and wherein the $C_{(3-5)}$cycloalkyl is unsubstituted or substituted with -CN;

R^{1a}, R^{1b} and R^{2a} are each independently fluorine, $C_{(3-5)}$cycloalkyl, -CN, -OH, $OC_{(1-3)}$alkyl or $OC_{(3-4)}$cycloalkyl, wherein the $OC_{(1-3)}$alkyl and $OC_{(3-4)}$cycloalkyl groups are unsubstituted or substituted with one to three fluorine atoms;

each R^{1c} is independently OCH_3, OCF_3, $OCHF_2$, or $C_{(1-4)}$alkyl that is unsubstituted or substituted with one to six fluorine atoms;

R^3 is $C_{(0-1)}$alkyl$C_{(3-6)}$cycloalkyl, $C_{(3-6)}$alkyl or $C_{(1-2)}$alkyl-O-$C_{(1-3)}$alkyl, wherein the $C_{(0-1)}$alkyl$C_{(3-6)}$cycloalkyl, $C_{(3-6)}$alkyl and $C_{(1-2)}$alkyl-O-$C_{(1-3)}$alkyl are unsubstituted or substituted with one to five R^{3a} groups each independently selected from fluorine, CH_3, CHF_2, CF_3, OH and =O;

R^4 is $C_{(3-6)}$cycloalkyl, phenyl, or a 5 to 6-membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S;

wherein the $C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to three R^{4a} groups each independently selected from halogen, $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl wherein the $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms;

alternatively, two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a $C_{(3-6)}$cycloalkyl;

wherein the phenyl is unsubstituted or substituted with one to three R^{4b} groups each independently selected from halogen, $-CN$, $-C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(1-3)}$alkyl, $-C_{(1-4)}$alkyl and a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-OC_{(1-3)}$alkyl, $-C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;

wherein the 5- to 6-membered heteroaryl is unsubstituted or substituted with one or two R^{4e} groups;

each R^{4e} is independently halogen, $-CN$, $-OH$, $-N(R^{4c1})(R^{4c2})$, $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl, or a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;

alternatively, two R^{4e} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;

each R^{4d} is independently fluorine, $-CN$, $-OH$, oxo, $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl, $-OC_{(3-4)}$cycloalkyl, $-C_{(0-2)}$alkyl-$N(R^{4d1})(R^{4d2})$, $-C_{(0-2)}$alkyl-$N(C_{(1-4)}$alkyl)$C(O)(C_{(1-4)}$alkyl) or a 3- to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl, $-OC_{(3-4)}$cycloalkyl and heterocyclyl groups are unsubstituted or substituted with one to three fluorine atoms;

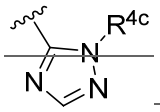
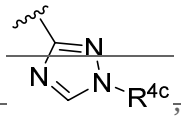
R^{4c1}, R^{4c2}, R^{4d1} and R^{4d2} are each independently H or $-C_{(1-3)}$alkyl, wherein the $-C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;

alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3- to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N, O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms; and

R^5 is hydrogen or halogen;

wherein

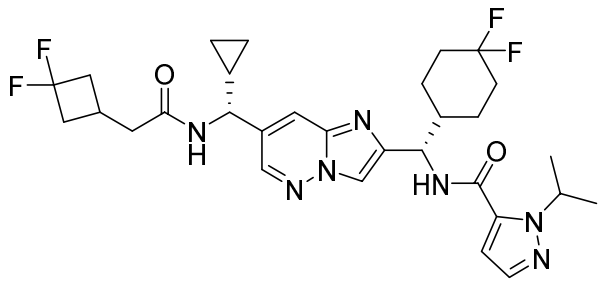
when R^4 is 1,2,4-triazolyl, then R^4 is

or , and

when R^4 is a substituted 6-membered heteroaryl, the substituted heteroaryl is unsubstituted at the para-position.

3. The compound of claim 1 or claim 2, having the following structure:



3. or a pharmaceutically acceptable salt thereof, wherein:

R^1 is $C_{(1-6)}$alkyl, $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, or piperidinyl;

wherein the $C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

wherein the $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to six R^{1b} groups; and

wherein the piperidinyl is unsubstituted or substituted with one to three R^{1c} groups;

R^{1a} and R^{1b} are each independently -OH, $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine;

each R^{1c} is independently $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

R^2 is H, $C_{(3-5)}$cycloalkyl, or $C_{(1-4)}$alkyl;

R^3 is $C_{(5-6)}$cycloalkyl that is unsubstituted or substituted with one to two fluorine atoms;

R^4 is $C_{(3-4)}$cycloalkyl, phenyl, or a 5-membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S;

wherein the $C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to three R^{4a} groups each independently selected from halogen and $C_{(1-4)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

alternatively, two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a $C_{(3-6)}$cycloalkyl;

wherein the phenyl is unsubstituted or substituted with one or two R^{4b} groups each independently selected from halogen, –CN, $C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-OC_{(1-3)}$alkyl, $C_{(1-4)}$alkyl, and a 3- to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-OC_{(1-3)}$alkyl, $-C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;

wherein the 5-membered heteroaryl is unsubstituted or substituted with one or two R^{4c} groups;

each R^{4c} is independently halogen, –CN, $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl, or a 3- to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;

each R^{4d} is independently fluorine, –CN, oxo, $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl, $-OC_{(3-4)}$cycloalkyl, $-C_{(0-2)}$alkyl-N(R^{4d1})(R^{4d2}), or $-C_{(0-2)}$alkyl-N($C_{(1-4)}$alkyl)C(O)($C_{(1-4)}$alkyl), wherein the $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl and $-OC_{(3-4)}$cycloalkyl groups are unsubstituted or substituted with one to three fluorine atoms;

R^{4d1} and R^{4d2} are each independently H or $-C_{(1-3)}$alkyl, wherein the $-C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;

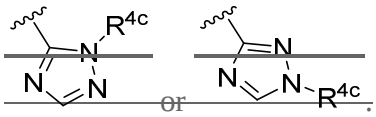
alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3- to 6-membered heterocyclyl having 1 to 3 heteroatoms selected from N,

O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms; and

R^5 is hydrogen or fluorine;

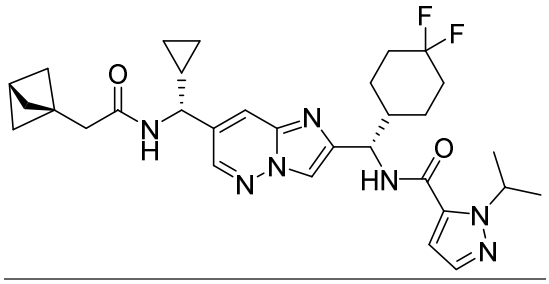
wherein:

when R^4 is 1,2,4-triazolyl, then R^4 is



or .

4. The compound of claim 2, 1, having the following structure:



4. or a pharmaceutically acceptable salt thereof, wherein:.

R^1 is $-C_{(1-6)}$alkyl, $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-C_{(0-2)}$alkyl-cyclopropyl-$C_{(1-3)}$perfluoroalkyl, pyrrolidinyl, or piperidinyl;

wherein the $-C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

wherein the $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to six R^{1b} groups; and

wherein the pyrrolidinyl and piperidinyl are unsubstituted or substituted with one to three R^{1c} groups;

R^{1a} and R^{1b} are each independently $-OH$, $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine;

each R^{1c} is independently $-C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

R^2 is H, $-C_{(3-5)}$cycloalkyl, or $-C_{(1-4)}$alkyl; wherein the $-C_{(3-5)}$cycloalkyl is unsubstituted or substituted with $-CN$;

R^3 is $-C_{(5-6)}$cycloalkyl that is unsubstituted or substituted with one to two fluorine atoms;

R^4 is $-C_{(3-4)}$cycloalkyl, phenyl, or a 5-membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S;

wherein the $C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to three R^{4a} groups each independently selected from halogen and $C_{(1-4)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

alternatively, two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a $C_{(3-6)}$cycloalkyl;

wherein the phenyl is unsubstituted or substituted with one or two R^{4b} groups each independently selected from halogen, -CN, -$C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, $C_{(1-4)}$alkyl, and a 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$OC_{(1-3)}$alkyl, -$C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and -$C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;

wherein the 5-membered heteroaryl is unsubstituted or substituted with one or two R^{4c} groups;

each R^{4c} is independently halogen, -CN, -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl, or a 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;

each R^{4d} is independently fluorine, -CN, oxo, -$C_{(1-3)}$alkyl, -$OC_{(1-3)}$alkyl, -$OC_{(3-4)}$cycloalkyl, -$C_{(0-2)}$alkyl-N(R^{4d1})(R^{4d2}), or -$C_{(0-2)}$alkyl-N($C_{(1-4)}$alkyl)C(O)($C_{(1-4)}$alkyl), wherein the -$C_{(1-3)}$alkyl, -$OC_{(1-3)}$alkyl and -$OC_{(3-4)}$cycloalkyl groups are unsubstituted or substituted with one to three fluorine atoms;

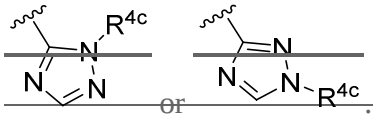
R^{4d1} and R^{4d2} are each independently H or -$C_{(1-3)}$alkyl, wherein the -$C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;

alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3 to 6 membered heterocyclyl having 1 to 3 heteroatoms selected from N, O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms; and

R^5 is hydrogen or fluorine;

wherein

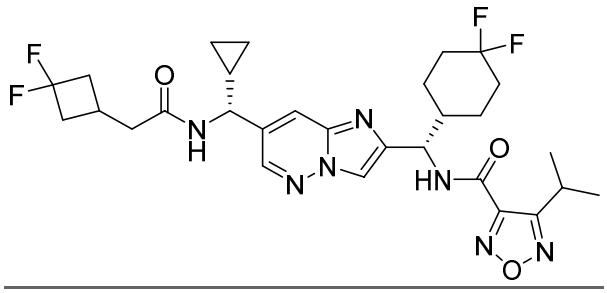
when R^4 is 1,2,4-triazolyl, then R^4 is



or

.

5. The compound of any one of claims 1-4, claim 1, having the following structure:



5. or a pharmaceutically acceptable salt thereof, wherein:.

R^1 is $-C_{(1-6)}$alkyl, $-CH_2C_{(3-6)}$cycloalkyl, or piperidinyl

wherein the $-C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

wherein the $-CH_2C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to four fluorine atoms; and

wherein the piperidinyl is unsubstituted or substituted with $-C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

each R^{1a} is independently -OH, $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine;

R^2 is H, $-C_{(3-5)}$cycloalkyl, or $-C_{(1-3)}$alkyl;

R^3 is cyclohexyl that is unsubstituted or substituted with one to two fluorine atoms;

R^4 is $-C_{(3-4)}$cycloalkyl, spiropentanyl, spirohexanyl, spiroheptanyl, spirooctanyl, phenyl, pyrrolyl, pyrazolyl, oxazolyl, oxadiazolyl, isoxazolyl, triazolyl, tetrazolyl, imidazolyl, thienyl, thiazolyl, isothiazolyl or thiadiazolyl; wherein the $-C_{(3-4)}$cycloalkyl is unsubstituted or substituted with one to three groups selected from halogen, and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

wherein the phenyl is unsubstituted or substituted with one or two groups selected from halogen, -CN, $-C_{(0-2)}$alkyl $C_{(3-4)}$cycloalkyl, -

~~$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, $C_{(1-4)}$alkyl, and a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$OC_{(1-3)}$alkyl, -$C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and -$C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;~~

~~wherein the pyrazolyl, oxazolyl, oxadiazolyl, isoxazolyl, triazolyl, tetrazolyl, imidazolyl, thiazolyl, isothiazolyl and thiadiazolyl are substituted with one or two R^{4c} groups;~~

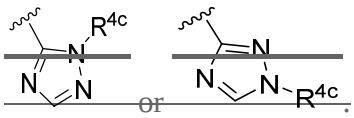
~~each R^{4c} is independently halogen, -CN, -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl, or a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to four R^{4d} groups;~~

~~each R^{4d} is independently -OCH_3, -OCF_3, -$OCHF_2$, or fluorine; and~~

~~R^5 is hydrogen or fluorine;~~

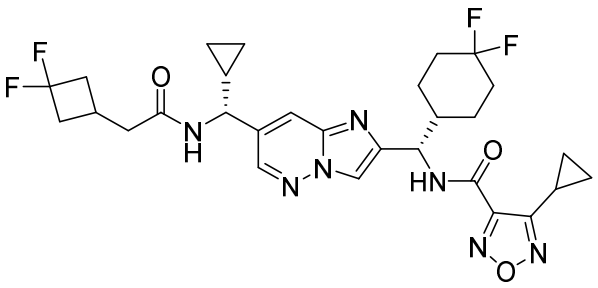
~~wherein~~

~~when R^4 is 1,2,4-triazolyl, then R^4 is~~



~~or~~ .

6. The compound of claim ~~2 or claim 4,~~ 1, having the following structure:



~~6.~~ or a pharmaceutically acceptable salt thereof~~, wherein:~~.

~~R^1 is -$C_{(1-6)}$alkyl, -$C_{(1-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$C_{(0-2)}$alkyl-cyclopropyl-CF_3, pyrrolidinyl, or piperidinyl~~

~~wherein the -$C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;~~

wherein the -$C_{(1-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to four fluorine atoms; and

wherein the pyrrolidinyl and piperidinyl are unsubstituted or substituted with -$C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

each R^{1a} is independently -OH, -OCH_3, -OCF_3, -$OCHF_2$, or fluorine;

R^2 is H, -$C_{(3-5)}$cycloalkyl, or -$C_{(1-3)}$alkyl; wherein the -$C_{(3-5)}$cycloalkyl is unsubstituted or substituted with -CN;

R^3 is cyclohexyl that is unsubstituted or substituted with one to two fluorine atoms;

R^4 is -$C_{(3-4)}$cycloalkyl, spiropentanyl, spirohexanyl, spiroheptanyl, spirooctanyl, phenyl, pyrrolyl, pyrazolyl, oxazolyl, oxadiazolyl, isoxazolyl, triazolyl, tetrazolyl, imidazolyl, thienyl, thiazolyl, isothiazolyl or thiadiazolyl; wherein the -$C_{(3-4)}$cycloalkyl is unsubstituted or substituted with one to three groups selected from halogen, and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

wherein the phenyl is unsubstituted or substituted with one or two groups selected from halogen, -CN, -$C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, $C_{(1-4)}$alkyl, and a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$OC_{(1-3)}$alkyl, -$C_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl and -$C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms, and wherein the heterocyclyl is unsubstituted or substituted with 1 oxo;

wherein the pyrazolyl, oxazolyl, oxadiazolyl, isoxazolyl, triazolyl, tetrazolyl, imidazolyl, thiazolyl, isothiazolyl and thiadiazolyl are substituted with one or two R^{4e} groups;

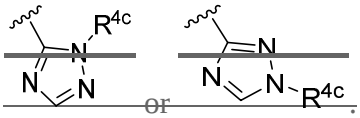
each R^{4e} is independently halogen, -CN, -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl, or a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, -$C_{(1-4)}$alkyl, -$OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to four R^{4d} groups;

each R^{4d} is independently -OCH_3, -OCF_3, -$OCHF_2$, or fluorine; and

R^5 is hydrogen or fluorine;

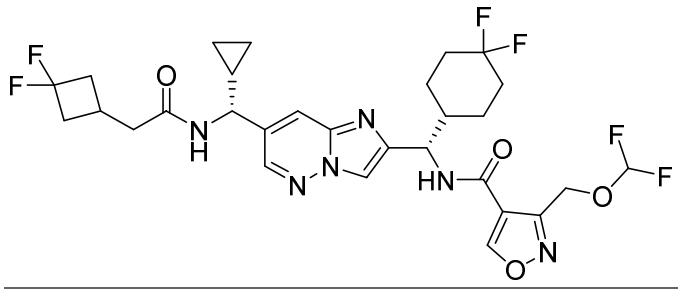
wherein

when R^4 is 1,2,4-triazolyl, then R^4 is

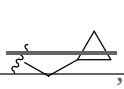
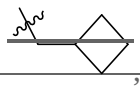
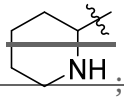


or .

7. The compound of any one of claims 1 to 6, claim 1, having the following structure:

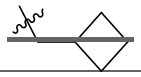


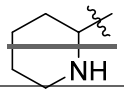
7. or a pharmaceutically acceptable salt thereof, wherein:.

R^1 is $C_{(3-5)}$alkyl, , , or ;

wherein the $C_{(3-5)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

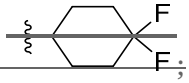
wherein the  is unsubstituted or substituted with one to four fluorine atoms;

wherein the  is unsubstituted or substituted with one to four fluorine atoms; and

wherein the  is unsubstituted or substituted with $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

each R^{1a} is independently -OH or fluorine;

R^2 is H, methyl, isopropyl or cyclopropyl;

R^3 is cyclohexyl or ;

~~R^4 is cyclopropyl, spiropentanyl, spirohexanyl, phenyl, pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, thienyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl or 1,2,5-thiadiazolyl;~~

~~wherein the cyclopropyl is unsubstituted or substituted with one to three groups selected from fluorine and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;~~

~~wherein the phenyl is unsubstituted or substituted with one to two groups selected from chlorine and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;~~

~~wherein the 1,2,3-thiadiazolyl is unsubstituted or substituted with $C_{(1-3)}$alkyl, wherein the $C_{(1-3)}$alkyl is unsubstituted or substituted with one- to three fluorine atoms;~~

~~wherein the pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, thiazolyl, isothiazolyl, or 1,2,5-thiadiazolyl are unsubstituted or substituted with one or two R^{4c} groups;~~

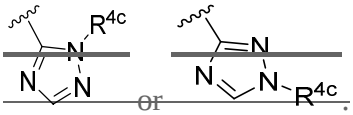
~~each R^{4c} is independently $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl, or $C_{(1-4)}$alkyl, wherein the $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl and $C_{(1-4)}$alkyl groups are unsubstituted or substituted with one to four R^{4d} groups;~~

~~each R^{4d} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine; and~~

~~R^5 is hydrogen or fluorine;~~

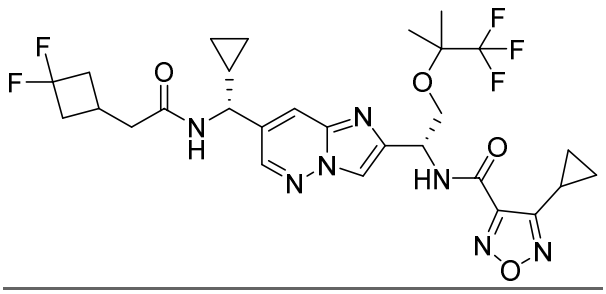
~~wherein~~

~~when R^4 is 1,2,4-triazolyl, then R^4 is~~

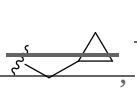
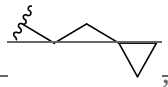
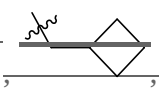
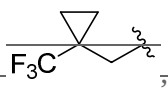
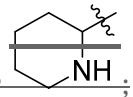


~~or~~ .

8. The compound of ~~any one of claims 2, 4, or 6,~~ claim 1, having the following structure:

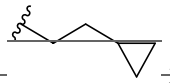


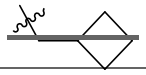
8. or a pharmaceutically acceptable salt thereof, wherein:

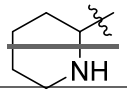
R^1 is $C_{(3-5)}$alkyl, , , , , or ;

wherein the $C_{(3-5)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;

wherein the  is unsubstituted or substituted with one to four fluorine atoms;

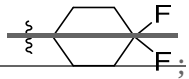
wherein the  is unsubstituted or substituted with one to four fluorine atoms;

wherein the  is unsubstituted or substituted with one to four fluorine atoms; and

wherein the  is unsubstituted or substituted with $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

each R^{1a} is independently -OH or fluorine;

R^2 is H, methyl, isopropyl, cyclopropyl, or cyclobutyl; wherein the cyclopropyl and cyclobutyl are unsubstituted or substituted with -CN;

R^3 is cyclohexyl or ;

R^4 is cyclopropyl, spiropentanyl, spirohexanyl, phenyl, pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, thienyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl or 1,2,5-thiadiazolyl;

wherein the cyclopropyl is unsubstituted or substituted with one to three groups selected from fluorine and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

wherein the phenyl is unsubstituted or substituted with one to two groups selected from chlorine and $C_{(1-2)}$alkyl that is unsubstituted or substituted with one to three fluorine atoms;

wherein the 1,2,3-thiadiazolyl is unsubstituted or substituted with $C_{(1-3)}$alkyl, wherein the $C_{(1-3)}$alkyl is unsubstituted or substituted with one to three fluorine atoms;

wherein the pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, thiazolyl, isothiazolyl, or 1,2,5-thiadiazolyl are unsubstituted or substituted with one or two R^{4c} groups;

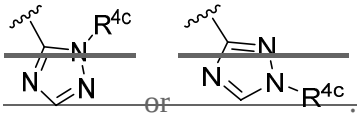
each R^{4c} is independently $-C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl, or $-C_{(1-4)}$alkyl, wherein the $-C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl and $-C_{(1-4)}$alkyl groups are unsubstituted or substituted with one to four R^{4d} groups;

each R^{4d} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine; and

R^5 is hydrogen or fluorine;

wherein

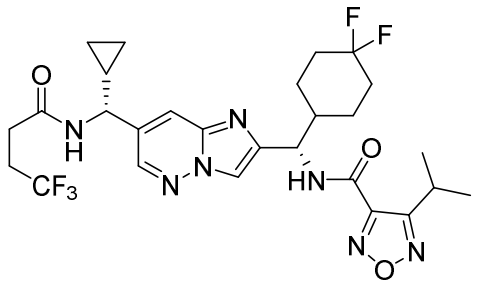
when R^4 is 1,2,4-triazolyl, then R^4 is



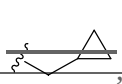
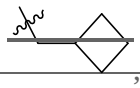
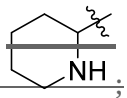
or

.

9. The compound of any one of claims 1 to 8, claim 1, having the following structure:



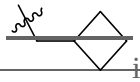
9. or a pharmaceutically acceptable salt thereof, wherein:.

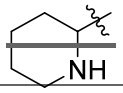
R^1 is $C_{(3-5)}$alkyl, , , or 

;

wherein the $C_{(3-5)}$alkyl is substituted with one to six R^{1a} groups;

wherein the  is unsubstituted or substituted with one to two fluorine atoms;

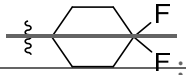
wherein the  is substituted with two fluorine atoms; and

wherein the 

is substituted with $-CF_3$;

each R^{1a} is independently -OH or fluorine;

R^2 is H, methyl, isopropyl or cyclopropyl;

R^3 is cyclohexyl or 

;

R^4 is cyclopropyl, spiropentanyl, spirohexanyl, phenyl, pyrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, 1,2,3-thiadiazolyl or 1,2,5-thiadiazolyl;

wherein the cyclopropyl is substituted with one to two groups selected from fluorine and $C_{(1)}$alkyl that is unsubstituted or substituted with three fluorine atoms;

wherein the phenyl is unsubstituted or substituted with -chlorine, or $-C_{(1-2)}$alkyl;

wherein the 1,2,3-thiadiazolyl and 1,2,5-thiadiazolyl are substituted with $C_{(2-3)}$alkyl;

wherein the pyrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl and imidazolyl are substituted with one or two R^{4e} groups;

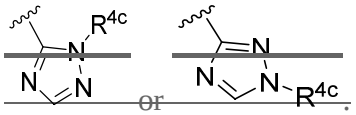
each R^{4e} is independently $-C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl, or $-C_{(1-3)}$alkyl, wherein the $-C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl and $-C_{(1-3)}$alkyl groups are unsubstituted or substituted with one to four R^{4d} groups;

each R^{4d} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine; and

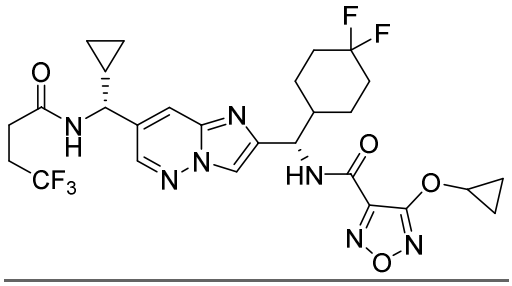
R^5 is hydrogen;

wherein

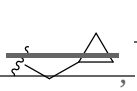
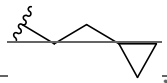
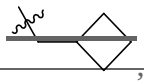
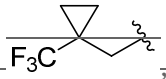
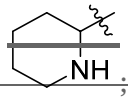
~~when R^4 is 1,2,4-triazolyl, then R^4 is~~



10. The compound of ~~any one of claims 2, 4, 6, or 8,~~ claim 1, having the following structure:

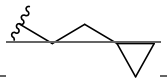


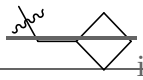
~~10.~~ or a pharmaceutically acceptable salt thereof~~, wherein:~~.

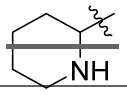
~~R^1 is $C_{(3-5)}$alkyl,~~     ~~, or~~  ~~;~~

~~wherein the $C_{(3-5)}$alkyl is substituted with one to six R^{1a} groups;~~

~~wherein the~~  ~~is unsubstituted or substituted with one to two fluorine atoms;~~

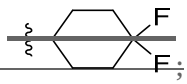
~~wherein the~~  ~~is unsubstituted or substituted with one to four fluorine atoms;~~

~~wherein the~~  ~~is substituted with two fluorine atoms; and~~

~~wherein the~~  ~~is substituted with CF_3;~~

~~each R^{1a} is independently -OH or fluorine;~~

~~R^2 is H, methyl, isopropyl, cyclopropyl, or cyclobutyl; wherein the cyclopropyl and cyclobutyl are unsubstituted or substituted with -CN;~~

~~R^3 is cyclohexyl or~~  ~~;~~

R^4 is cyclopropyl, spiropentanyl, spirohexanyl, phenyl, pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, 1,2,3-thiadiazolyl or 1,2,5-thiadiazolyl;

wherein the cyclopropyl is substituted with one to two groups selected from fluorine and $C_{(1)}$alkyl that is unsubstituted or substituted with three fluorine atoms;

wherein the phenyl is unsubstituted or substituted with chlorine, or $C_{(1-2)}$alkyl;

wherein the 1,2,3-thiadiazolyl and 1,2,5-thiadiazolyl are substituted with $C_{(2-3)}$alkyl;

wherein the pyrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, triazolyl, tetrazolyl and imidazolyl are substituted with one or two R^{4c} groups;

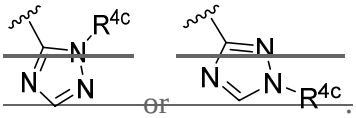
each R^{4c} is independently $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl, or $C_{(1-3)}$alkyl, wherein the $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl and $C_{(1-3)}$alkyl groups are unsubstituted or substituted with one to four R^{4d} groups;

each R^{4d} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, or fluorine; and

R^5 is hydrogen;

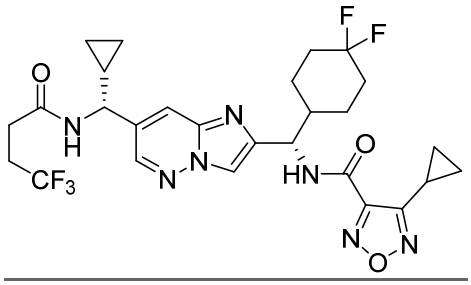
wherein

when R^4 is 1,2,4-triazolyl, then R^4 is



or .

11. The compound of any one of claims 1 to 4, claim 1, having the following structure:



11. or a pharmaceutically acceptable salt thereof, wherein R^1 is.

~~R^1 is $C_{(3-6)}$alkyl, $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, or a 6-membered heterocyclyl having 1 to 2 nitrogen atoms;~~

~~wherein the $C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;~~

~~wherein the $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one to three R^{1b} groups; and~~

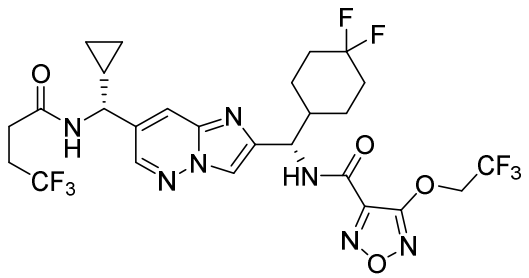
~~wherein the 6-membered heterocyclyl is substituted with one R^{1c} group;~~

~~each R^{1a} is independently fluorine or –OH;~~

~~each R^{1b} is independently fluorine;~~

~~R^{1c} is $C_{(1-4)}$alkyl that is substituted with one to three fluorine atoms.~~

12. The compound of claim ~~2,~~ 1, having the following structure:



~~12.~~ or a pharmaceutically acceptable salt thereof~~, wherein:~~.

~~R^1 is $C_{(3-6)}$alkyl, $C_{(1-2)}$alkyl$C_{(3-6)}$cycloalkyl, or $C_{(1-2)}$alkyl-cyclopropyl-CF_3;~~

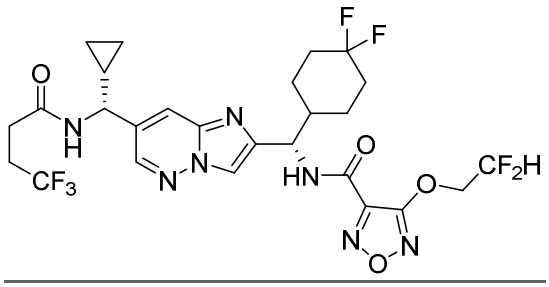
~~wherein the $C_{(1-6)}$alkyl is unsubstituted or substituted with one to six R^{1a} groups;~~

~~wherein the $C_{(1-2)}$alkyl$C_{(3-6)}$cycloalkyl is unsubstituted or substituted with one or two R^{1b} groups;~~

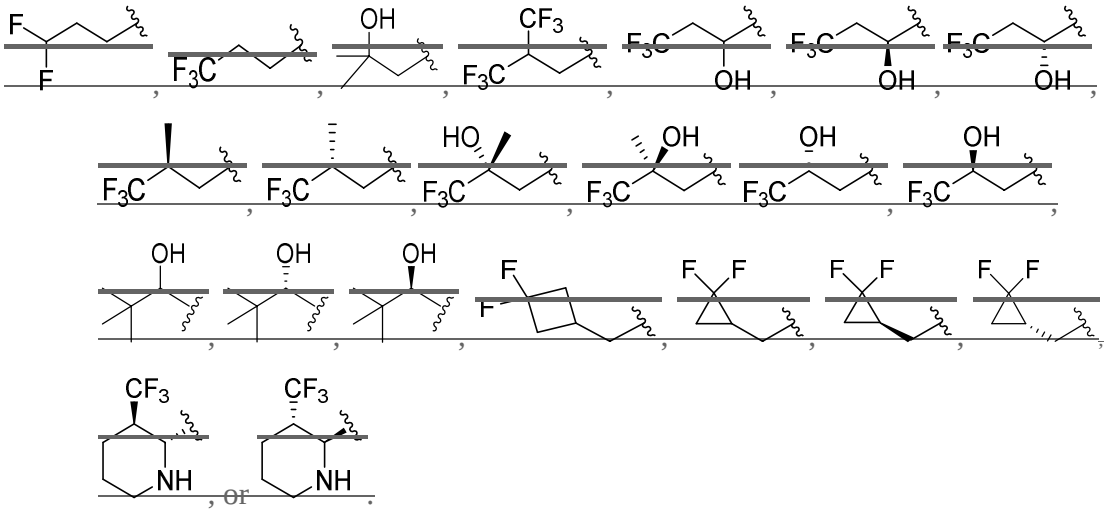
~~each R^{1a} is independently fluorine;~~

~~each R^{1b} is independently fluorine.~~

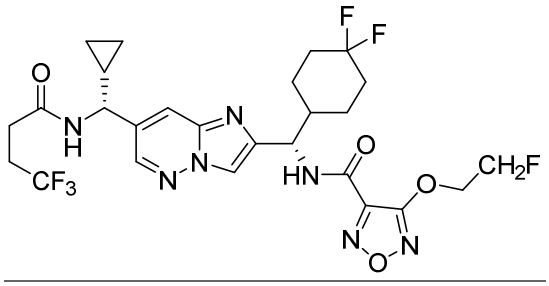
13. The compound of ~~any one of claims 1 to 11,~~ claim 1, having the following structure:



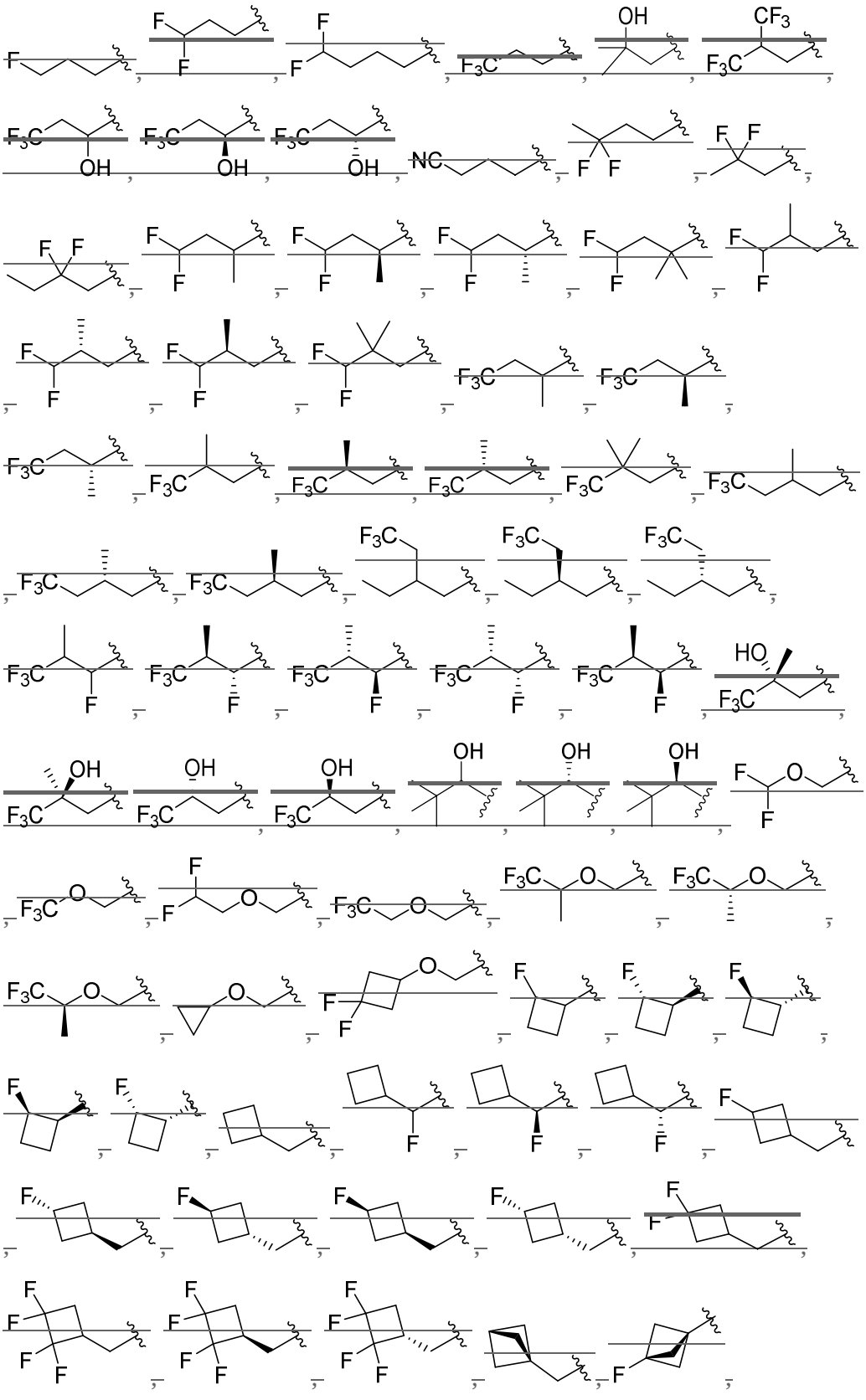
~~13.~~ or a pharmaceutically acceptable salt thereof~~, wherein R^1 is:~~.

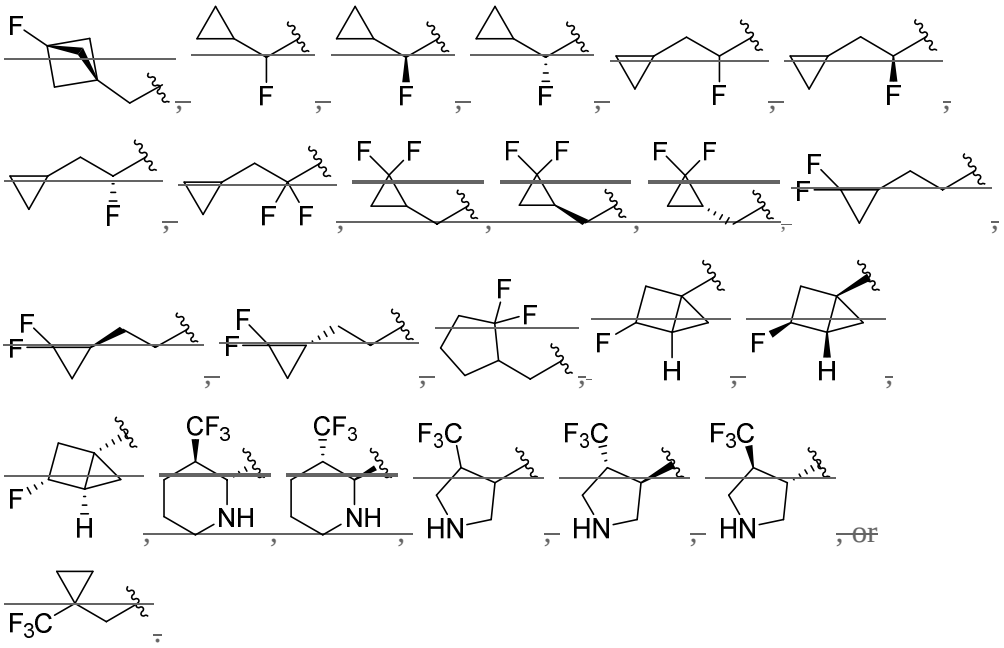


14. The compound of claim ~~2,~~ 1, having the following structure:

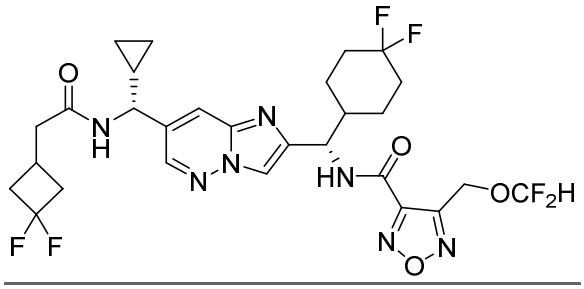


~~14.~~ or a ~~pharmceutically~~pharmaceutically acceptable salt thereof~~, wherein R^1 is:~~.

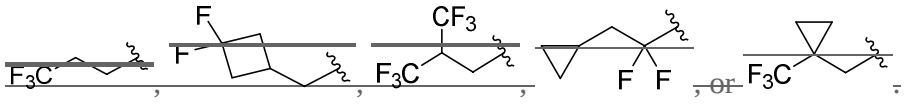




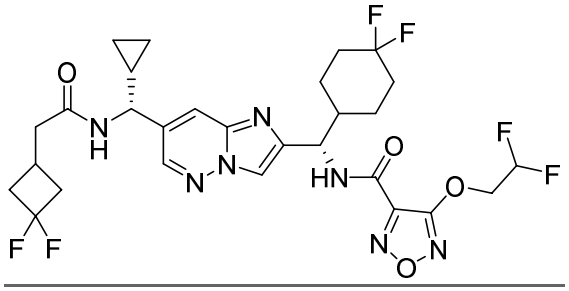
15. The compound of claim ~~2, 12, or 14,~~ 1, having the following structure:



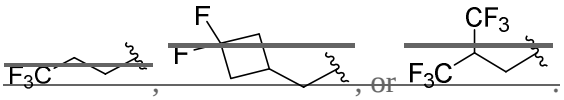
~~15.~~ or a pharmaceutically acceptable salt thereof~~, wherein R^1 is:~~.



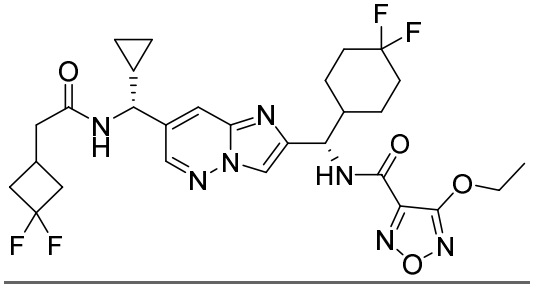
16. The compound of ~~any one of claims~~claim 1 ~~to 15,~~, having the following structure:

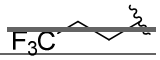


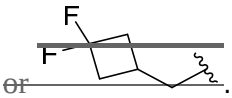
~~16.~~ or a pharmaceutically acceptable salt thereof~~, wherein R^1 is: .~~



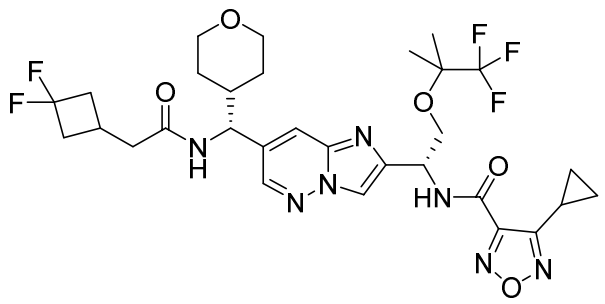
17. The compound of ~~any one claims~~claim 1~~ to 16,~~, having the following structure:



~~17.~~ or a pharmaceutically acceptable salt thereof~~, wherein R^1 is~~ 



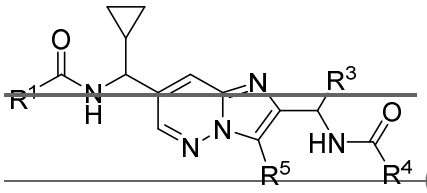
18. The compound of ~~any one of claims~~claim 1~~ to 6 or 11 to 17,~~, having the following structure:



~~18.~~ or a pharmaceutically acceptable salt thereof~~, wherein R^2 is H, methyl, isopropyl or cyclopropyl~~.

19. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^2 is unsubstituted cyclopropyl.

20. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, which is a compound of formula Ia:

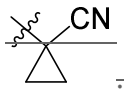


(Ia).

21. The compound of any one of claims 2, 4, 6, 12, 14, or 15, or a pharmaceutically acceptable salt thereof, wherein R^2 is H, methyl, isopropyl, cyclopropyl, or cyclobutyl; wherein the cyclopropyl and cyclobutyl are unsubstituted or substituted with -CN.

22. The compound of any one of claims 2, 4, 6, 8, 10, 12, 14, 15, or 21, or a pharmaceutically acceptable salt thereof, wherein R^2 is cyclopropyl substituted with -CN.

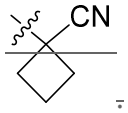
23. The compound of any one of claims 2, 4, 6, 8, 10, 12, 14, 15, 21, or 22, or a pharmaceutically acceptable salt thereof, wherein R^2 is



.

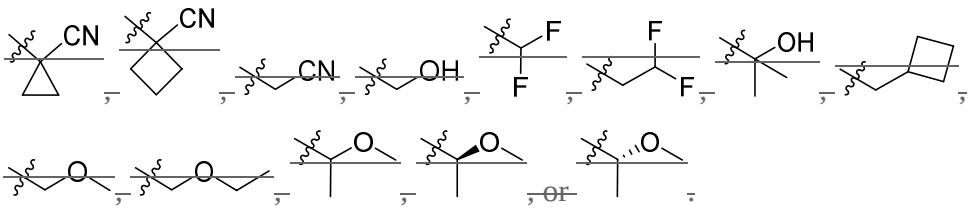
23. The compound of any one of claims 2, 4, 6, 8, 10, 12, 14, 15, or 21, or a pharmaceutically acceptable salt thereof, wherein R^2 is cyclobutyl substituted with -CN.

23. The compound of any one of claims 2, 4, 6, 8, 10, 12, 14, 15, 21, or 24, or a pharmaceutically acceptable salt thereof, wherein R^2 is:



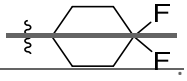
.

23. The compound of claim 2, or a pharmaceutically acceptable salt thereof, wherein R^2 is H, methyl, ethyl, isopropyl, trifluoromethyl, cyclopropyl, cyclobutyl, tetrahydropyranyl,

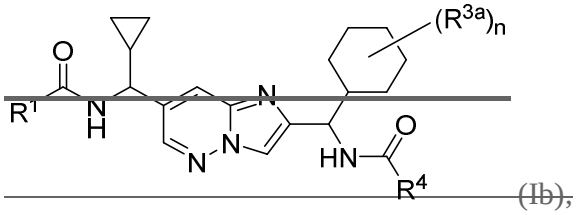


~~23. The compound of any one of claims 1, 2, or 11 to 26, or a pharmaceutically acceptable salt thereof, wherein R^3 is -$C_{(0-1)}$alkyl$C_{(3-6)}$cycloalkyl that is unsubstituted or substituted with one to two fluorine atoms.~~

~~23. The compound of any one of claims 1 to 4, or 11 to 27, or a pharmaceutically acceptable salt thereof, wherein R^3 is cyclohexyl that is unsubstituted or substituted with one to two fluorine atoms.~~

~~23. The compound of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, wherein R^3 is~~  .

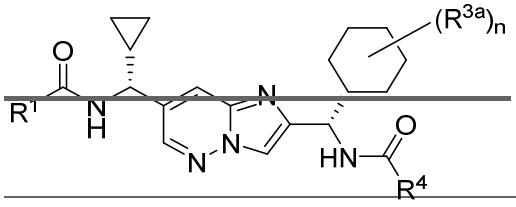
~~23. The compound of any one of claims 1 to 6, 11 to 19, 27, or 28, or a pharmaceutically acceptable salt thereof, which is a compound of formula Ib:~~



~~(Ib),~~

~~wherein R^{3a} is fluorine and n is 0, 1, or 2.~~

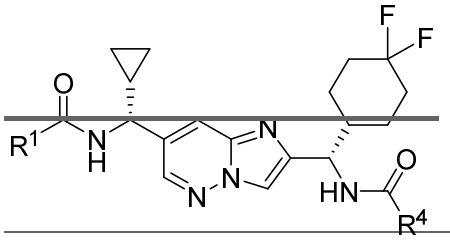
~~23. The compound of any one of claims 1 to 6, 11 to 19, 27, 28, or 30, or a pharmaceutically acceptable salt thereof, which is a compound of formula Ib-2a:~~



~~(Ib-2a),~~

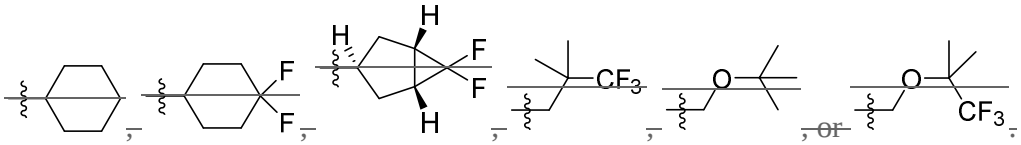
~~wherein R^{3a} is fluorine and n is 2.~~

24. The compound of any one of claims 1 to 19 or 27-31, or a pharmaceutically acceptable salt thereof, which is a compound of formula Ib-3a:



(Ib-3a).

24. The compound of any one of claims 1, 2, or 11-26, or a pharmaceutically acceptable salt thereof, wherein R^3 is



24. The compound of any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein

R^4 is $C_{(3-6)}$cycloalkyl that is unsubstituted or substituted with one to three R^{4a} groups; and

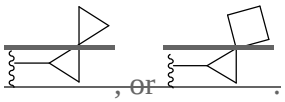
each R^{4a} is independently selected from halogen, $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl, wherein the $-OC_{(1-3)}$alkyl, and $-C_{(1-4)}$alkyl are unsubstituted or substituted with one to three fluorine atoms;

alternatively, two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a $C_{(3-6)}$cycloalkyl.

24. The compound of any one of claims 1 to 34, or a pharmaceutically acceptable salt thereof, wherein each R^{4a} group is fluorine, methyl, or $-CF_3$, or two R^{4a} groups attached to the same ring atom can be combined with the atom to which they are attached to form a cyclopropyl, cyclobutyl or cyclopentyl.

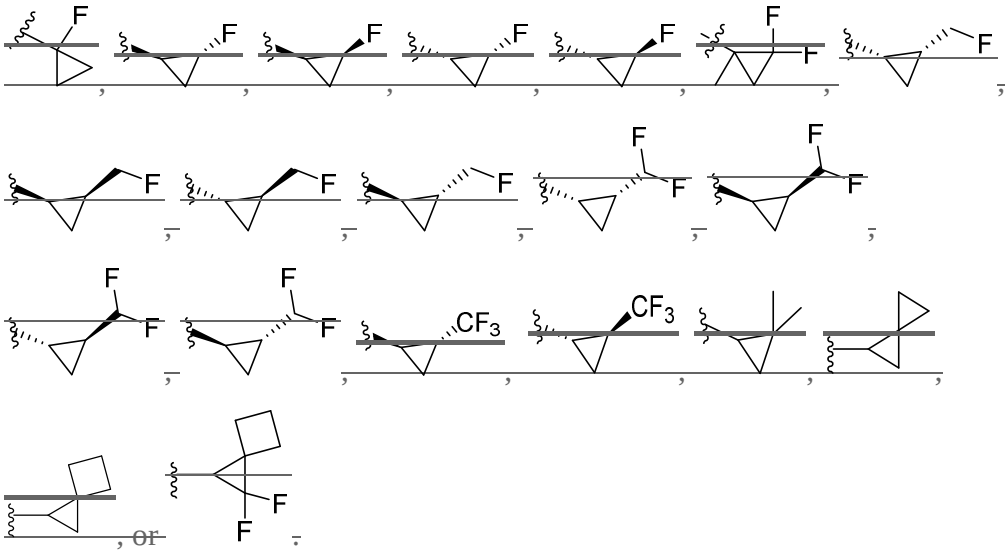
24. The compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, wherein R^4 is cyclopropyl that is unsubstituted or substituted with one to three groups selected from fluorine, CH_3, and CF_3.

25. The compound of any one of claims 1 to 35, or a pharmaceutically acceptable salt thereof, wherein R^4 is

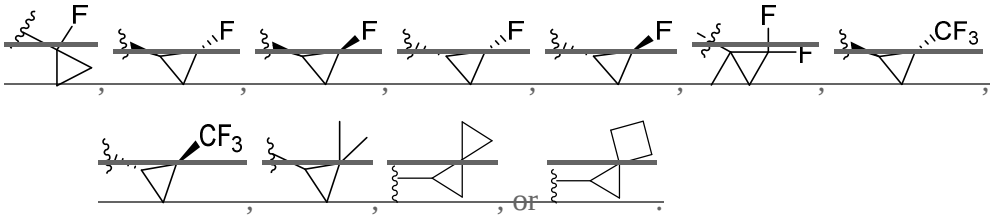


, or .

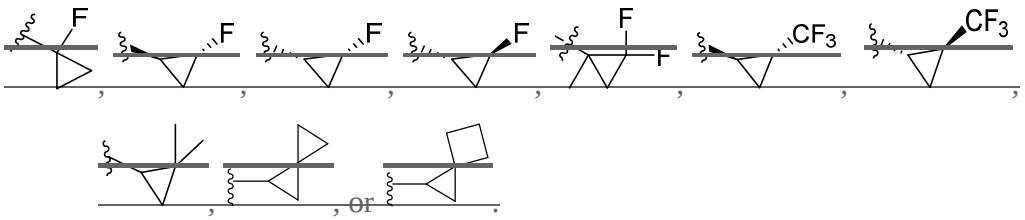
25. The compound of any one of claims 1, 2, or 11-33, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



25. The compound of any one of claims 1 to 35 or 38, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



25. The compound of any one of claims 1 to 35, 38, or 39, or a pharmaceutically acceptable salt thereof, wherein R^4 is:

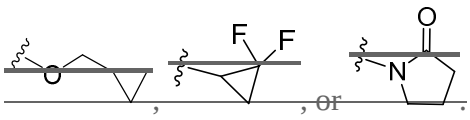


26. The compound of any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein

R^4 is phenyl that is unsubstituted or substituted with one to two R^{4b} groups; and

each R^{4b} is independently selected from chlorine, fluorine, -CN, cyclopropyl, -OCH_2-cyclopropyl, -$OC_{(1-2)}$alkyl, -$C_{(1-2)}$alkyl and pyrrolidin-2-one, wherein the cyclopropyl, -$OC_{(1-2)}$alkyl, and $C_{(1-2)}$alkyl are unsubstituted or substituted with one to three fluorine atoms.

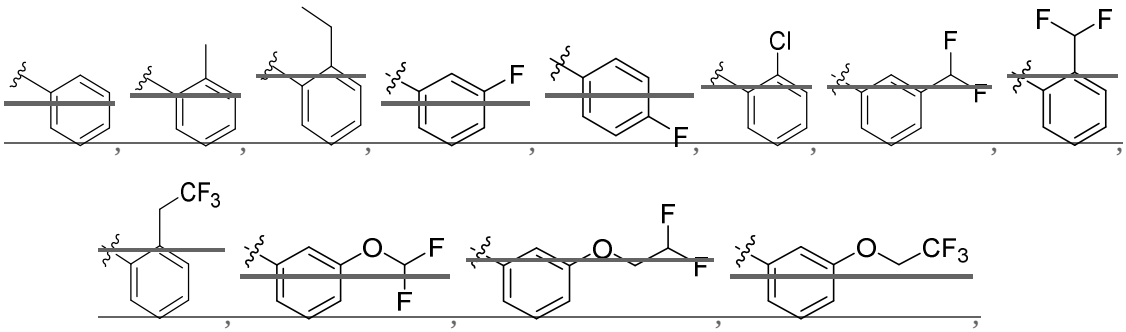
The compound of any one of claims 1 to 33 or 41, or a pharmaceutically acceptable salt thereof, wherein each R^{4b} group is independently H, fluorine, chlorine, -CN, methyl, ethyl, -CHF_2, -CH_2CF_3, -$OCHF_2$, -OCH_2CHF_2, -OCH_2CF_3, cyclopropyl,

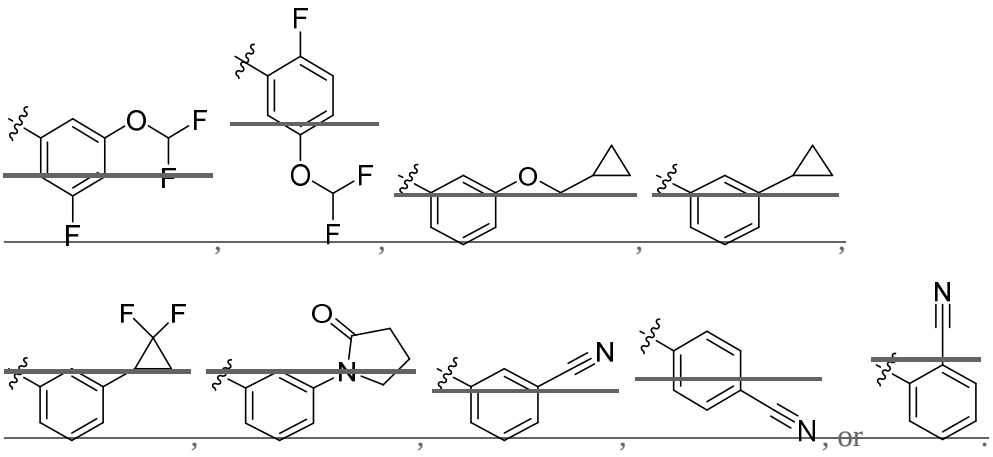


, or .

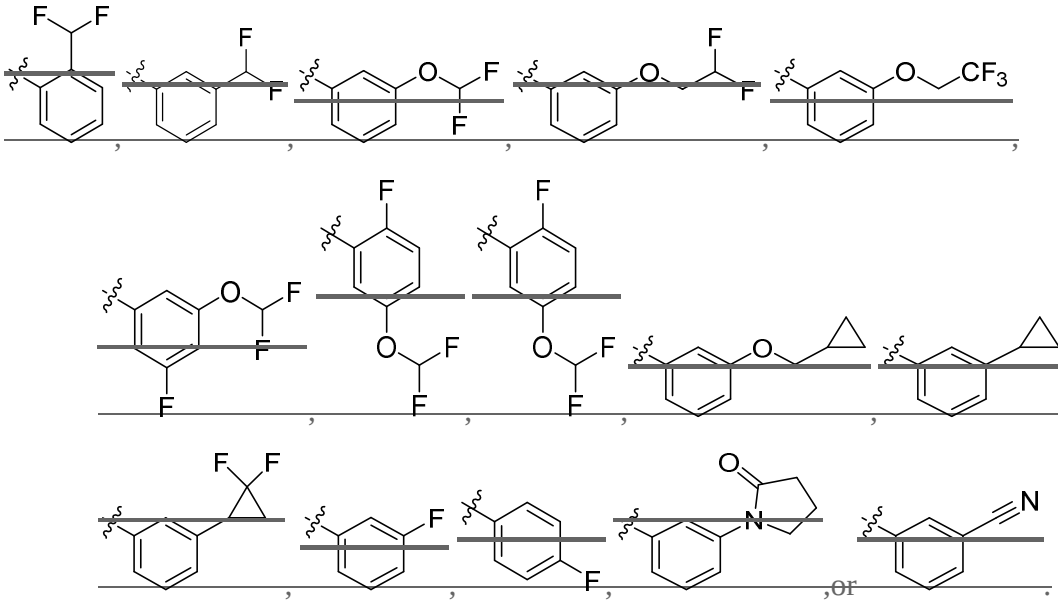
27. The compound of any one of claims 1 to 33, 41 or 42, or a pharmaceutically acceptable salt thereof, wherein R^4 is phenyl that is unsubstituted or substituted with chlorine, -CH_3, or -CH_2CH_3.

27. The compound of any one of claims 1 to 33 or 41 to 43, or a pharmaceutically acceptable salt thereof, wherein R^4 is:





28. The compound of any one of claims 1 to 33 or 41 to 44, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



28. The compound of any one of claims 1, 2 or 11 to 33, or a pharmaceutically acceptable salt thereof, wherein

R^4 is a 5 to 6 membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S, that is substituted with one or two R^{4e} groups;

each R^{4e} is independently halogen, -CN, $-C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $-OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $-C_{(1-4)}$alkyl, $-OC_{(1-3)}$alkyl, or a 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $-C_{(0-}$

~~$_{2)}$alkyl$C_{(3-6)}$cycloalkyl, $C_{(1-4)}$alkyl, $OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;~~

~~alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;~~

~~each R^{4d} is independently fluorine, CN, oxo, $C_{(1-3)}$alkyl, $OC_{(1-3)}$alkyl, $OC_{(3-4)}$cycloalkyl, $C_{(0-2)}$alkyl-N(R^{4d1})(R^{4d2}), or $C_{(0-2)}$alkyl-N($C_{(1-4)}$alkyl)C(O)($C_{(1-4)}$alkyl), wherein the $C_{(1-3)}$alkyl, $OC_{(1-3)}$alkyl and $OC_{(3-4)}$cycloalkyl groups are unsubstituted or substituted with one to three fluorine atoms; and~~

~~R^{4d1} and R^{4d2} are each independently H or $C_{(1-3)}$alkyl, wherein the $C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;~~

~~alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3 to 6 membered heterocyclyl having 1 to 3 heteroatoms selected from N, O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms;~~

~~wherein~~

~~when R^4 is 1,2,4-triazolyl, then R^4 is 1*H*-1,2,4-triazolyl, and~~

~~when R^4 is a 6-membered heteroaryl, the heteroaryl is unsubstituted at the para-position.~~

~~28. The compound of any one of claims 1, 2 or 11 to 33, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^4 is a 5 to 6-membered heteroaryl having 1 to 4 heteroatoms selected from N, O, and S, that is substituted with one or two R^{4c} groups;~~

~~each R^{4c} is independently halogen, CN, NH_2, $N(CH_3)_2$, $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $OC_{(0-2)}$alkyl-$C_{(3-4)}$cycloalkyl, $C_{(1-4)}$alkyl, $OC_{(1-3)}$alkyl, or a 3 to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the $C_{(0-2)}$alkyl$C_{(3-6)}$cycloalkyl, $C_{(1-4)}$alkyl, $OC_{(1-3)}$alkyl and heterocyclyl groups are unsubstituted or substituted with one to six R^{4d} groups;~~

~~alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;~~

~~each R^{4d} is independently fluorine, CN, OH, oxo, $C_{(1-3)}$alkyl, $OC_{(1-3)}$alkyl, $OC_{(3-4)}$cycloalkyl, $C_{(0-2)}$alkyl-N(R^{4d1})(R^{4d2}), $C_{(0-2)}$alkyl-N($C_{(1-4)}$alkyl)C(O)($C_{(1-$~~

$_{4)}$alkyl), or a 3- to 6-membered heterocyclyl having 1 to 2 heteroatoms selected from N and O, wherein the -$C_{(1-3)}$alkyl, -$OC_{(1-3)}$alkyl, -$OC_{(3-4)}$cycloalkyl, and heterocyclyl groups are unsubstituted or substituted with one to three fluorine atoms; and

R^{4d1} and R^{4d2} are each independently H or -$C_{(1-3)}$alkyl, wherein the -$C_{(1-3)}$alkyl is unsubstituted or substituted with one to six groups selected from fluorine and chlorine;

alternatively R^{4d1} and R^{4d2} can be combined with the atom to which they are attached to form a 3 to 6 membered heterocyclyl having 1 to 3 heteroatoms selected from N, O and S, wherein the heterocyclyl is unsubstituted or substituted with 1 to 4 fluorine atoms;

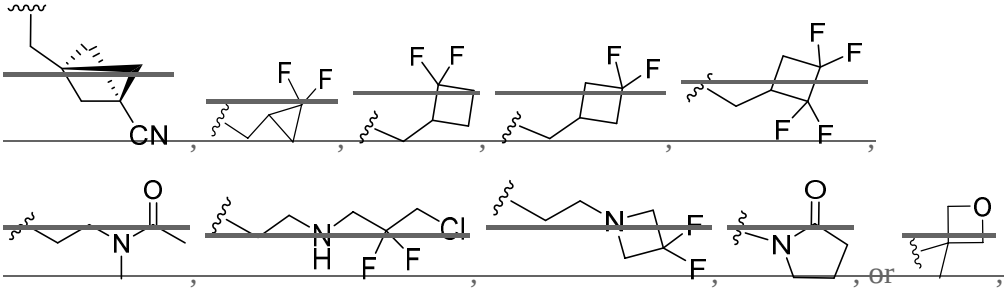
wherein

when R^4 is 1,2,4-triazolyl, then R^4 is 1*H*-1,2,4-triazolyl, and

when R^4 is a 6-membered heteroaryl, the heteroaryl is unsubstituted at the para-position.

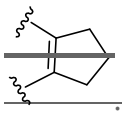
28. The compound of any one of claims 1 to 6, 11 to 33, 46, or 47, or a pharmaceutically acceptable salt thereof, wherein

each R^{4e} is independently fluorine, -CN, methyl, ethyl, isopropyl, -CD_2CD_3, -OCH_3, -OCH_2CH_3, -$OCH(CH_3)_2$, -CHF_2, -CF_3, -CH_2CH_2F, -CH_2CHF_2, -CH_2CF_3, -CF_2CH_3, -$CH_2CH_2CH_2F$, -$CH_2CH_2CHF_2$, -$CH_2CH_2CF_3$, -$CH(CH_3)CF_3$, -$CH(CH_2F)_2$, -CH_2OCH_3, -$CH_2CH_2OCH_3$, -$CH_2CH_2OCHF_2$, -$CH_2CH_2OCF_3$, -$OCHF_2$, -OCH_2CHF_2, -OCH_2CF_3, cyclopropyl, cyclobutyl, cyclopentyl, -CH_2-cyclopropyl, -O-cyclopropyl, -O-cyclobutyl,

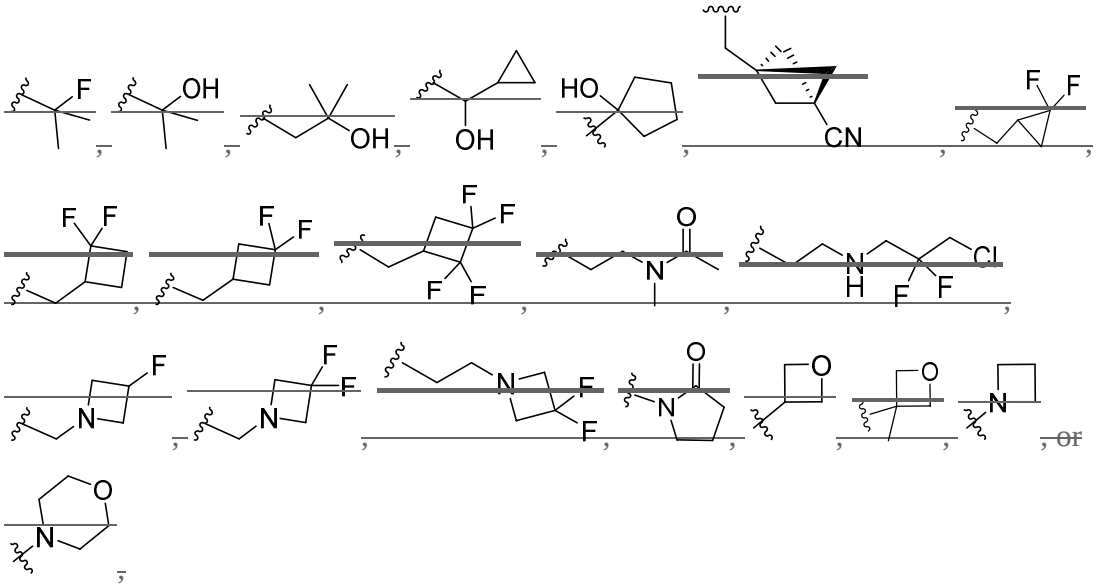


, or

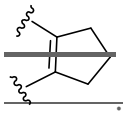
alternatively two R^{4e} groups attached to adjacent ring atoms can be combined to form the group:



28. The compound of any one of claims 1, 2, 11 to 33, or 47, or a pharmaceutically acceptable salt thereof, wherein each $R^{4\epsilon}$ is independently fluorine, -CN, $-NH_2$, $-N(CH_3)_2$, methyl, ethyl, isopropyl, $-CD_3$, $-CD_2CD_3$, $-OCH_3$, $-OCH_2CH_3$, $-OCH(CH_3)_2$, $-OC(CH_3)_3$, $-CH(CH_3)OH$, $-CHF_2$, $-CF_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CF_2CH_3$, $-CH_2CH_2CH_2F$, $-CH_2CH_2CHF_2$, $-CH_2CH_2CF_3$, $-CH(CH_3)CHF_2$, $-CH(CH_3)CF_3$, $-CH(CH_2F)_2$, $-CH_2CF_2CH_3$, $-CH_2CH_2CF_2CH_3$, $-CH_2OCH_3$, $-CH_2CH_2OCH_3$, $-CH_2CH_2OCHF_2$, $-CH_2CH_2OCF_3$, $-CH_2OCHF_2$, $-OCHF_2$, $-OCH_2CHF_2$, $-OCH_2CH_2F$, $-OCH_2CF_3$, cyclopropyl, cyclobutyl, cyclopentyl, $-CH_2$-cyclopropyl, -O-cyclopropyl, -O-cyclobutyl,



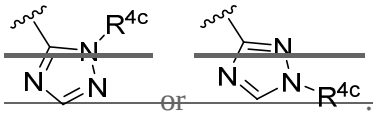
alternatively two $R^{4\epsilon}$ groups attached to adjacent ring atoms can be combined to form the group:



28. The compound of any one of claims 1-4, 11-33, or 46 to 49, or a pharmaceutically acceptable salt thereof, wherein

R^4 is a 5 membered heteroaryl ring having from 1 to 4 heteroatoms selected from N, O and S, that is substituted with one or two $R^{4\epsilon}$ groups,

wherein when R^4 is 1,2,4 triazolyl, then R^4 is

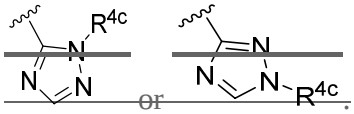


or .

28. The compound of any one of claims 1 to 6, 11 to 33 or 46 to 50, or a pharmaceutically acceptable salt thereof, wherein

R^4 is pyrrolyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, furanyl, oxazolyl, isoxazolyl, oxadiazolyl, thienyl, thiazolyl, isothiazolyl or thiadiazolyl, that is substituted with one or two R^{4c} groups,

wherein when R^4 is 1,2,4 triazolyl, then R^4 is



or .

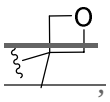
28. The compound of any one of claims 1 to 6, 11 to 33 or 46 to 51, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyrrolyl, pyrazolyl, imidazolyl, 1*H*-1,2,3-triazolyl, 2*H*-1,2,3-triazolyl, 1*H*-1,2,4-triazolyl, tetrazolyl, furanyl, oxazolyl, isoxazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, thienyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl or 1,3,4-thiadiazolyl, that is substituted with one or two R^{4c} groups.

28. The compound of any one of claims 1 to 6, 11 to 33 or 46 to 52, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyrazolyl, imidazolyl, 1*H*-1,2,3-triazolyl, 2*H*-1,2,3-triazolyl, 1*H*-1,2,4-triazolyl, tetrazolyl, oxazolyl, isoxazolyl, 1,2,5-oxadiazolyl, thienyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, or 1,2,5-thiadiazolyl, that is substituted with one or two R^{4c} groups.

28. The compound of any one of claims 1 to 33 or 46 to 51, or a pharmaceutically acceptable salt thereof, wherein

R^4 is oxazolyl, isoxazolyl or oxadiazolyl that is substituted with one or two R^{4c} groups,

wherein each R^{4c} is independently $C_{(3-5)}$cycloalkyl, $C_{(1-3)}$alkyl or

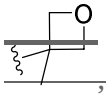


,

wherein the $C_{(3-5)}$cycloalkyl and $C_{(1-3)}$alkyl groups are unsubstituted or substituted with OCH_3, or one to three fluorine atoms.

29. The compound of any one of claims 1 to 33, 46 to 51 or 54, or a pharmaceutically acceptable salt thereof, wherein R^4 is

isoxazolyl substituted with one or two R^{4c} groups each independently methyl, ethyl, isopropyl, $-CF_3$, $-CH_2CH_2F$, $-CH_2CH_2CF_3$, $-CH_2$-OCH_3, cyclopropyl, cyclopentyl, or

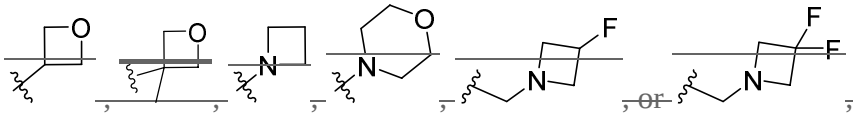


oxazolyl substituted with one isopropyl, or

oxadiazolyl substituted with one methyl or ethyl.

29. The compound of any one of claims 1, 2, 11 to 33, 47, or 49 to 51, or a pharmaceutically acceptable salt thereof, wherein R^4 is

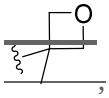
oxazolyl, isoxazolyl or oxadiazolyl that is substituted with one or two R^{4c} groups, wherein each R^{4c} is independently $-NH_2$, $-N(CH_3)_2$, $-C_{(0-1)}$alkyl$C_{(3-5)}$cycloalkyl, $-OC_{(3-4)}$cycloalkyl, $-C_{(1-3)}$alkyl, $-OC_{(1-3)}$alkyl,



wherein the $-C_{(0-1)}$alkyl$C_{(3-5)}$cycloalkyl, $-C_{(1-3)}$alkyl, and $-OC_{(1-3)}$alkyl groups are unsubstituted or substituted with one to three groups selected from -OH, $-OCH_3$, $-OCHF_2$, $-CH_3$, and fluorine.

29. The compound of any one of claims 1, 2, 11 to 33, 47, 49 to 51, or 56, or a pharmaceutically acceptable salt thereof, wherein R^4 is

isoxazolyl substituted with one or two R^{4c} groups each independently methyl, ethyl, isopropyl, $-CF_3$, $-CH_2CH_2F$, $-CH_2CH_2CF_3$, $-CH_2OCH_3$, cyclopropyl, cyclopentyl, or



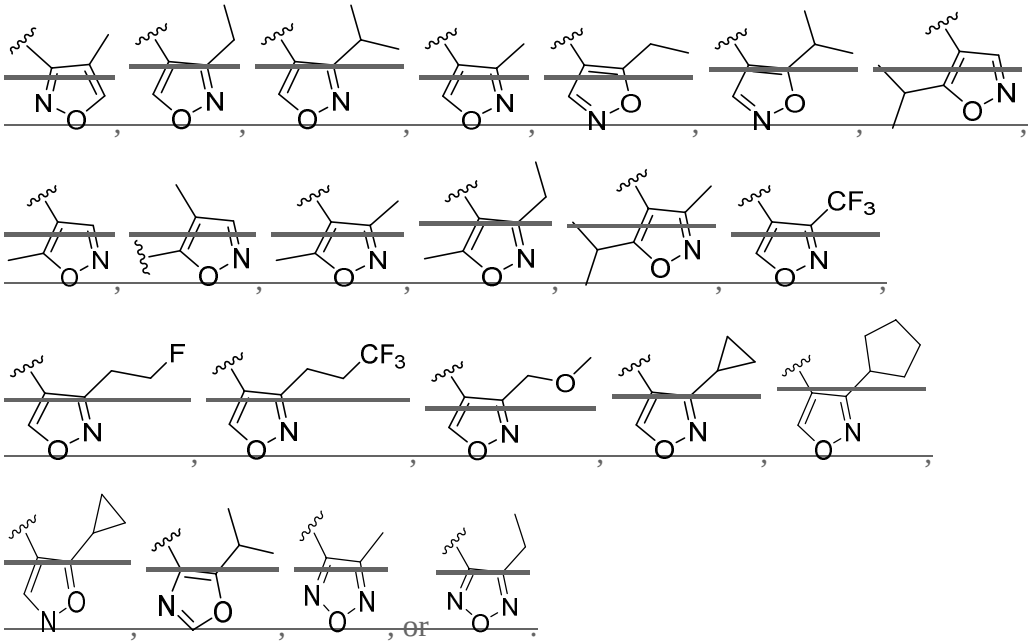
oxazolyl substituted with one isopropyl, or

oxadiazolyl substituted with one methyl, ethyl, $-OCH_2CHF_2$, or cyclopropyl.

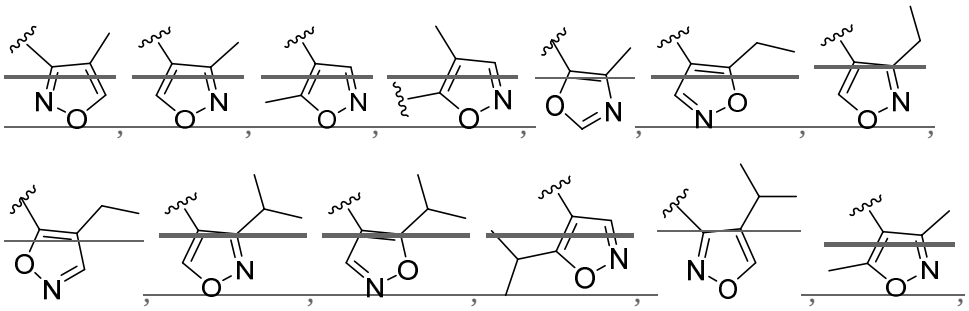
30. The compound of any one of claims 1 to 33, 46 to 51, or 54 to 57, or a pharmaceutically acceptable salt thereof, wherein R^4 is oxadiazolyl substituted with one -$C_{(1-3)}$alkyl.

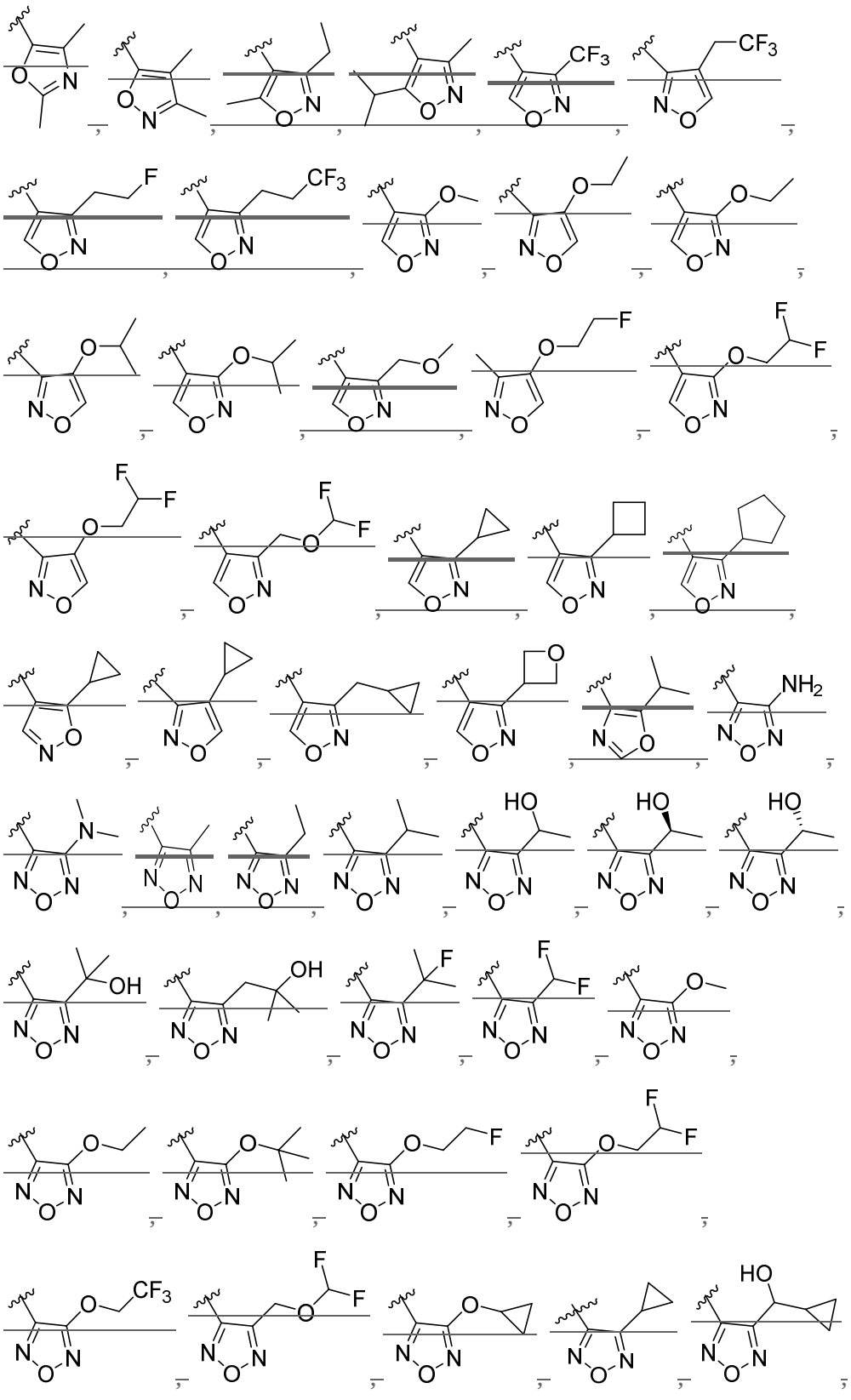
The compound of any one of claims 1 to 33 or 46 to 54, 56, or 57, or a pharmaceutically acceptable salt thereof, whrein R^4 is 1,2,5-oxadiazolyl substituted with cyclopropyl.

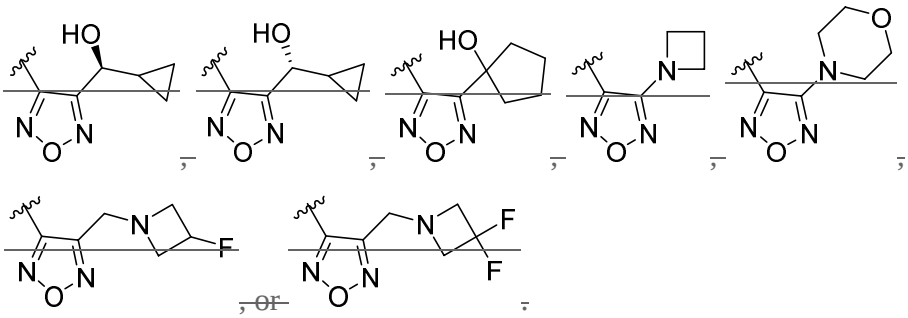
31. The compound of any one of claims 1 to 33 or 46 to 56, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



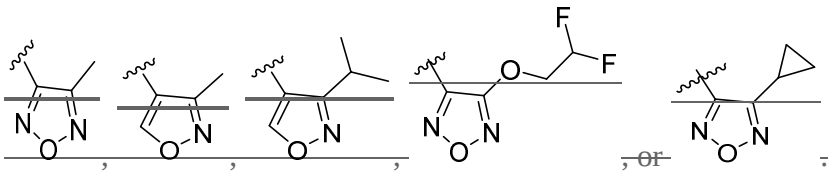
31. The compound of any one of claims 1, 2, 11 to 33, 47, 49, or 56, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



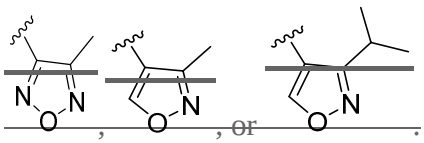




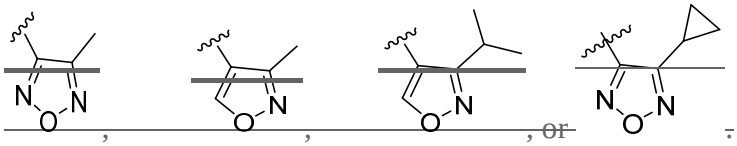
31. The compound of any one of claims 1 to 6, 11 to 33 or 47, 49, 56, or 61, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



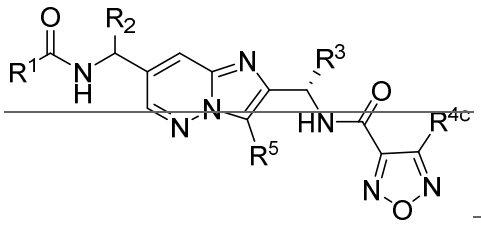
31. The compound of any one of claims 1 to 33, 46 to 57, or 60 to 62, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



31. The compound of any one of claims 1 to 33, 46 to 54, 56, 57, 61 or 62, or a pharmaceutically acceptable salt thereof, wherein R^4 is:

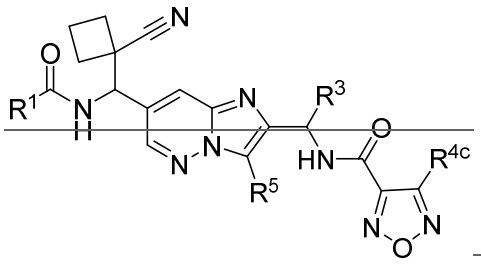


31. The compound of any one of claims 1 to 19, 21 to 29, 33, or 46 to 59, or a pharmaceutically acceptable salt thereof, which is a compound of formula I'f:



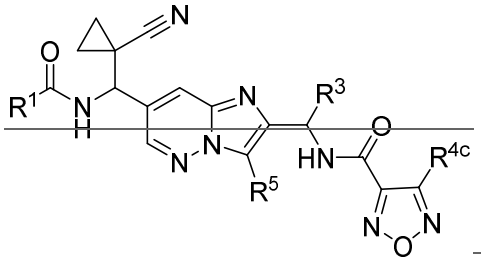
(I'f).

32. The compound of any one of claims 2, 4, 6, 8, 12, 14, 15, 21, 24, 25, 27 to 29, 33, or 46 to 59, or a pharmaceutically acceptable salt thereof, which is a compound of formula I'g:



(I'g).

32. The compound of any one of claims 2, 4, 6, 8, 10, 12, 14, 15, 21 to 23, 27 to 29, 33, or 46 to 59, or a pharmaceutically acceptable salt thereof, which is a compound of formula I'h:



(I'h).

32. The compound of any one of claims 1 to 33 or 46 to 53, or a pharmaceutically acceptable salt thereof, wherein

R^4 is pyrazolyl or imidazolyl that is unsubstituted or substituted with one or two R^{4c} groups,

wherein each R^{4c} is independently fluorine or $-C_{(1-3)}$alkyl that is unsubstituted or substituted with one to three groups selected from $-CHF_2$, $-CF_3$, $-OCHF_2$, $-OCF_3$ and fluorine.

32. The compound of any one of claims 1 to 33, 46 to 53 or 68, or a pharmaceutically acceptable salt thereof, wherein R^4 is

pyrazolyl substituted with one or two R^{4c} groups each independently methyl, ethyl, isopropyl, $-CD_2CD_3$, fluorine, $-CHF_2$, $-CF_3$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)CF_3$, $-CH(CH_2F)_2$, $-CH_2CH_2OCHF_2$, or $-CH_2CH_2OCF_3$, or

imidazolyl substituted with one isopropyl.

33. The compound of any one of claims 1 to 33 or 46 to 53, or a pharmaceutically acceptable salt thereof, wherein R^4 is

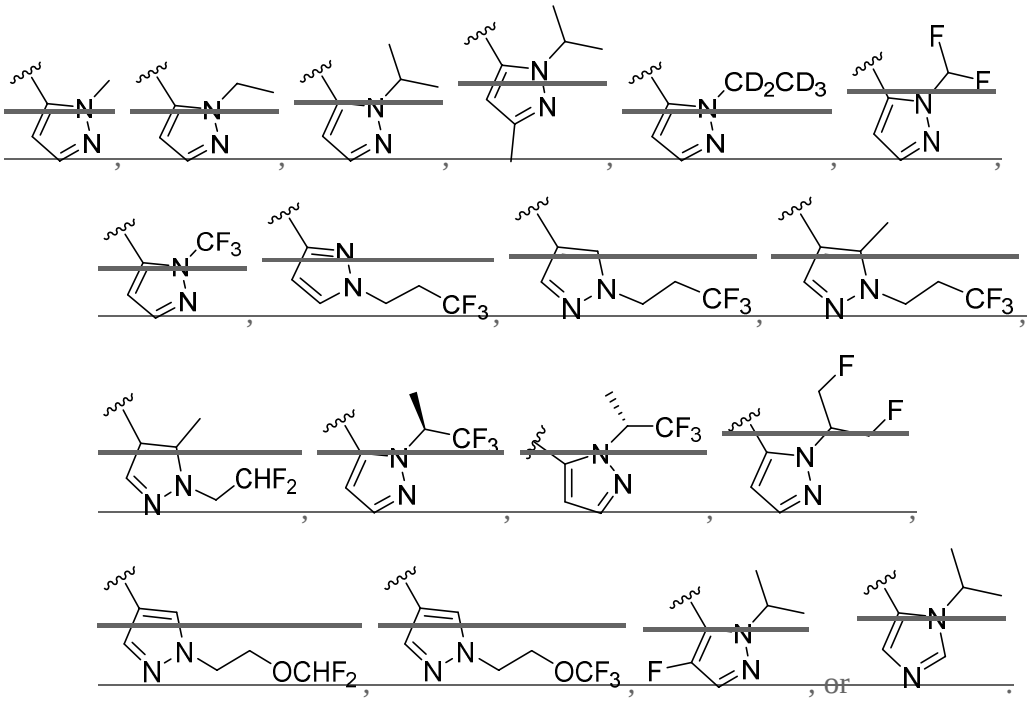
pyrazolyl substituted with one or two R^{4c} groups each independently cyclopropyl, methyl, ethyl, isopropyl, $-CD_3$, $-CD_2CD_3$, fluorine, $-CHF_2$, $-CF_3$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)CF_3$, $-CH(CH_2F)_2$, $-CH_2CH_2OCHF_2$, or $-CH_2CH_2OCF_3$, or

imidazolyl substituted with one methyl or isopropyl.

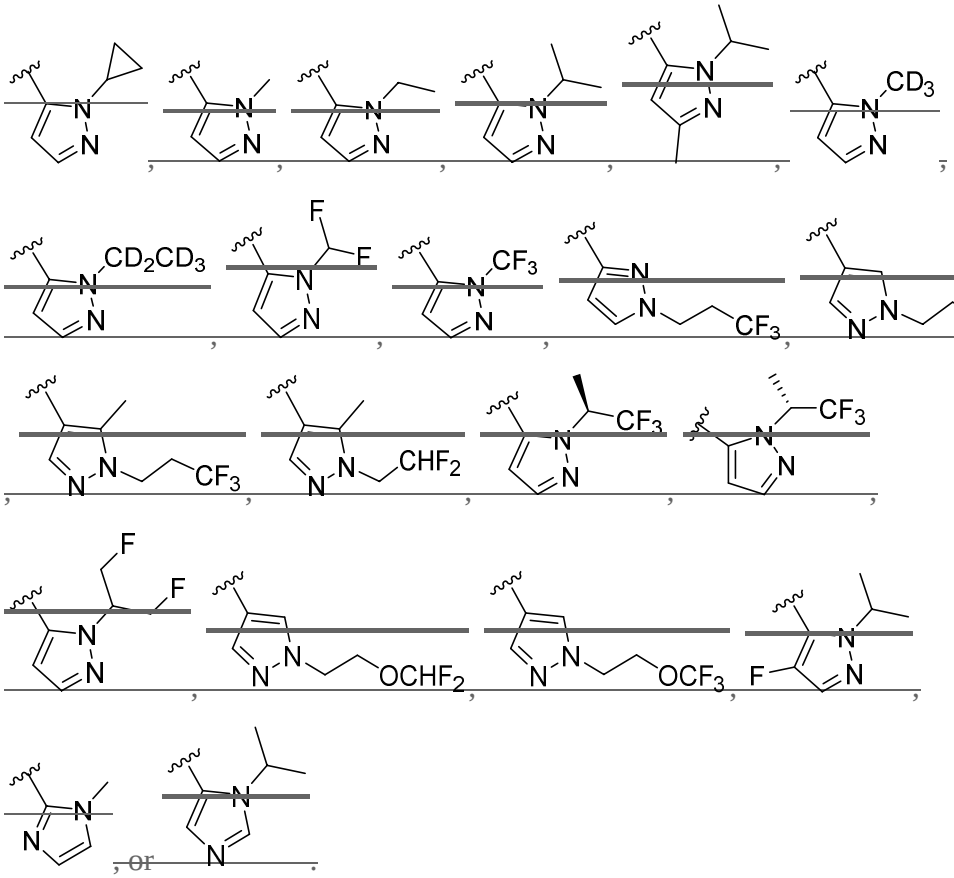
The compound of any one of claims 1 to 33, 46 to 53, or 68 to 70, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyrazolyl substituted with one $-C_{(1-3)}$alkyl.

34. The compound of any one of claims 1 to 33, 46 to 53, or 68 to 71, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyrazolyl substituted with isopropyl, $-CD_3$, or $-CD_2CD_3$.

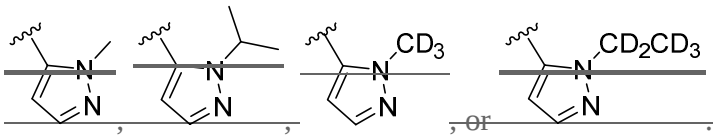
34. The compound of any one of claims 1 to 33, 46 to 53, 68, or 69, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



34. The compound of any one of claims 1 to 33, 46 to 53, 68, or 70, or a pharmaceutically acceptable salt thereof, wherein R^4 is



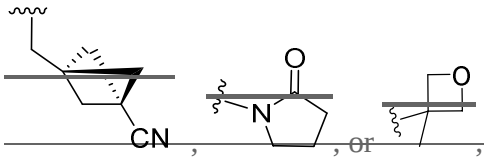
~~The compound of any one of claims 1 to 33, 46 to 53, 68, 70, or 74, or a pharmaceutically acceptable salt thereof, wherein R^4 is~~



~~35. The compound of any one of claims 1 to 33 or 46 to 51, or a pharmaceutically acceptable salt thereof, wherein~~

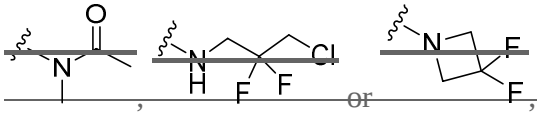
~~R^4 is triazolyl that is unsubstituted or substituted with one or two R^{4e} groups;~~

~~each R^{4e} is independently $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl, $C_{(1-3)}$alkyl,~~

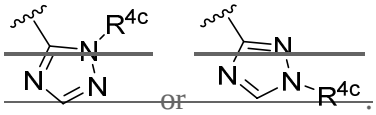


~~wherein the $C_{(0-1)}$alkyl$C_{(3-4)}$cycloalkyl and $C_{(1-3)}$alkyl groups are unsubstituted or substituted with one to four R^{4d} groups; and~~

each R^{4d} is independently $-OCH_3$, $-OCF_3$, $-OCHF_2$, fluorine,



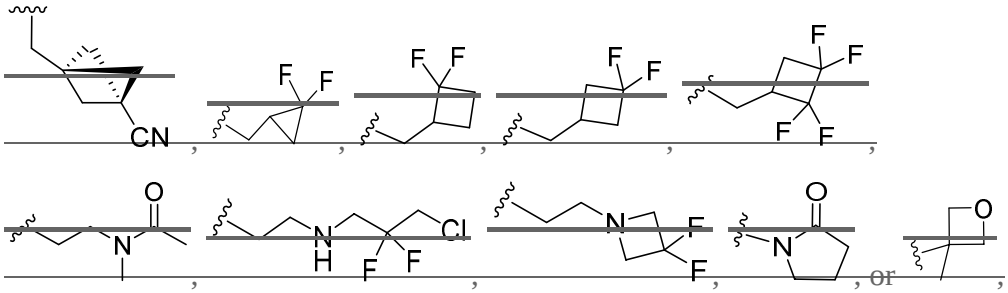
wherein when R^4 is 1,2,4-triazolyl, then R^4 is



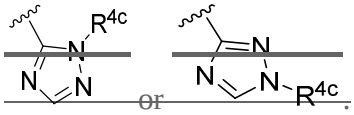
The compound of any one of claims 1 to 33, 46 to 51, or 76, or a pharmaceutically acceptable salt thereof, wherein

R^4 is triazolyl that is unsubstituted or substituted with one or two R^{4c} groups; and

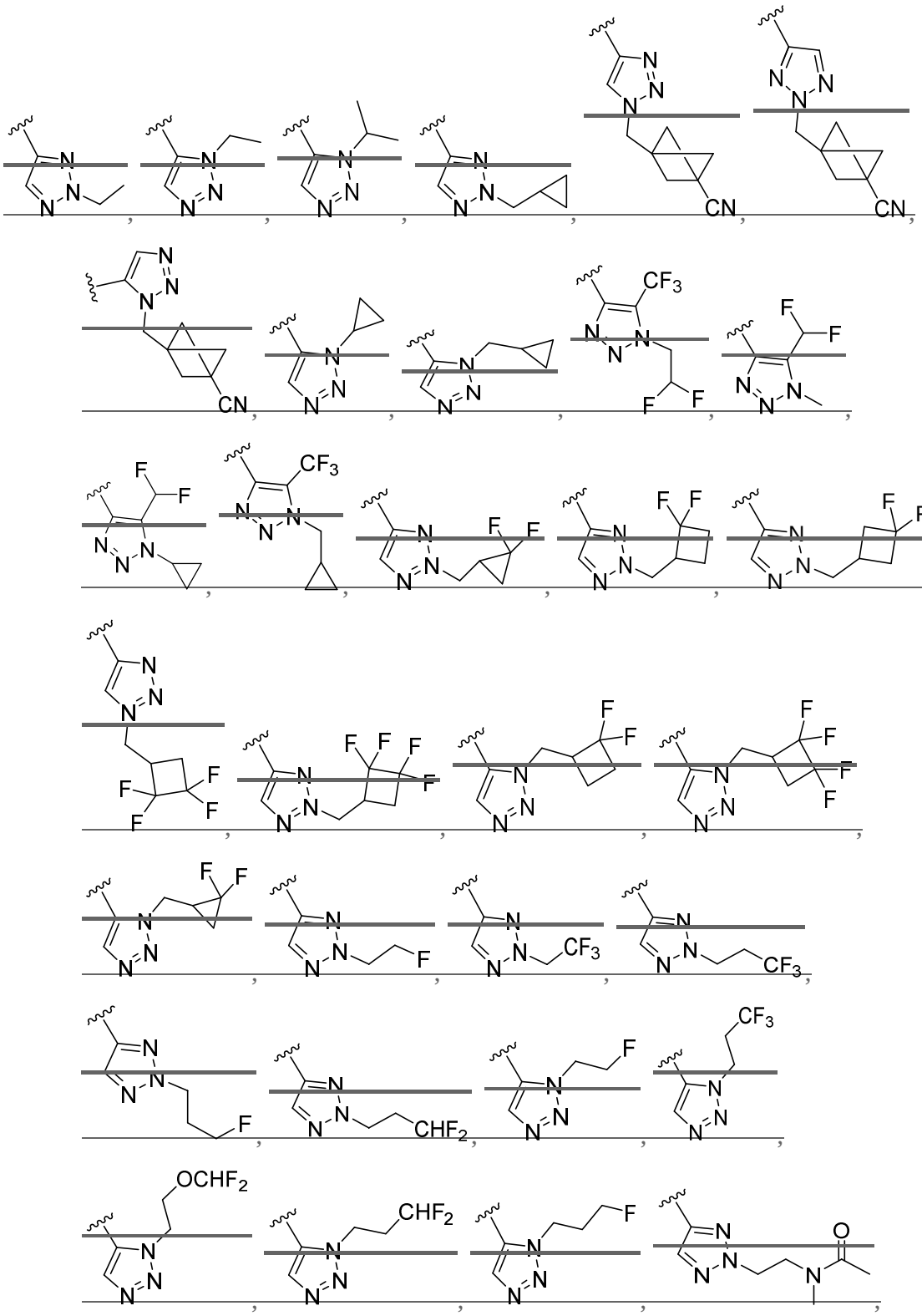
each R^{4c} is independently methyl, ethyl, isopropyl, $-CH_2CH_2OCH_3$, $-CHF_2$, $-CF_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2CH_2CH_2F$, $-CH_2CH_2CHF_2$, $-CH_2CH_2CF_3$, $-CH_2CH_2OCHF_2$, $-CH_2CH_2OCF_3$, cyclopropyl, $-CH_2$-cyclopropyl,

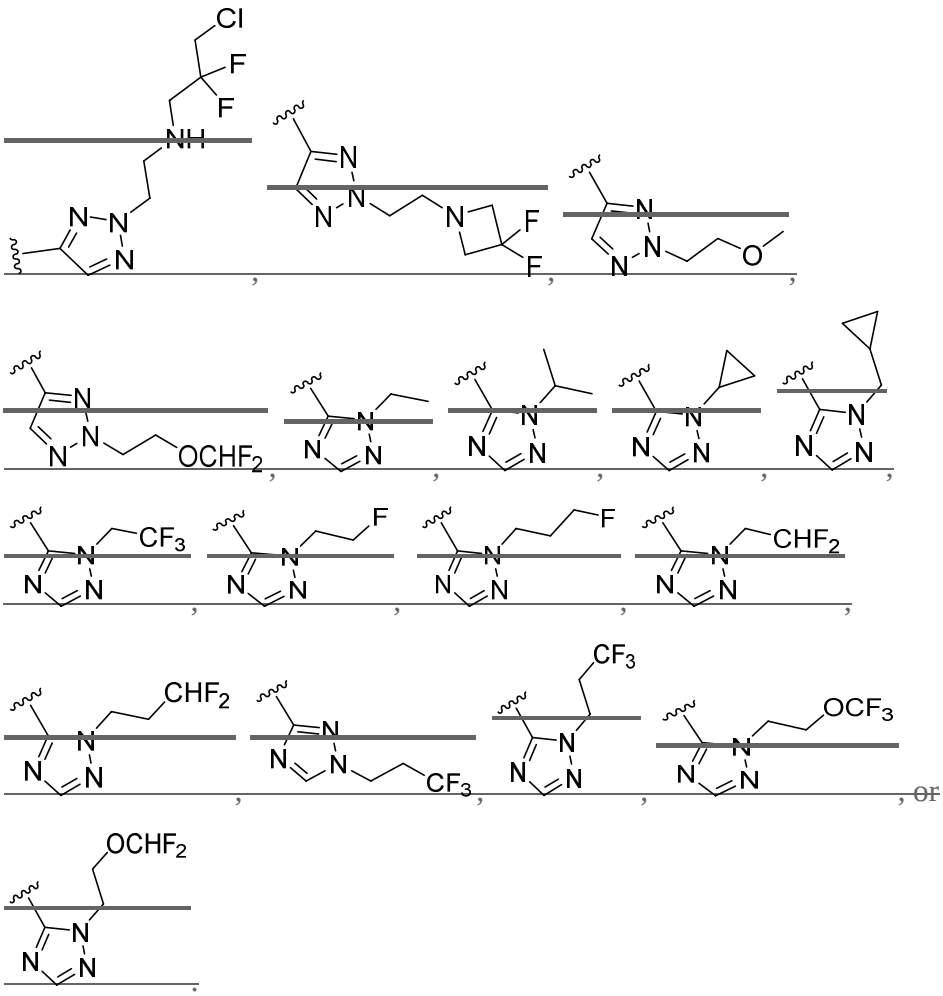


wherein when R^4 is 1,2,4-triazolyl, then R^4 is

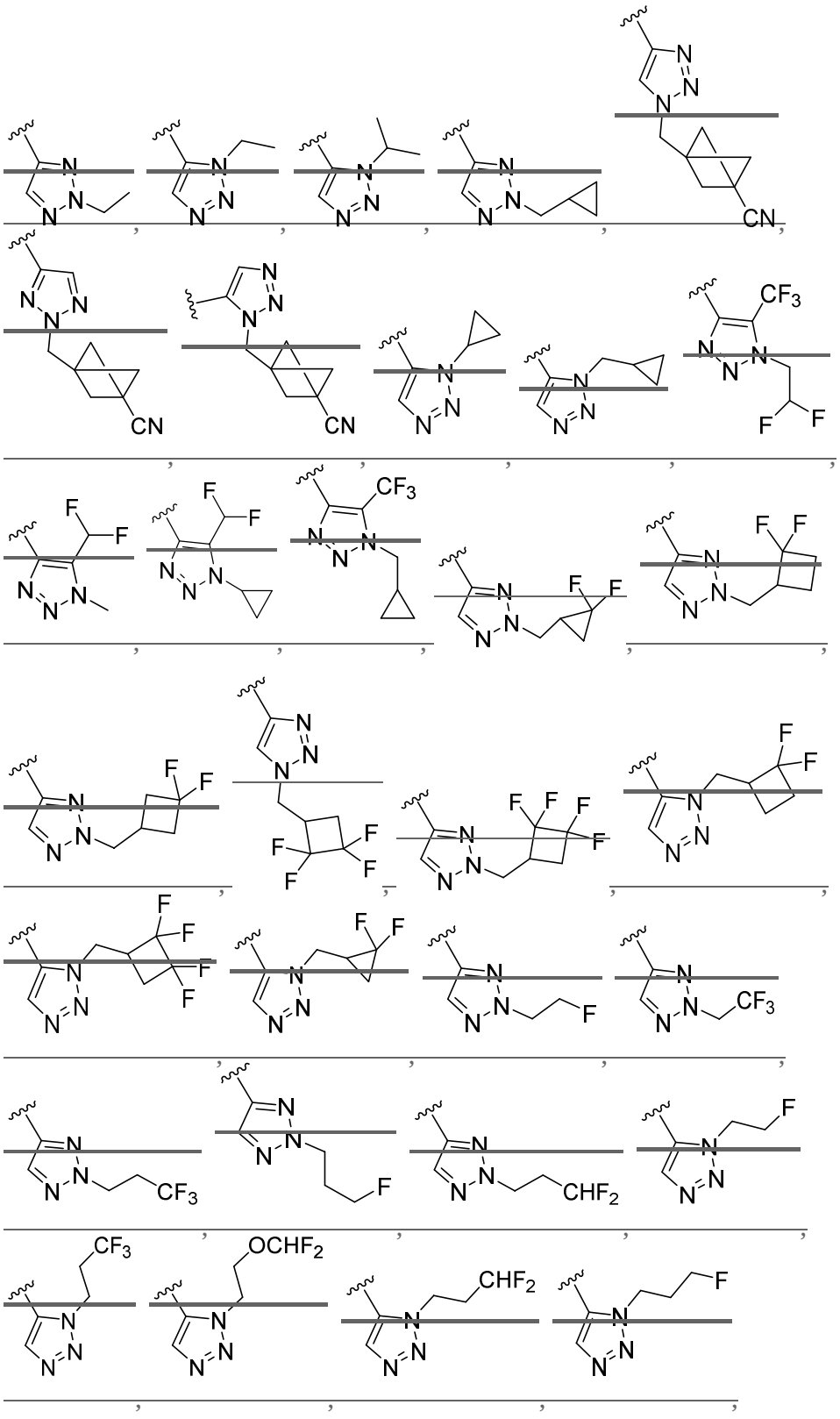


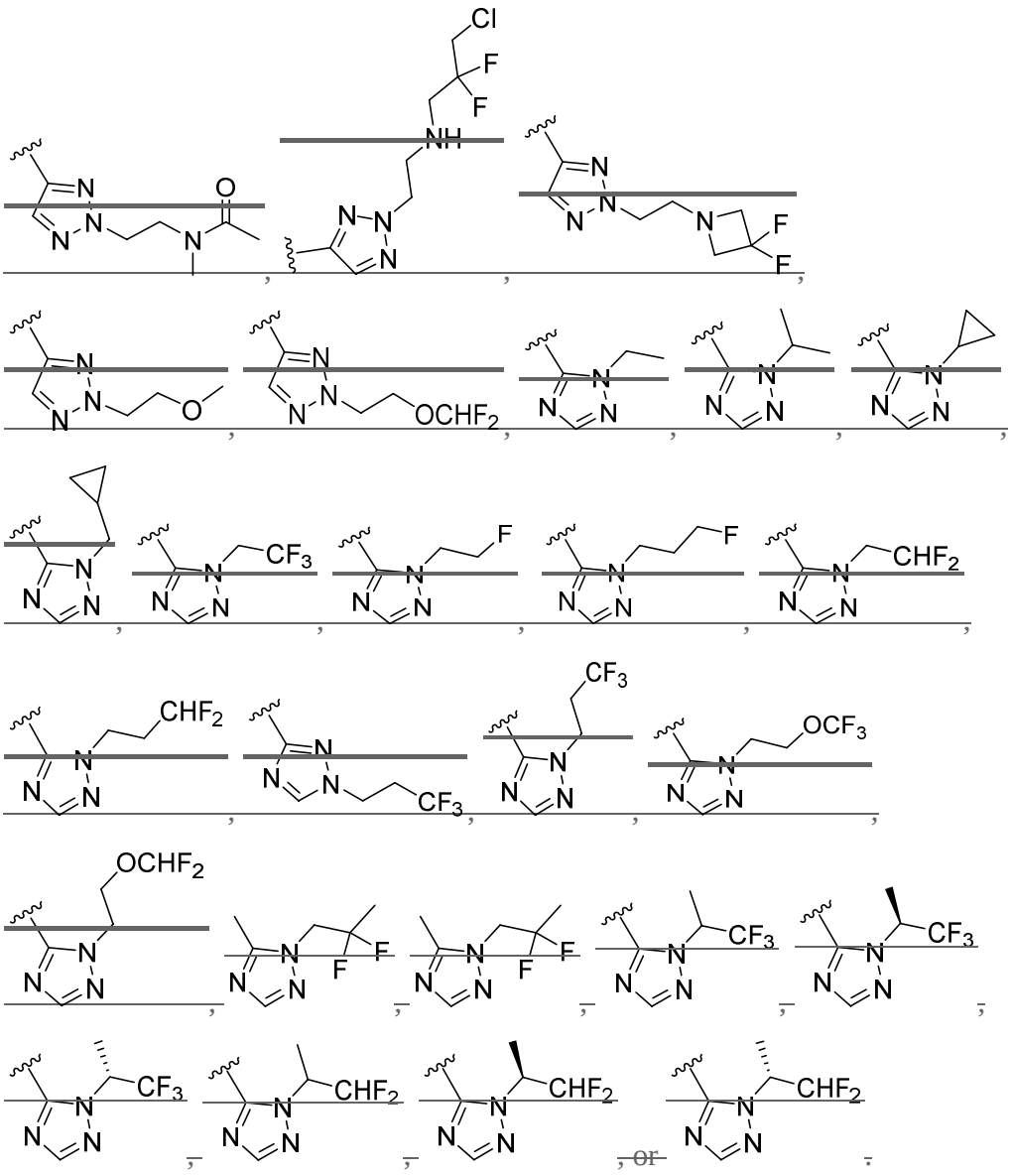
36. The compound of any one of claims 1 to 33, 46 to 51, 76, or 77, or a pharmaceutically acceptable salt thereof, wherein R^4 is:





~~The compound of any one of claims 1 to 33 or 46 to 51, or a pharmaceutically acceptable salt thereof, wherein R^4 is~~

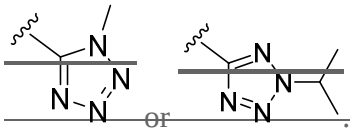




~~37. The compound of any one of claims 1 to 33 or 46 to 53, or a pharmaceutically acceptable salt thereof, wherein R^4 is tetrazolyl substituted with $C_{(1-4)}$alkyl.~~

~~37. The compound of any one of claims 1 to 33, 46 to 53 or 80, or a pharmaceutically acceptable salt thereof, wherein R^4 is tetrazolyl substituted with methyl or isopropyl.~~

~~37. The compound of any one of claims 1 to 33, 46 to 53, 80 or 81, or a pharmaceutically acceptable salt thereof, wherein R^4 is:~~



37. The compound of any one of claims 1 to 33 or 46 to 51, or a pharmaceutically acceptable salt thereof, wherein R^4 is thienyl, thiazolyl, isothiazolyl or thiadiazolyl, each substituted with $-C_{(1-3)}$alkyl, or $-C_{(3-6)}$cycloalkyl.

37. The compound of any one of claims 1 to 33, 46 to 51 or 83, or a pharmaceutically acceptable salt thereof, wherein R^4 is thienyl, thiazolyl, isothiazolyl or thiadiazolyl, each substituted with methyl, isopropyl or cyclopropyl.

37. The compound of any one of claims 1 to 33, 46 to 51, 83 or 84, or a pharmaceutically acceptable salt thereof, wherein R^4 is

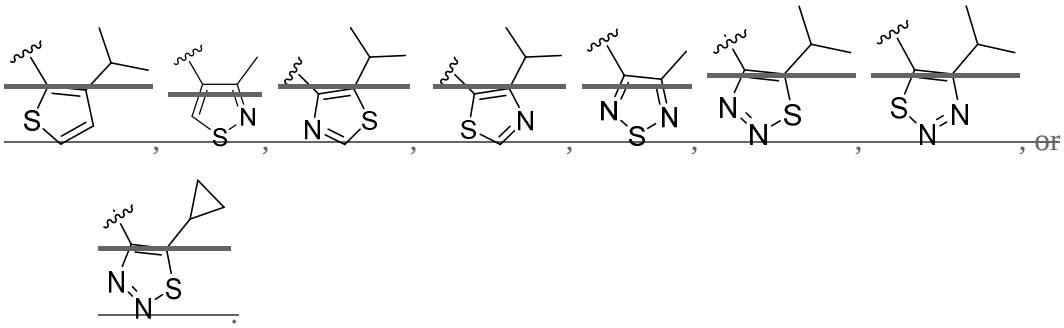
thienyl substituted with isopropyl,

isothiazolyl substituted with methyl,

thiazolyl substituted with isopropyl, or

thiadiazolyl substituted with methyl, isopropyl or cyclopropyl.

37. The compound of any one of claims 1 to 33, 46 to 51, or 83 to 85, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



37. The compound of any one of claims 1, 2, 11 to 33, or 46 to 49, or a pharmaceutically acceptable salt thereof, wherein

R^4 is a 6-membered heteroaryl having 1 to 2 heteroatoms selected from N, that is

substituted with one or two R^{4c} groups; and

each R^{4c} group is independently fluorine, -CN, pyrrolidin-2-one, $C_{(3-4)}$cycloalkyl, -$OC_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, or $C_{(1-3)}$alkyl wherein the -$OC_{(1-3)}$alkyl, and $C_{(1-3)}$alkyl are unsubstituted or substituted with -OCH_3, or one to three fluorine atoms, alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;

wherein the heteroaryl is unsubstituted at the para-position.

38. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, or 87, or a pharmaceutically acceptable salt thereof, wherein

R^4 is a pyridinyl, pyridazinyl, pyrimidinyl, or pyrazinyl, that is substituted with one or two R^{4c} groups; and

each R^{4c} group is independently fluorine, -CN, pyrrolidin-2-one, $C_{(3-4)}$cycloalkyl, -$OC_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, or $C_{(1-3)}$alkyl wherein the -$OC_{(1-3)}$alkyl, and $C_{(1-3)}$alkyl are unsubstituted or substituted with -OCH_3, or one to three fluorine atoms;

alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;

wherein the heteroaryl is unsubstituted at the para-position.

38. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87 or 88, or a pharmaceutically acceptable salt thereof, wherein

R^4 is pyridyl that is unsubstituted or substituted with 1 to 2 R^{4c} groups; and

each R^{4c} group is independently fluorine, -CN, pyrrolidin-2-one, $C_{(3-4)}$cycloalkyl, -$OC_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl, or $C_{(1-3)}$alkyl wherein the -$OC_{(1-3)}$alkyl, and $C_{(1-3)}$alkyl are unsubstituted or substituted with -OCH_3, or one to three fluorine atoms;

alternatively, two R^{4c} groups attached to adjacent ring atoms can be combined to form a $C_{(4-6)}$cycloalkyl;

wherein the pyridyl is unsubstituted at the para-position.

38. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, or 87 to 89, or a pharmaceutically acceptable salt thereof, wherein R^4 is pyridyl unsubstituted or substituted with $C_{(1-2)}$alkyl unsubstituted or substituted with one to three fluorine atoms, wherein the pyridyl is unsubstituted at the para-position.

39. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, or 87 to 89, or a pharmaceutically acceptable salt thereof, wherein

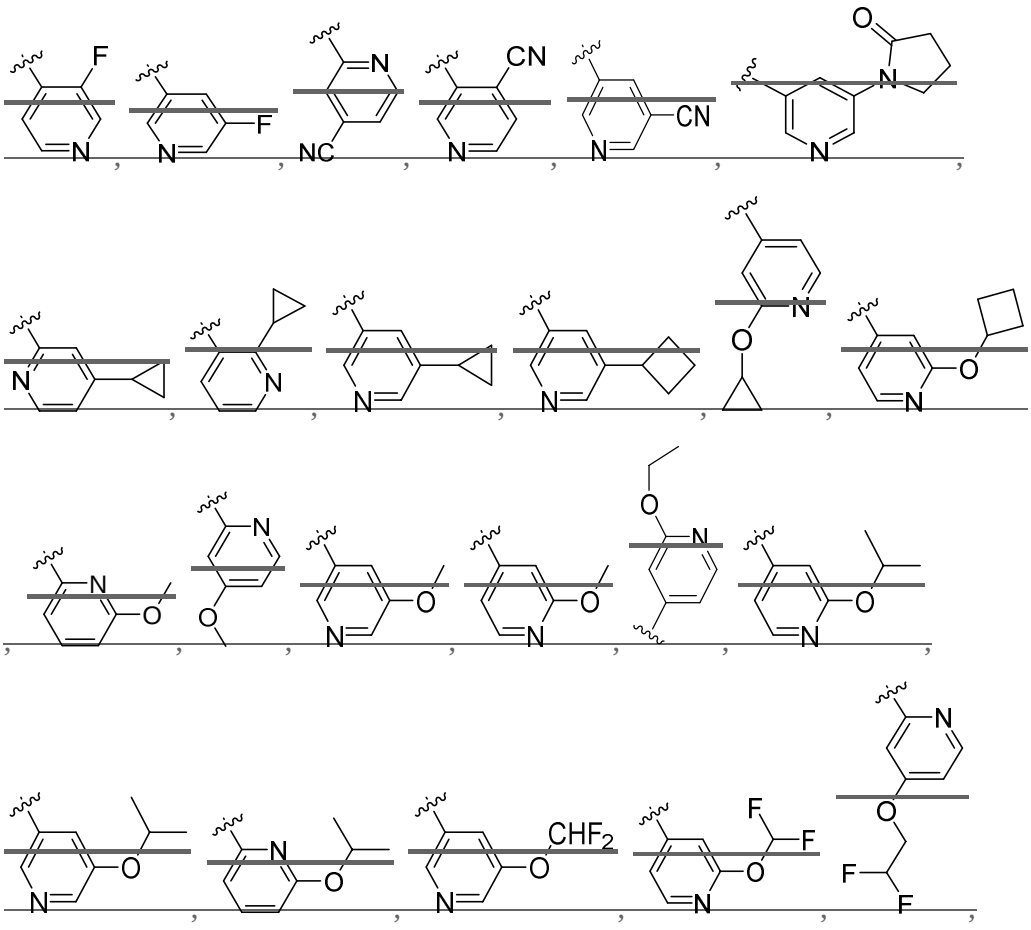
R^4 is pyridyl that is unsubstituted or substituted with 1 to 2 R^{4e} groups; and

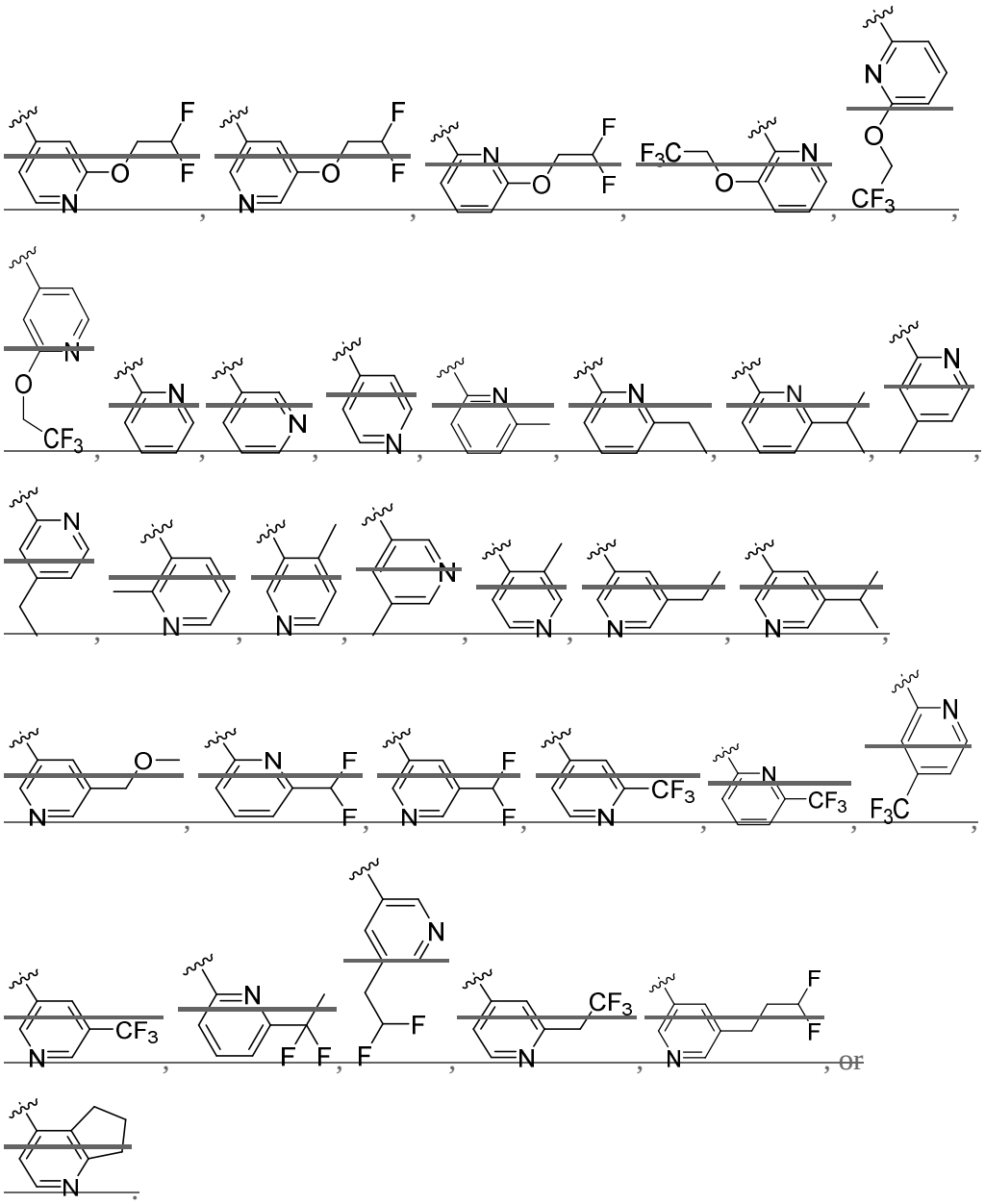
each R^{4e} group is independently fluorine, -CN, pyrrolidin-2-one, cyclopropyl, cyclobutyl, -O-cyclopropyl, -O-cyclobutyl, -OMe, -OEt, -O-isopropyl, $-OCHF_2$, $-OCH_2CHF_2$, $-OCH_2CF_3$, methyl, ethyl, isopropyl, $-CH_2OCH_3$, $-CHF_2$, $-CF_3$, $-C(CH_3)F_2$, $-CH_2CHF_2$, $-CH_2CF_3$, or $-CH_2CH_2CHF_2$;

alternatively, two R^{4e} groups attached to adjacent ring atoms can be combined to form a cyclopentyl,

wherein the pyridyl is unsubstituted at the para-position.

40. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87 to 89, or 91, or a pharmaceutically acceptable salt thereof, wherein R^4 is:





~~40. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87 or 88, or a pharmaceutically acceptable salt thereof, wherein~~

~~R^4 is pyridazinyl, pyrimidinyl, or pyrazinyl, wherein each is unsubstituted or substituted with one or two R^{4e} groups;~~

~~each R^{4e} is independently selected from -$C_{(3-4)}$cycloalkyl, -$OC_{(1-3)}$alkyl and -$C_{(1-4)}$alkyl, wherein the -$C_{(1-4)}$alkyl groups are unsubstituted or substituted with one to three fluorine atoms,~~

wherein the pyridazinyl, pyrimidinyl and pyrazinyl are unsubstituted at the para-position.

The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87, 88 or 93, or a pharmaceutically acceptable salt thereof, wherein

R^4 is pyridazinyl, pyrimidinyl, or pyrazinyl, wherein each is unsubstituted or substituted with one or two R^{4e} groups; and

each R^{4e} is independently selected from methyl, isopropyl, -OMe, cyclopropyl, $-CHF_2$, and $-CF_3$,

wherein the pyridazinyl, pyrimidinyl and pyrazinyl are unsubstituted at the para-position.

41. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87, 88, 93 or 94, or a pharmaceutically acceptable salt thereof, wherein R^4 is

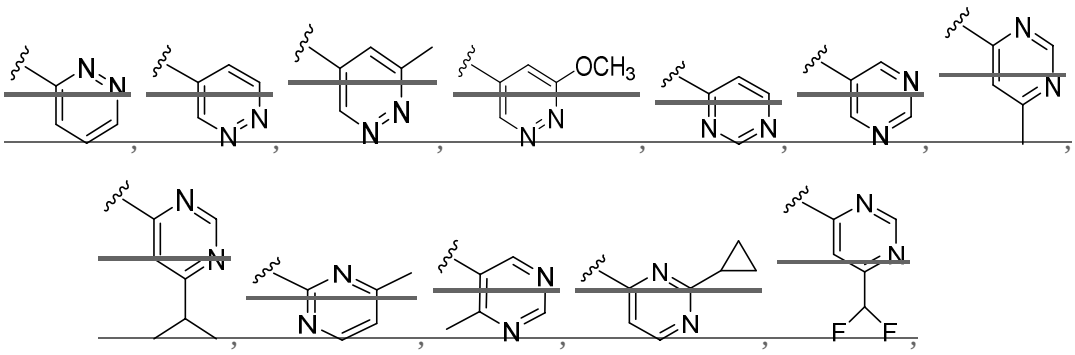
pyridazinyl unsubstituted or substituted with $-OCH_3$ or $-CH_3$,

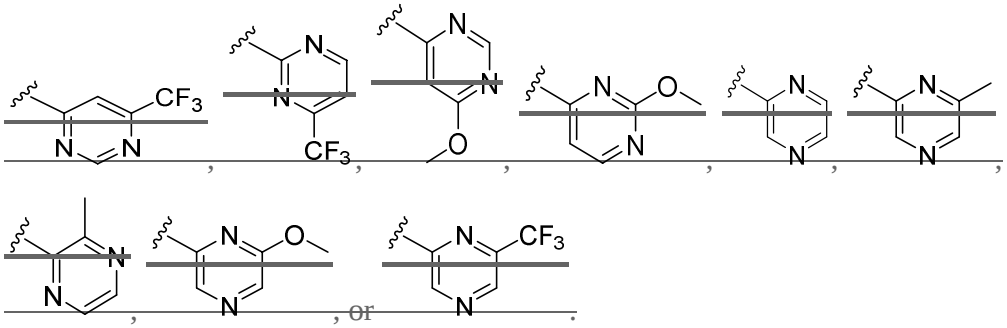
pyrimidinyl unsubstituted or substituted with methyl, isopropyl, $-OCH_3$, or cyclopropyl, wherein the methyl is unsubstituted or substituted with one to three fluorine atoms, or

pyrazinyl unsubstituted or substituted with $-OCH_3$, $-CH_3$, or $-CF_3$,

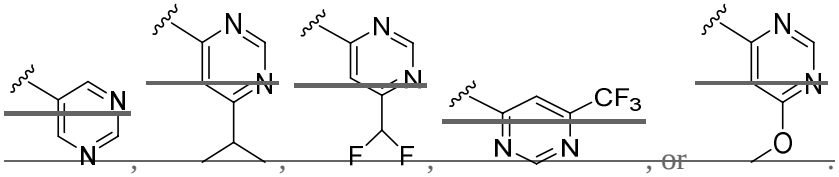
wherein the pyridazinyl, pyrimidinyl and pyrazinyl are unsubstituted at the para-position.

42. The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87, 88 or 93 to 95, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



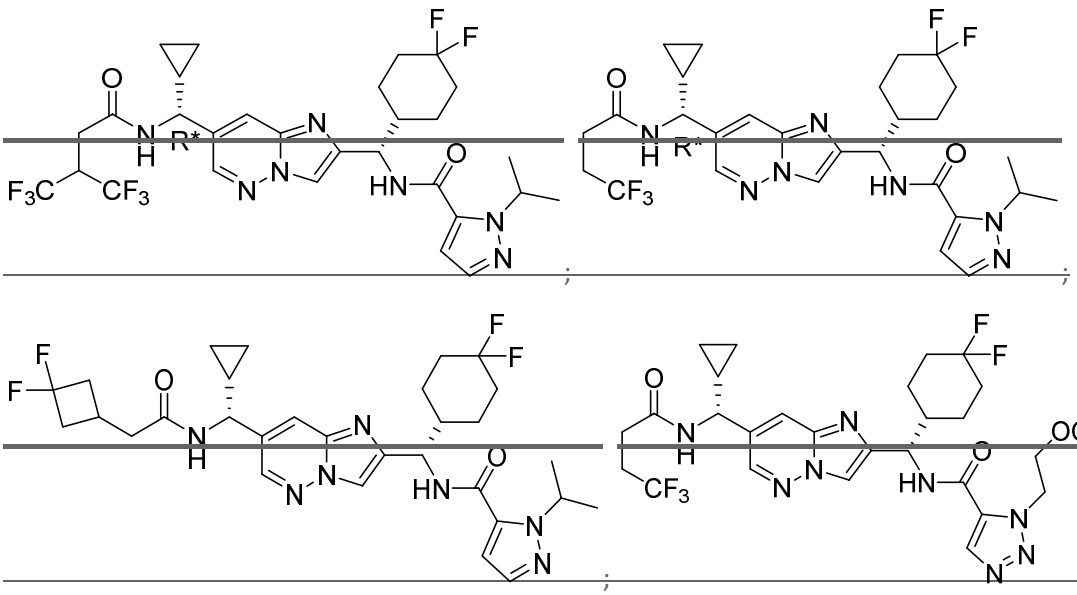


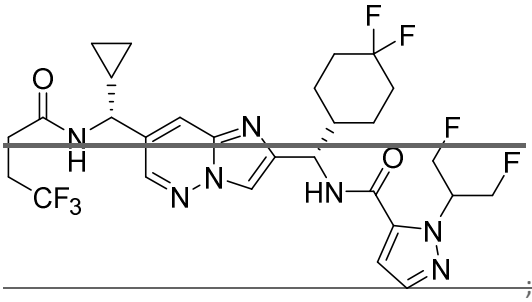
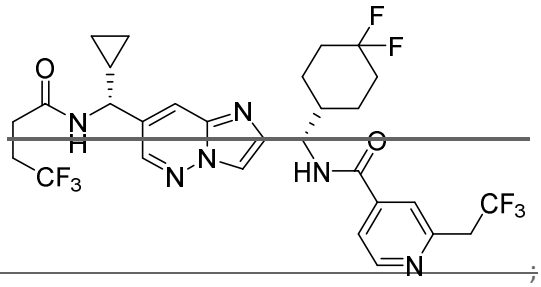
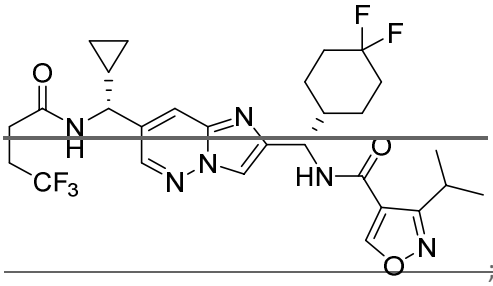
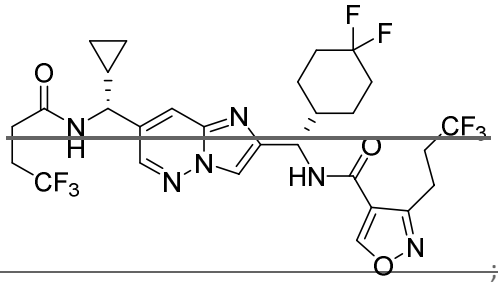
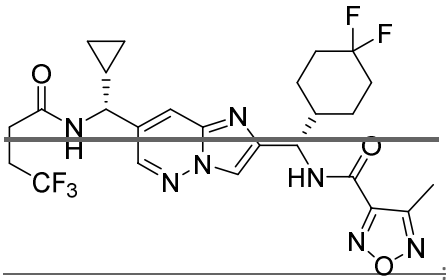
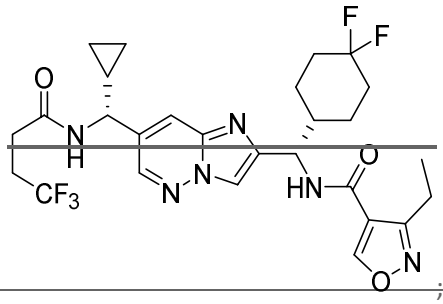
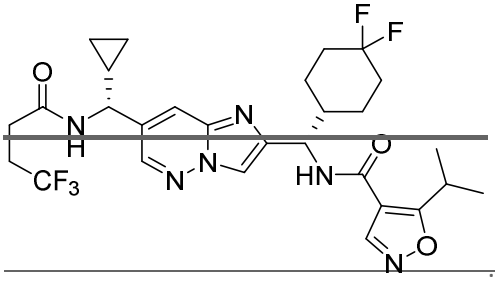
The compound of any one of claims 1, 2, 11 to 33, 46 to 49, 87, 88 or 93 to 96, or a pharmaceutically acceptable salt thereof, wherein R^4 is:



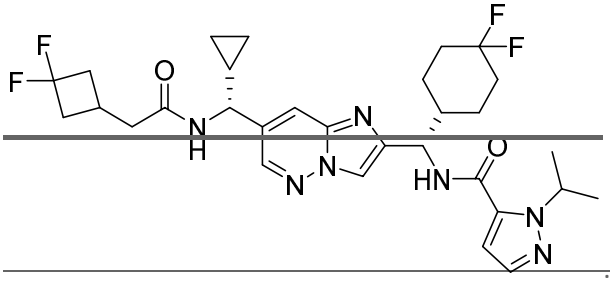
43. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, selected from the group consisting of the compounds in Table 1A, Table 1B, Table 1C, Table 1D, Table 1E, Table 1F, Table 1G, Table 1H, Table 1I and Table 1J.

43. The compound of claim 98, or a pharmaceutically acceptable salt thereof, selected from the group consisting of:

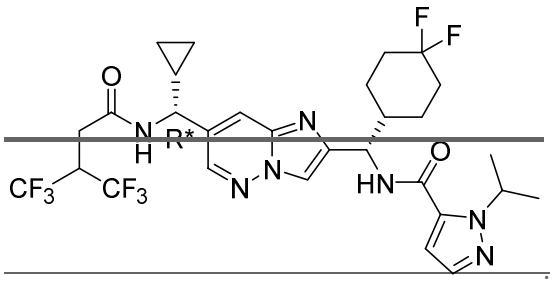



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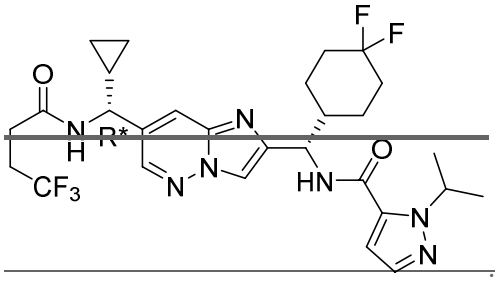
43. The compound of claim 98, or a pharmaceutically acceptable salt thereof, which is


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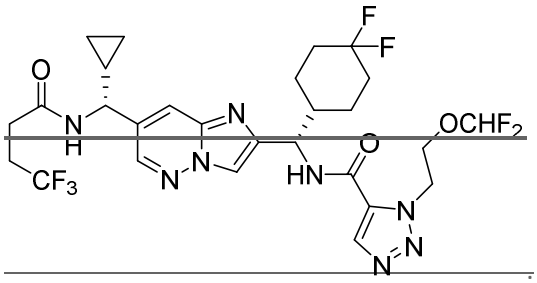
~~44. The compound of claim 98, or a pharmaceutically acceptable salt thereof, which is~~



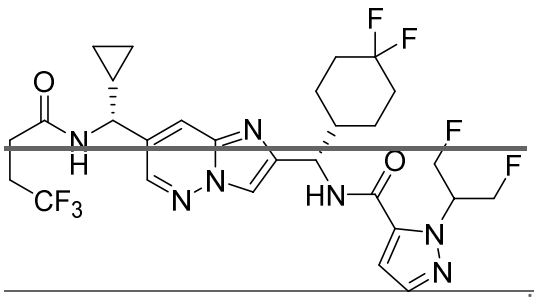
~~44. The compound of claim 98, or a pharmaceutically acceptable salt thereof, which is~~



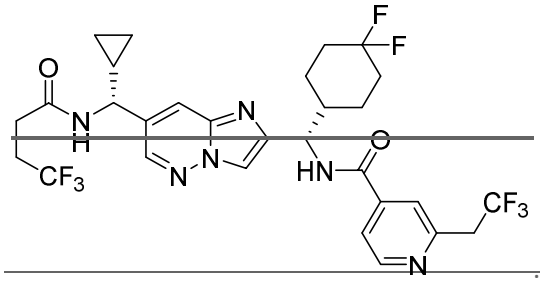
~~44. The compound of claim 98, or a pharmaceutically acceptable salt thereof, which is~~

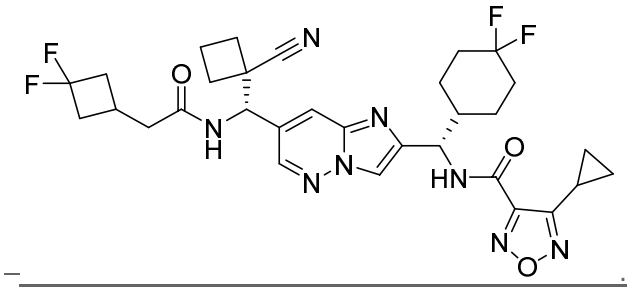


~~44. The compound of claim 98, or a pharmaceutically acceptable salt thereof, which is~~

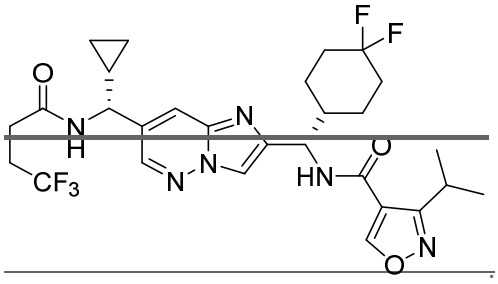


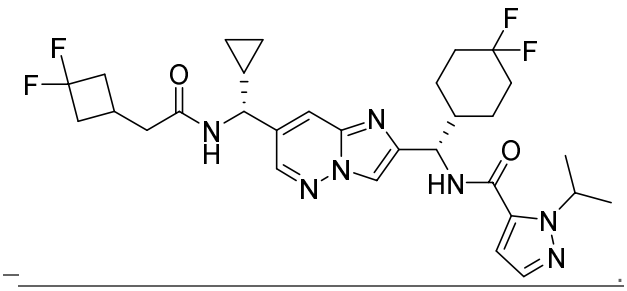
~~45.~~19. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



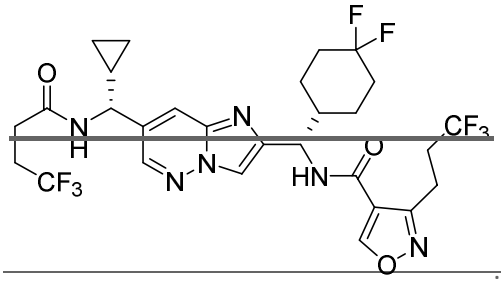


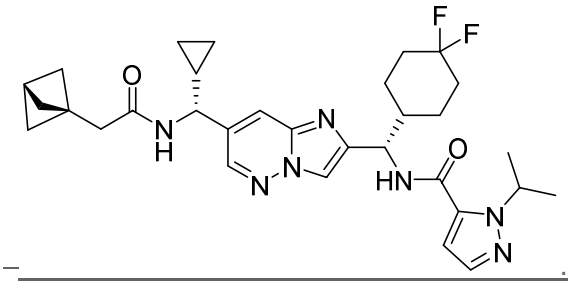
~~46.~~20. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



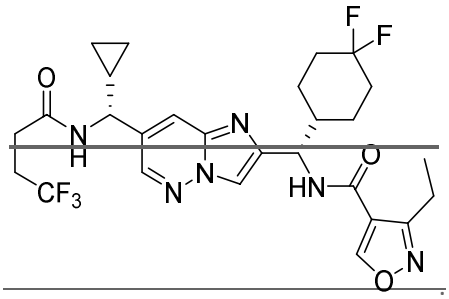


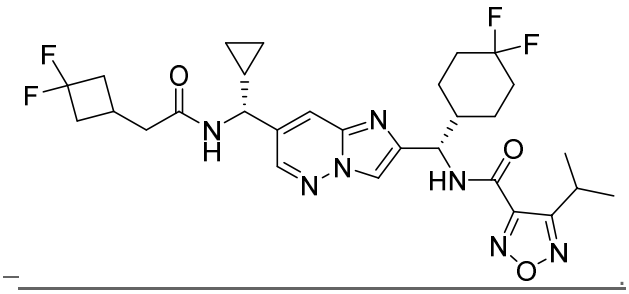
~~47.~~21. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



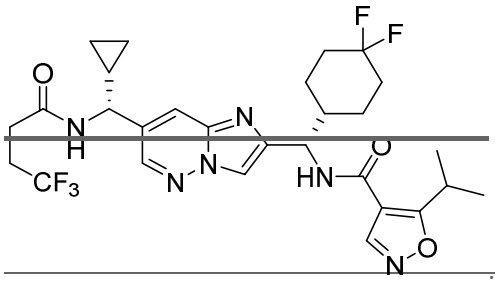


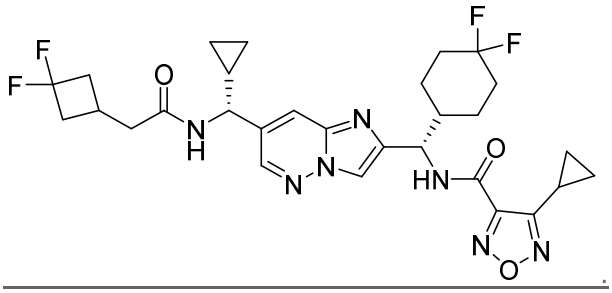
~~48.~~22. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



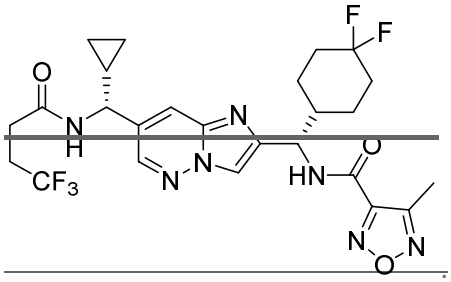


~~49.~~23. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:

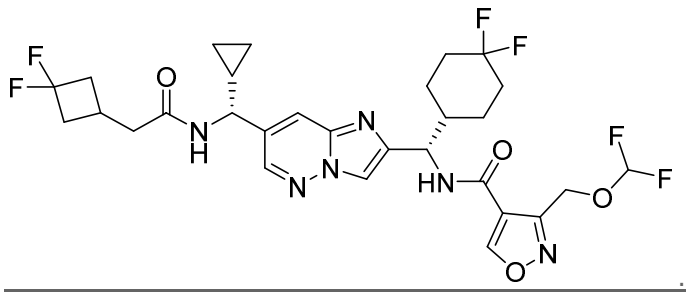




~~50.~~24. The compound of claim ~~98, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:

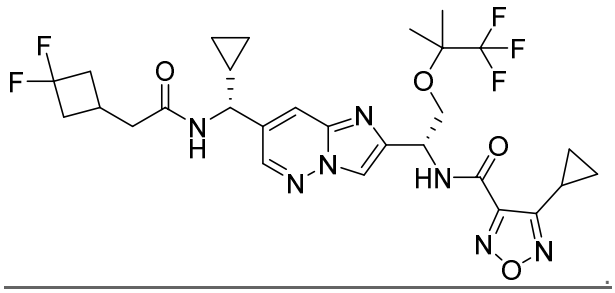


~~51. The compound of claim 2, or a pharmaceutically acceptable salt thereof, selected from the group consisting of the compounds in Table 2A, Table 2B, Table 2C, Table 2D, Table 2E, Table 2F, Table 2G, Table 2H, Table 2I, Table 2J, Table 2K, and Table 2M.~~



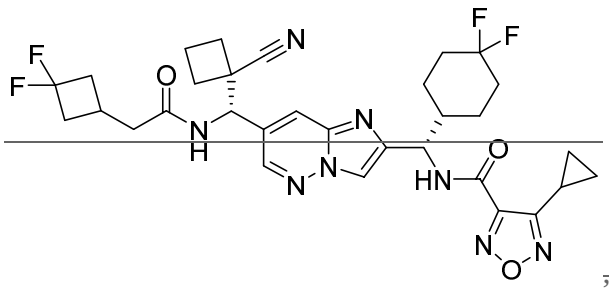
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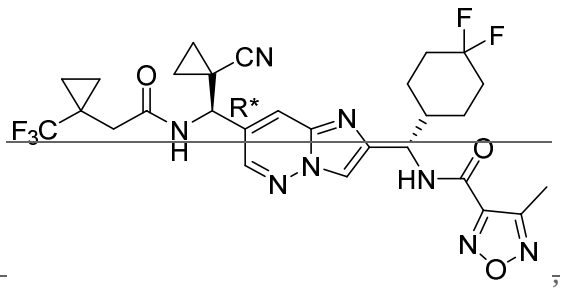
25. The compound of claim 1, having the following structure:

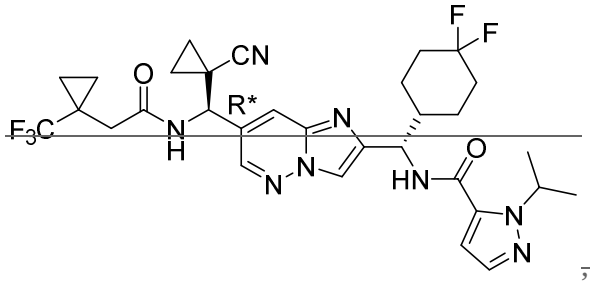


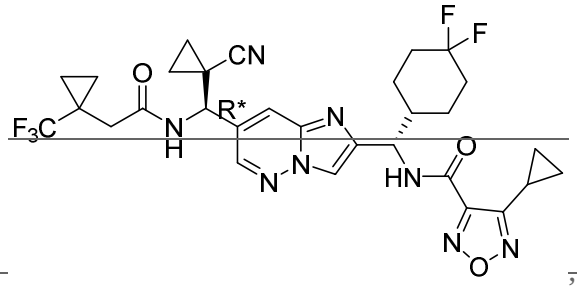
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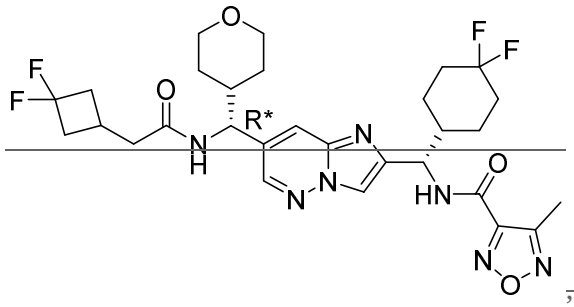
~~52.~~26. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, selected from the group consisting of~~1, having the following structure:

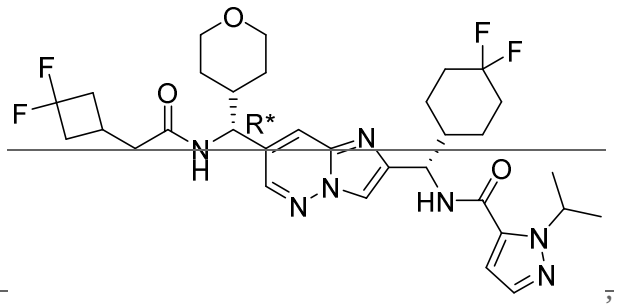


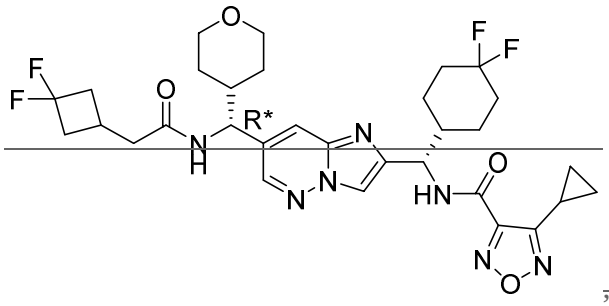


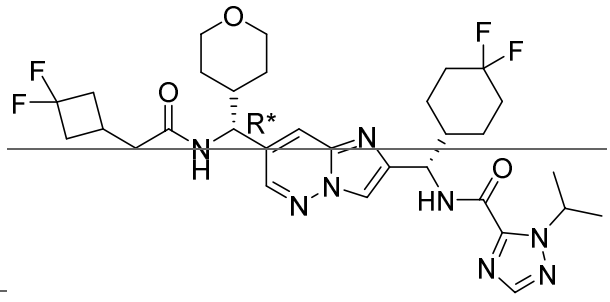


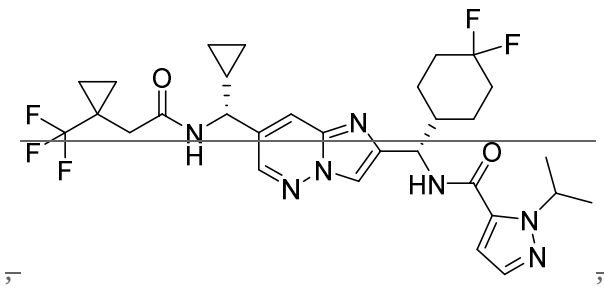


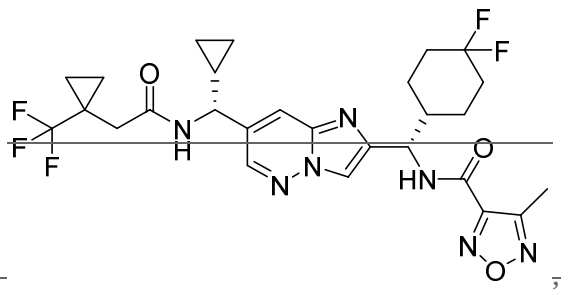


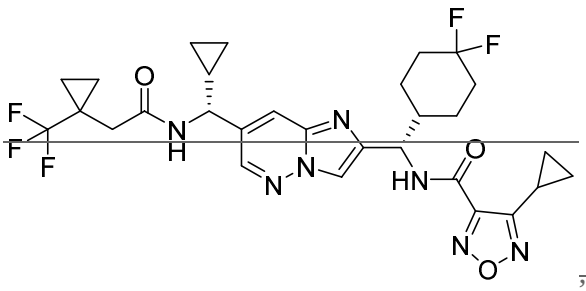


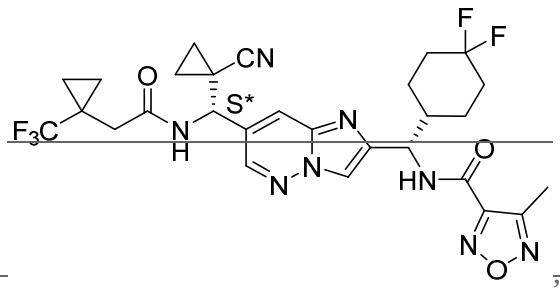


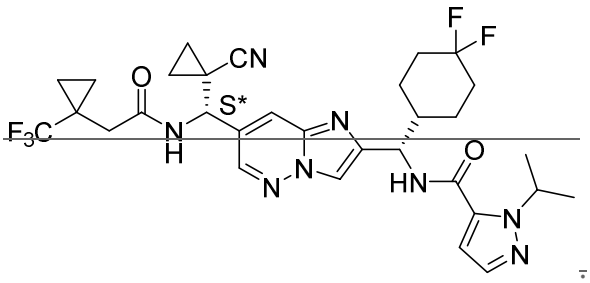


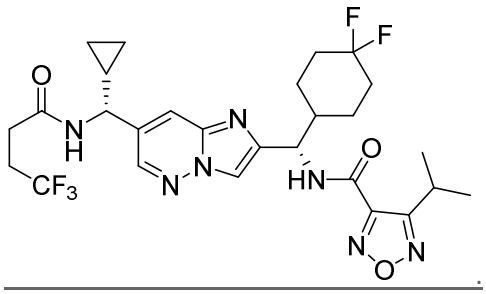




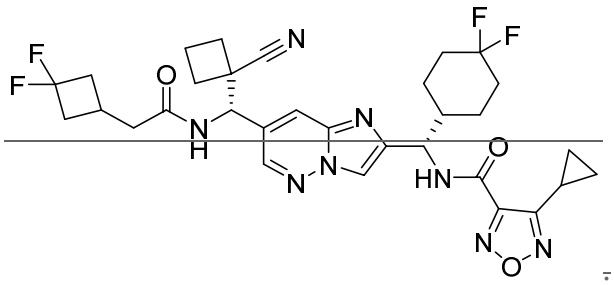

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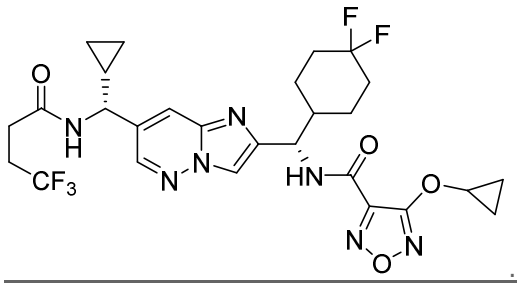

, and


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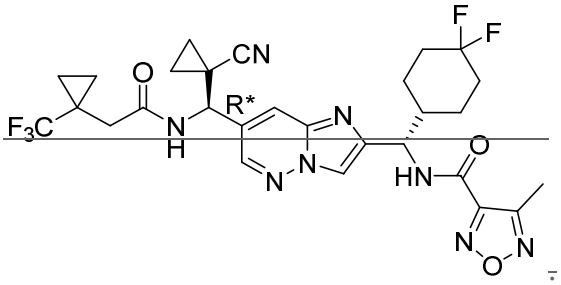

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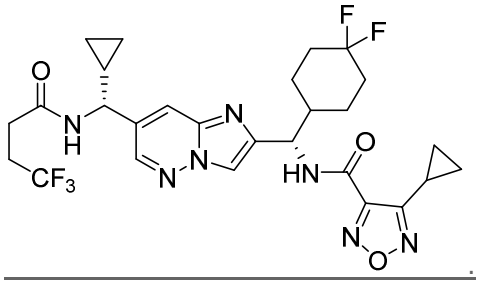
~~53.~~27. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:


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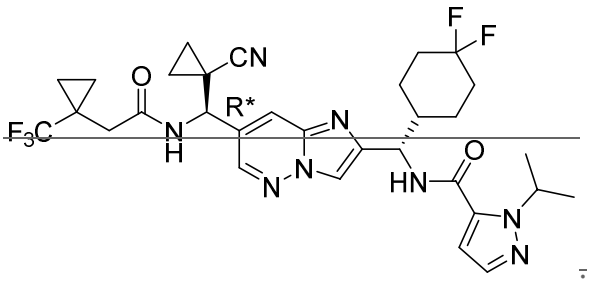


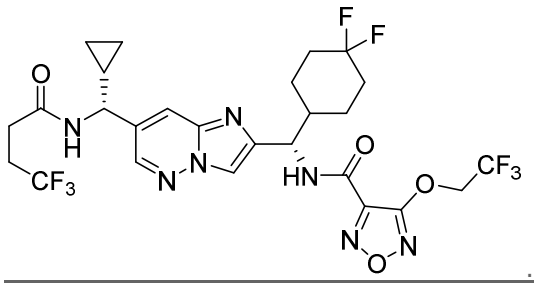
~~54.~~28. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



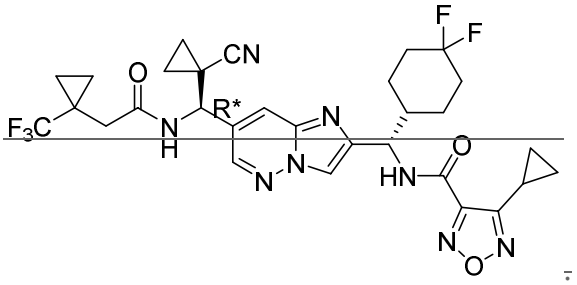


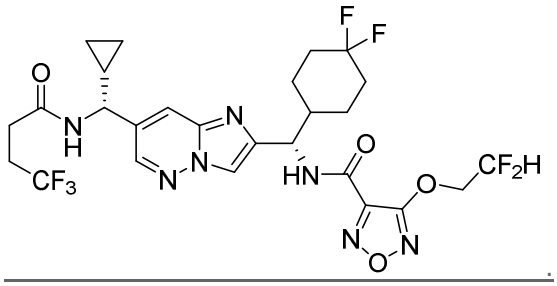
~~55.~~29. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



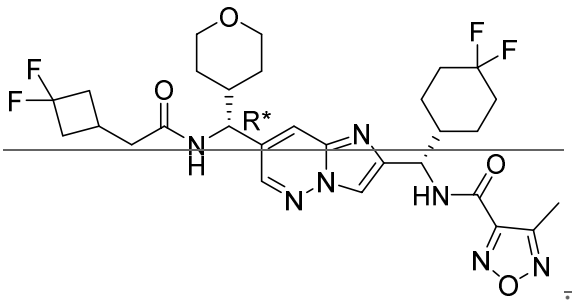


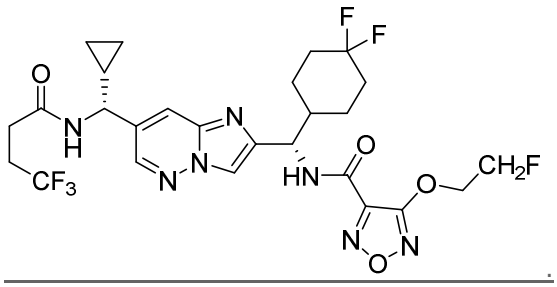
56.30. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is1, having the following structure:



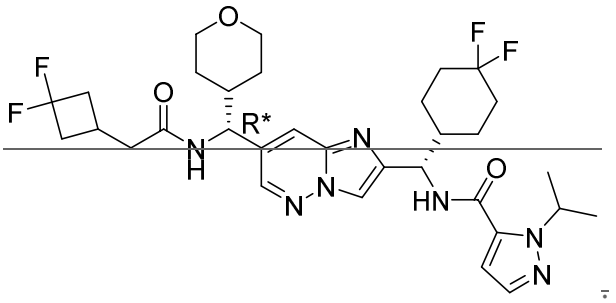


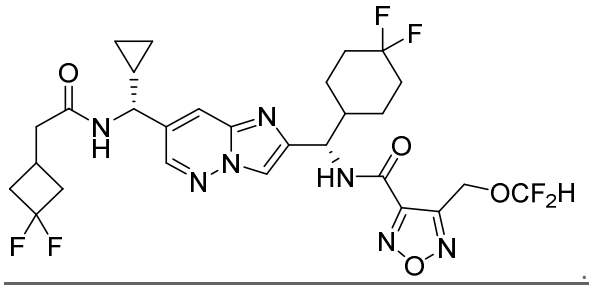
57.31. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is1, having the following structure:



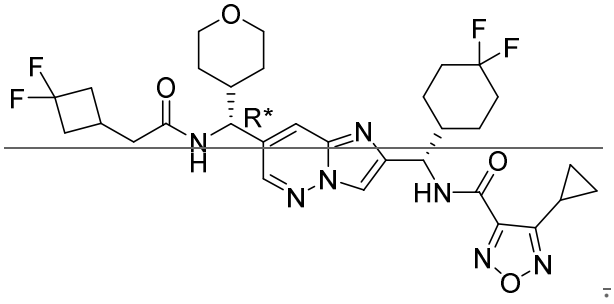


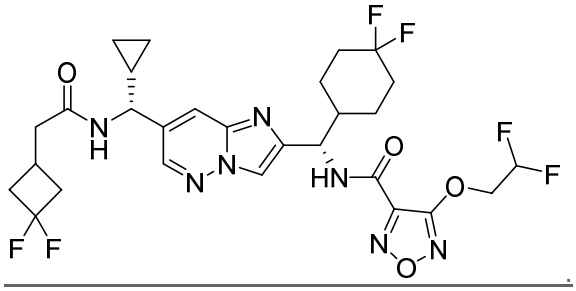
58.32. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is1, having the following structure:



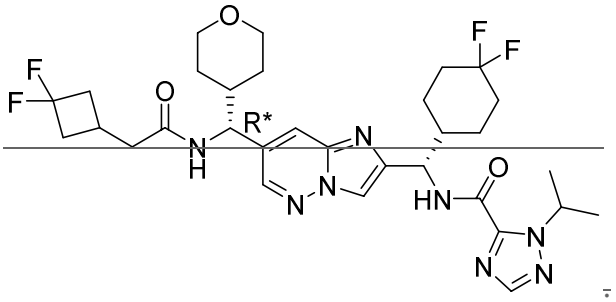


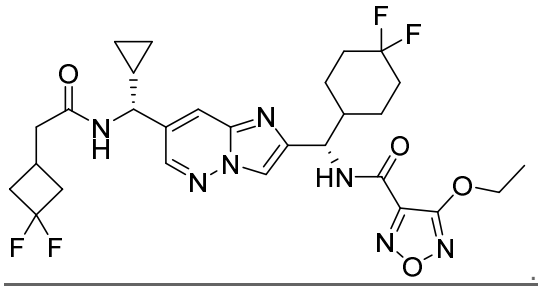
59.33. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is1, having the following structure:



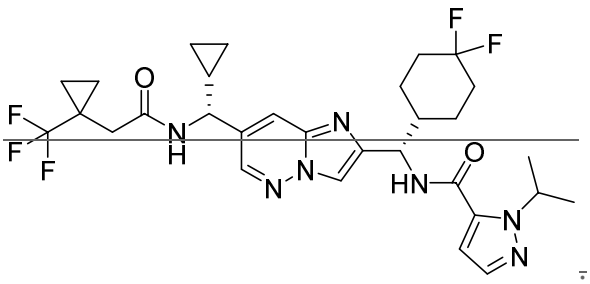


60.34. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:

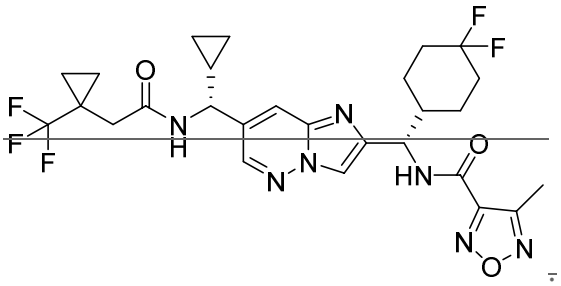




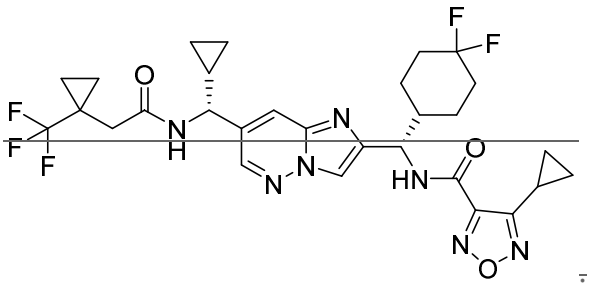
61.35. The compound of claim ~~111, or a pharmaceutically acceptable salt thereof, which is~~1, having the following structure:



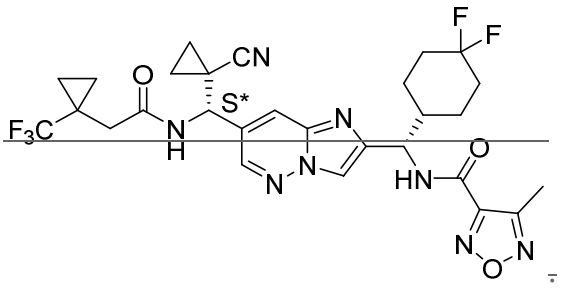
~~62. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is~~



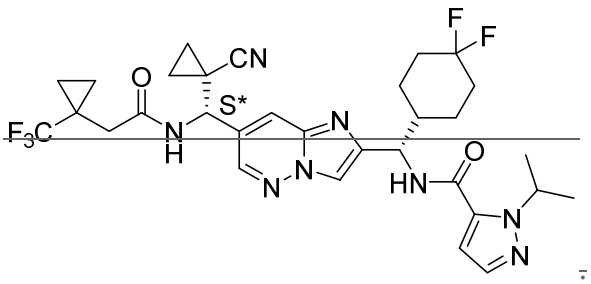
~~62. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is~~

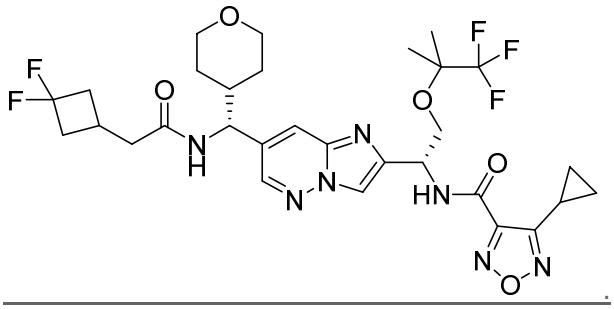


~~62. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is~~



~~62. The compound of claim 111, or a pharmaceutically acceptable salt thereof, which is~~





63.36. A pharmaceutical composition, comprising a compound of ~~any one of claims 1 to 125~~claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~64. A pharmaceutical composition made by mixing~~ Use of a compound of ~~any one of claims 1 to 125,~~claim 1 or a pharmaceutically acceptable salt thereof~~, and a pharmaceutically acceptable carrier.~~

~~65. The pharmaceutical composition of claim 126 or 127, which is administered orally.~~

~~66. The pharmaceutical composition of claim 128, which is administered as a tablet or a capsule.~~

~~67. A process~~ for ~~making a pharmaceutical composition comprising mixing a compound of any one of claims 1 to 125, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.~~

68.37. ~~A method for~~the manufacture of a medicament treating and/or ameliorating an IL-17A mediated inflammatory syndrome, disorder, or disease ~~comprising administering to a subject in need thereof a therapeutically effective amount of a compound of any one of claims 1 to 125, or a pharmaceutically acceptable salt thereof~~.

~~69.~~38. The ~~method~~use of claim ~~131~~37, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is selected from the group consisting of: psoriasis, psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, hidradenitis suppurativa, bullous pemphigold, atopic dermatitis, vitiligo, multiple sclerosis, asthma, uveitis, chronic obstructive pulmonary disorder, multiple myeloma, and systemic lupus erythematosus.

39. The ~~method~~use of claim ~~132~~37, wherein the compound, or pharmaceutically acceptable salt thereof, is to be administered orally.

40. The use of claim 37, wherein the compound, or pharmaceutically acceptable salt thereof, is to be administered as a tablet or a capsule.

~~70.~~41. The use of claim 37, wherein the IL-17A-mediated inflammatory syndrome, disorder, or disease is ~~psoriasis~~systemic lupus erythematosus.

~~71.~~42. The ~~method~~use of claim ~~132~~37, wherein the IL-17A-mediated inflammatory syndrome, disorder, or disease is psoriatic arthritis.

~~72.~~43. The ~~method~~use of claim ~~132~~37, wherein the IL-17A-mediated inflammatory syndrome, disorder, or disease is ~~rheumatoid arthritis~~psoriasis.

~~73. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is ankylosing spondylitis.~~

~~74. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is hidradenitis suppurativa.~~

~~75. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is bullous pemphigold.~~

~~76.~~44. ~~The method of claim 132, wherein the IL-17A~~-mediated inflammatory syndrome, disorder, or disease is atopic dermatitis.

45. The use of claim 37, wherein the compound, or a pharmaceutically acceptable salt thereof, is to be administered in combination with an additional therapeutic agent.

~~77.~~46. The ~~method~~use of claim ~~132~~37, wherein the ~~IL-17A mediated inflammatory syndrome, disorder, or disease is vitiligo~~compound, or a pharmaceutically acceptable salt thereof, and the additional therapeutic agent are to be administered concurrently.

~~78. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is multiple sclerosis.~~

~~79. The method of claim 132~~37, wherein the ~~IL-17A mediated inflammatory syndrome, disorder, or disease is systemic lupus erythematosus.~~

~~80. The method of claim 132, wherein~~compound, or a pharmaceutically acceptable salt thereof, and the ~~IL-17A mediated inflammatory syndrome, disorder, or disease is asthma.~~

~~81. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is uveitits.~~

~~82. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is chronic obstructive pulmonary disorder.~~

~~83. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is multiple myeloma.~~

~~84. The method of claim 132, wherein the IL-17A mediated inflammatory syndrome, disorder, or disease is systemic lupus erythematosus.~~

~~85. The method of any of claims 132 to 147, wherein the compound of any one of claims 1 to 125, or a pharmaceutically acceptable salt thereof, is administered orally.~~

~~86. The method of any of claims 132 to 148, wherein the compound of any one of claims 1 to 125, or a pharmaceutically acceptable salt thereof, is administered as a tablet or a capsule.~~

~~87. A compound as described herein.~~

~~88. A method as described herein.~~

47. additional therapeutic agent are to be administered sequentially.