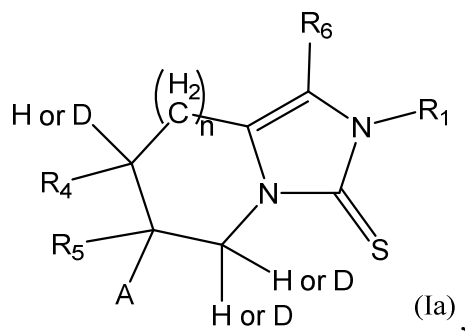


CLAIMS:

1. A compound of formula **Ia**, or a pharmaceutically acceptable salt or solvate thereof:



- 5 wherein:

R₁ is hydrogen, C₁-C₆ alkyl, partially or fully deuterated C₁-C₆ alkyl or C₃-C₆ cycloalkyl;

R₄ is hydrogen or C₁-C₃ alkyl;

R₅ is hydrogen;

or **R₄** and **R₅** combine, together with the carbon atoms to which they are attached, to form a

- 10 cyclopropyl ring;

R₆ is -COOH, -CHO, or -(CH₂)_m-X,

wherein:

m is 1, 2 or 3 and one -CH₂- moiety within -(CH₂)_m- may optionally be replaced by



- 15 **X** is hydroxy, C₁-C₃ alkoxy, cyano, -N=CH(NHCN)(NH₂), -NH-C(pyrrolidin-1-yl)=NCN, 5- or 6-membered heteroaryl optionally substituted with one methyl group, phenyl, -SO₂-R₇, -NR₈R₉, -CO₂R₁₀, -CH(CO₂R₁₀)₂, -CONR₁₁R₁₂ or -NR₁₃COR₁₄;

wherein:

R₇ is C₁-C₃ alkyl;

- 20 **R₈** is hydrogen or C₁-C₃ alkyl;

R₉ is hydrogen,

C₁-C₄ alkyl optionally substituted with up to three fluoro substituents or with one substituent selected from the group consisting of hydroxy, methylsulfonyl, C₃-C₆ cycloalkyl, phenyl, 5- or 6-membered

- 25 heterocyclyl and 5- or 6-membered heteroaryl optionally substituted with one methyl substituent,

C₃-C₆ cycloalkyl,

5- or 6-membered heteroaryl, or
 5- or 6-membered heterocyclyl optionally substituted with one or two
 oxo substituents;
 or **R₈** and **R₉** combine together with the N atom to which they are attached to
 5 form a
 5- or 6-membered N-heterocyclyl group optionally substituted with
 one substituent selected from methyl, trifluoromethyl, hydroxy,
 hydroxymethyl, methoxymethyl, methylsulfonyl, amido, (N,N-
 dimethyl)acetamide and pyridyl or with one or two substituents
 10 selected from fluoro and oxo, or a
 9- or 10-membered heterospirocyclyl group;
R₁₀ is hydrogen or C₁-C₃ alkyl;
R₁₁ is hydrogen or C₁-C₃ alkyl;
R₁₂ is hydrogen,
 15 C₁-C₄ alkyl optionally substituted with up to three fluoro substituents
 or with one substituent selected from the group consisting of cyano,
 hydroxy, methylsulfonyl, C₁-C₂ alkoxy, dimethylamino, C₃-C₆
 cycloalkyl, phenyl, 5- or 6-membered heteroaryl optionally substituted
 with one methyl substituent and 5- or 6-membered heterocyclyl
 20 optionally substituted with one t-Boc group or with one or two fluoro
 substituents,
 C₃-C₆ cycloalkyl optionally substituted with one substituent selected
 from the group consisting of cyano, hydroxy, hydroxymethyl and oxo,
 cyano,
 25 methylsulfonyl,
 CH₂COO(C₁-C₃ alkyl),
 5- or 6-membered heteroaryl optionally substituted with one methyl
 substituent,
 4-, 5- or 6-membered heterocyclyl optionally substituted with one or
 30 two substituents selected from oxo and methyl,
 CH₂CH(NH₂)(COOH), or
 CH(CH₃)CONH₂;
 or **R₁₁** and **R₁₂** combine together with the N atom to which they are attached to
 form a

5- or 6-membered N-heterocyclyl group optionally substituted with one substituent selected from monofluoromethyl, trifluoromethyl, hydroxy, hydroxymethyl, methoxymethyl, methylsulfonyl, cyano, amido, (N,N-dimethyl)acetamide and pyridyl, or with one or two substituents selected from fluoro, methyl and oxo, or optionally fused to a cyclopropyl ring which may be substituted with one or two methyl substituents, or a

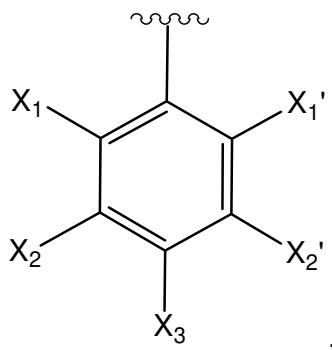
9- or 10-membered heterospirocyclyl group;

R₁₃ is hydrogen or C₁-C₃ alkyl;

R₁₄ is C₁-C₄ alkyl optionally substituted with up to three fluoro substituents or with one substituent selected from the group consisting of hydroxy, methylsulfonyl, C₃-C₆ cycloalkyl and phenyl, C₃-C₆ cycloalkyl, 5- or 6-membered heteroaryl, or

5- or 6-membered heterocyclyl optionally substituted with one or two oxo substituents;

A is C₅-C₇ cycloalkyl, furanyl, thiophenyl, methylthiophenyl or



wherein:

X₁ is hydrogen, halo or methyl;

X₁' is hydrogen or halo;

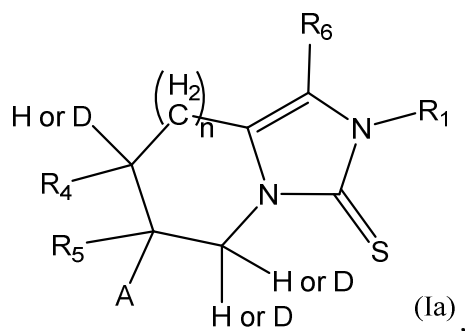
X₂ is hydrogen, halo or methyl;

X₂' is hydrogen or halo;

X₃ is hydrogen or fluoro;

n is 0 or 1, and when **n** is 0 a single bond joins the carbon atoms to which the CH₂ moiety would be attached when **n** is 1 for use in therapy.

2. A compound of formula **Ia**, or a pharmaceutically acceptable salt or solvate thereof:



wherein:

R₁ is hydrogen, C₁-C₆ alkyl, partially or fully deuterated C₁-C₆ alkyl or C₃-C₆ cycloalkyl;

5 **R₄** is hydrogen or C₁-C₃ alkyl;

R₅ is hydrogen;

or **R₄** and **R₅** combine, together with the carbon atoms to which they are attached, to form a cyclopropyl ring;

R₆ is -COOH, -CHO, or -(CH₂)_m-X,

10 wherein:

m is 1, 2 or 3 and one -CH₂- moiety within -(CH₂)_m- may optionally be replaced by



X is hydroxy, C₁-C₃ alkoxy, cyano, -N=CH(NHCN)(NH₂), -NH-C(pyrrolidin-1-yl)=NCN, 5- or 6-membered heteroaryl optionally substituted with one methyl group, phenyl, -SO₂-R₇, -NR₈R₉, -CO₂R₁₀, -CH(CO₂R₁₀)₂, -CONR₁₁R₁₂ or -NR₁₃COR₁₄;

15

wherein:

R₇ is C₁-C₃ alkyl;

R₈ is hydrogen or C₁-C₃ alkyl;

R₉ is hydrogen,

20

C₁-C₄ alkyl optionally substituted with up to three fluoro substituents or with one substituent selected from the group consisting of hydroxy, methylsulfonyl, C₃-C₆ cycloalkyl, phenyl, 5- or 6-membered heterocyclyl and 5- or 6-membered heteroaryl optionally substituted with one methyl substituent,

25

C₃-C₆ cycloalkyl,
5- or 6-membered heteroaryl, or

5- or 6-membered heterocyclyl optionally substituted with one or two oxo substituents;

or **R₈** and **R₉** combine together with the N atom to which they are attached to form a

5 5- or 6-membered N-heterocyclyl group optionally substituted with one substituent selected from methyl, trifluoromethyl, hydroxy, hydroxymethyl, methoxymethyl, methylsulfonyl, amido, (N,N-dimethyl)acetamide and pyridyl or with one or two substituents selected from fluoro and oxo, or a

10 9- or 10-membered heterospirocyclyl group;

R₁₀ is hydrogen or C₁-C₃ alkyl;

R₁₁ is hydrogen or C₁-C₃ alkyl;

R₁₂ is hydrogen,

15 C₁-C₄ alkyl optionally substituted with up to three fluoro substituents or with one substituent selected from the group consisting of cyano, hydroxy, methylsulfonyl, C₁-C₂ alkoxy, dimethylamino, C₃-C₆ cycloalkyl, phenyl, 5- or 6-membered heteroaryl optionally substituted with one methyl substituent and 5- or 6-membered heterocyclyl optionally substituted with one t-Boc group or with one or two fluoro substituents,

20 C₃-C₆ cycloalkyl optionally substituted with one substituent selected from the group consisting of cyano, hydroxy, hydroxymethyl and oxo, cyano, methylsulfonyl,

25 CH₂COO(C₁-C₃ alkyl),

 5- or 6-membered heteroaryl optionally substituted with one methyl substituent,

 4-, 5- or 6-membered heterocyclyl optionally substituted with one or two substituents selected from oxo and methyl,

30 CH₂CH(NH₂)(COOH), or

 CH(CH₃)CONH₂;

or **R₁₁** and **R₁₂** combine together with the N atom to which they are attached to form a

5- or 6-membered N-heterocyclyl group optionally substituted with one substituent selected from monofluoromethyl, trifluoromethyl, hydroxy, hydroxymethyl, methoxymethyl, methylsulfonyl, cyano, amido, (N,N-dimethyl)acetamide and pyridyl, or with one or two substituents selected from fluoro, methyl and oxo, or optionally fused to a cyclopropyl ring which may be substituted with one or two methyl substituents, or a

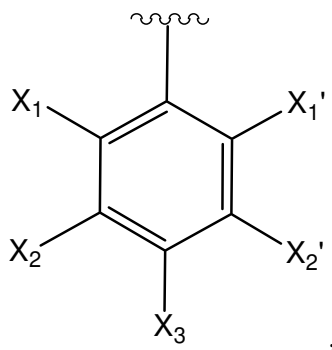
9- or 10-membered heterospirocyclyl group;

R₁₃ is hydrogen or C₁-C₃ alkyl;

R₁₄ is C₁-C₄ alkyl optionally substituted with up to three fluoro substituents or with one substituent selected from the group consisting of hydroxy, methylsulfonyl, C₃-C₆ cycloalkyl and phenyl, C₃-C₆ cycloalkyl, 5- or 6-membered heteroaryl, or

5- or 6-membered heterocyclyl optionally substituted with one or two oxo substituents;

A is C₅-C₇ cycloalkyl, furanyl, thiophenyl, methylthiophenyl or



wherein:

X₁ is hydrogen, halo or methyl;

X₁' is hydrogen or halo;

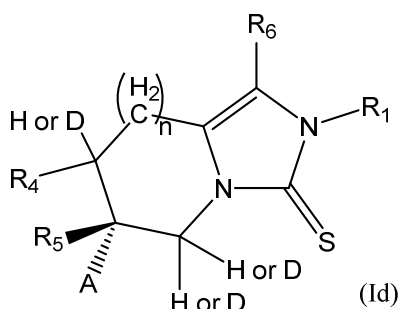
X₂ is hydrogen, halo or methyl;

X₂' is hydrogen or halo;

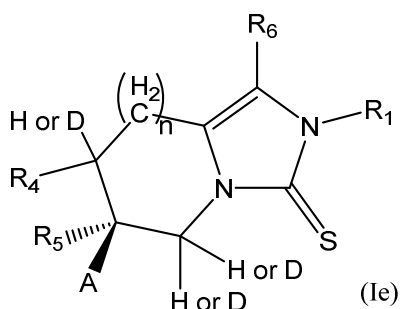
X₃ is hydrogen or fluoro;

n is 0 or 1, and when **n** is 0 a single bond joins the carbon atoms to which the CH₂ moiety would be attached when **n** is 1.

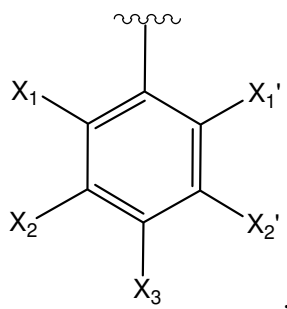
3. A compound for use in therapy according to claim 1, or a compound according to claim 2, wherein **n** is 0.
4. A compound for use in therapy according to claims 1 or 3, or a compound according to claims 2 or 3, wherein **R₄** and **R₅** combine, together with the carbon atom to which they are attached, to form a cyclopropyl ring.
5. A compound for use in therapy according to claims 1 or 3 to 4, or a compound according to claims 2 to 4, wherein more than 50% of substituents **R₅** and **A** have the stereochemical configuration of formula **Id**



6. A compound for use in therapy according to claims 1 or 3 to 4, or a compound according to claims 2 to 4, wherein more than 50% of substituents **R₅** and **A** have the stereochemical configuration of formula **Ie**



7. A compound for use in therapy according to claims 1 or 3 to 6, or a compound according to claims 2 to 6, wherein **A** is



wherein **X**₁, **X**₁', **X**₂, **X**₂' and **X**₃ are as defined in claim 1.

8. A compound for use in therapy according to claims 1 or 3 to 7, or a compound
5 according to claims 2 to 7, wherein **R**₁ is hydrogen, methyl or *d*3-methyl.
9. A compound for use in therapy according to claims 1, 3 or 5 to 8, or a compound
according to claims 2, 3 or 5 to 8, wherein **R**₄ is hydrogen or methyl.
10. A compound for use in therapy according to claims 1, 3 or 5 to 9, or a compound
according to claims 2, 3 or 5 to 9, wherein **R**₅ is hydrogen.
11. A compound for use in therapy according to claims 1 or 3 to 10, or a compound
according to claims 2 to 10, wherein **R**₆ is -COOH, -CHO,
15 or -(CH₂)_m-X,
wherein:
m is 1, 2 or 3 and one -CH₂- moiety within -(CH₂)_m- may optionally be replaced by

X is hydroxy, ethoxy, cyano, -N=C(NHCN)(NH₂), -NH-C(pyrrolidin-1-yl)=NCN, 1-
20 methylimidazol-2-yl, 3-methyl-1,2,4-oxadiazol-5-yl, tetrazol-5-yl, pyridin-2-yl,
pyridin-3-yl, pyridin-4-yl, phenyl,
-SO₂-R₇, -NR₈R₉, -COOR₁₀, -CH(COOR₁₀)₂, -CONR₁₁R₁₂ or -NR₁₃COR₁₄;
wherein:
R₇ is methyl;
25 **R**₈ is hydrogen or methyl;
R₉ is hydrogen, methyl, cyclopropylmethyl, benzyl, 2-hydroxyethyl, 2,2,2-
trifluoroethyl, 2-methylsulfonyl, 1-cyclohexylethyl, isopropyl, butyl,
cyclopropyl, cyclobutyl, cyclopentyl, tetrahydrofuran-3-yl, (tetrahydrofuran-2-

yl)methyl, (1,1-dioxido)tetrahydrothiopyran-4-yl, (tetrahydro-2*H*-pyran-4-yl)methyl, pyridin-2-yl, pyridin-3-yl, tetrahydropyran-3-yl, cyclohexyl, (pyridin-2-yl)methyl or (1-methylpyrazol-4-yl)methyl;

or **R₈** and **R₉** combine together with the N atom to which they are attached to form a pyrrolidinyl, piperidinyl, 4-methylsulfonyl-piperidinyl, 4,4-difluoropiperidinyl or morpholinyl group;

R₁₀ is hydrogen, methyl or ethyl;

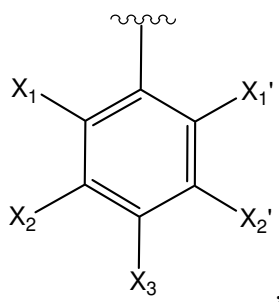
R₁₁ is hydrogen or methyl;

R₁₂ is hydrogen, methyl, cyanomethyl, cyclopropylmethyl, benzyl, (pyridin-2-yl)methyl, (pyridin-3-yl)methyl, (N-*t*-Boc-pyrrolidin-2-yl)methyl, 2-hydroxyethyl, 2-methoxyethyl, 2,2,2-trifluoroethyl, 2-methylsulfonyl-ethyl, 1-cyclohexylethyl, 2-(pyridin-2-yl)ethyl, 2-(1*H*-pyrazol-1-yl)ethyl, 2-(4,4-difluoropiperidin-1-yl)ethyl, propyl, isopropyl, 3-(*N,N*-dimethylamino)propyl, 3-(morpholin-1-yl)propyl, butyl, cyclopropyl, 1-cyanocyclopropyl, cyclobutyl, cyclopentyl, 2-hydroxycyclopentyl, 2-hydroxymethylcyclopentyl, 2-oxocyclopentyl, cyclohexyl, 2-hydroxycyclohexyl, 4-hydroxycyclohexyl, cyano, methylsulfonyl, CH₂COOEt, tetrahydrofuran-3-yl, 2-oxotetrahydrofuran-3-yl, tetrahydropyran-3-yl, tetrahydropyran-4-yl, (1,1-dioxido)tetrahydrothiopyran-4-yl, 1,3,4-thiadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, CH₂CH(NH₂)(COOH), CH(CH₃)CONH₂, oxazol-2-yl, (pyrazine-2-yl)methyl, oxetan-3-yl, (tetrahydrofuran-2-yl)methyl, (1-methylpyrazol-4-yl)methyl, thiazol-2-yl, 2-oxopyrrolidin-3-yl, 2-cyanocyclopentyl, isoxazol-4-yl, 3-methyl-1,2,4-oxadiazol-5-yl, (tetrahydropyran-4-yl)methyl, 2-oxopiperidin-3-yl, 1-methylpyrazol-4-yl, isothiazol-4-yl, 1-methyl-2-oxopiperidin-5-yl, 1-methyl-2-oxopyrrolidin-3-yl, 1-methyl-5-oxopyrrolidin-3-yl or 1-methyl-2-oxopyrrolidin-4-yl;

or **R₁₁** and **R₁₂** combine together with the N atom to which they are attached to form a pyrrolidinyl, 2-hydroxymethyl-pyrrolidinyl, 2-methoxymethyl-pyrrolidinyl, 2-trifluoromethyl-pyrrolidinyl, 3-(fluoromethyl)pyrrolidinyl, 3-methylsulfonyl-pyrrolidinyl, *N,N*-dimethylpyrrolidinyl-3-carboxamide, piperidinyl, 3-hydroxy-piperidinyl, 4-hydroxy-piperidinyl, 4-methyl-piperidinyl, 4-hydroxymethyl-piperidinyl, 4-amido-piperidinyl, 4-methylsulfonyl-piperidinyl, 4,4-difluoro-piperidinyl, *N,N*-dimethylpiperidinyl-4-carboxamide, N4-methyl-piperazinyl, N4-(*N,N*-dimethyl)acetamide-

5 piperazinyl, N4-(pyridine-2-yl)piperazinyl, morpholinyl, thiomorpholinyl, 1-
 oxidothiomorpholinyl, 1,1-dioxidothiomorpholinyl, 2-oxa-7-
 azaspiro[4.4]nonanyl, 2-oxa-8-azaspiro[4.5]decanyl, 1,4-dioxa-8-
 azaspiro[4.5]decanyl group, 6,6-dimethyl-3-azabicyclo[3.1.0]hexanyl,
 10 piperazinyl, 3-oxopiperazinyl, 4-methyl-3-oxopiperazinyl, 2-
 cyanopyrrolidinyl, 3-cyanopyrrolidinyl, 3-fluoromethylpyrrolidinyl or 3-(N,N-
 dimethylacetamide)pyrrolidinyl;
R₁₃ is hydrogen or methyl;
R₁₄ is cyclopropyl, cyclopentyl, pyrrolidin-1-yl, tetrahydropyran-4-yl or
 pyridin-3-yl.

12. A compound for use in therapy according to claims 1 or 3 to 11, or a compound
 according to claims 2 to 11, wherein **A** is



15 wherein:
X₁ is hydrogen, fluoro, chloro or methyl;
X₁' is hydrogen, fluoro or chloro;
X₂ is hydrogen, fluoro, chloro, bromo or methyl;
X₂' is hydrogen, fluoro, chloro or bromo;
 20 **X₃** is hydrogen or fluoro.

13. A compound of formula **Ia**, as defined in any one of claims 2 to 12, or a
 pharmaceutically acceptable salt or solvate thereof, for use in the treatment of conditions
 ameliorated by inhibition of dopamine-beta-hydroxylase outside the central nervous system.

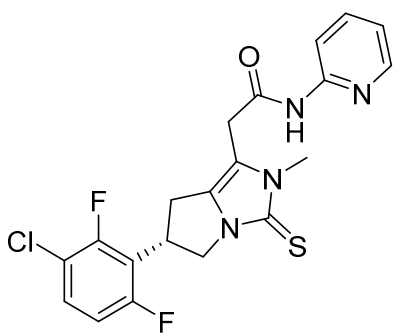
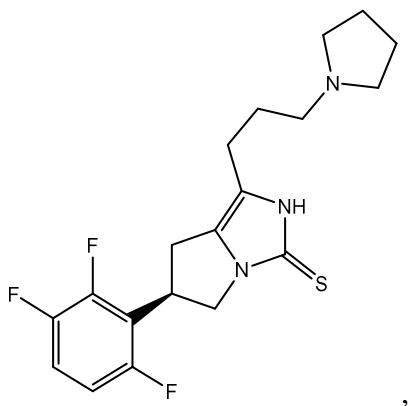
25 14. Use of a compound of formula **Ia**, as defined in any one of claims 2 to 12, or a
 pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for
 treatment of conditions ameliorated by inhibition of dopamine-beta-hydroxylase outside the
 central nervous system.

15. A pharmaceutical composition comprising (i) a therapeutically effective amount of a compound of formula **Ia**, as defined in any one of claims 2 to 12, or a pharmaceutically acceptable salt or solvate thereof; and (ii) a pharmaceutically acceptable excipient.

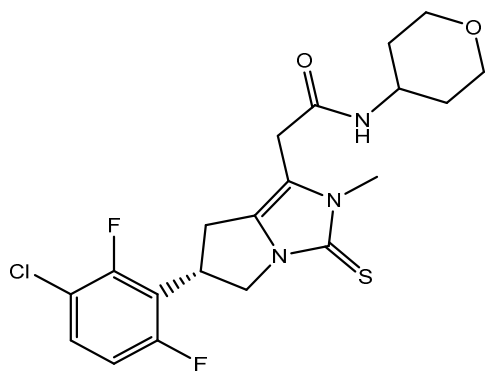
16. A compound of formula **Ia**, as defined in any one of claims 2 to 5 or 7 to 12, or a pharmaceutically acceptable salt or solvate thereof, with the proviso that the compound (*S*)-1-benzyl-6-(3,5-difluorophenyl)-6,7-dihydro-2*H*-pyrrolo[1,2-*c*]imidazole-3(5*H*)-thione is excluded.

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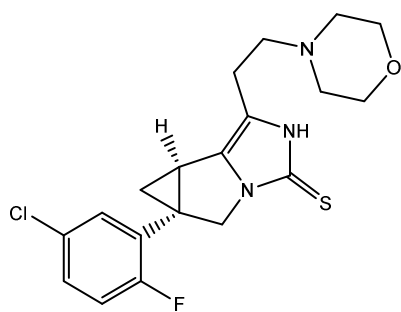
17. A compound according to claim 2, wherein the compound is selected from the group consisting of:



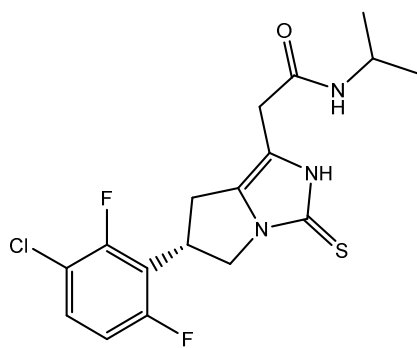
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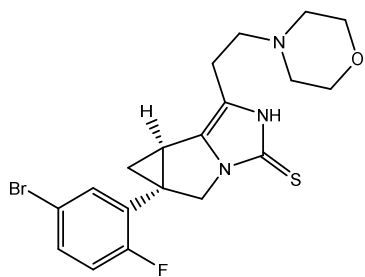


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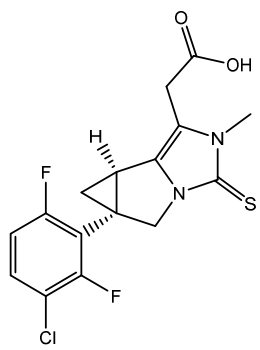
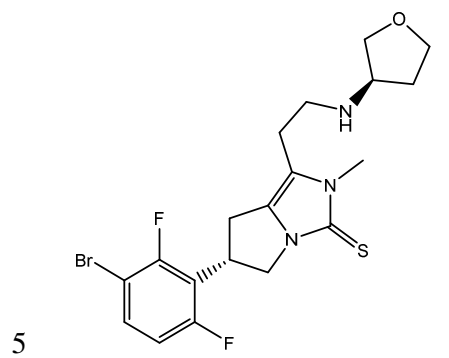
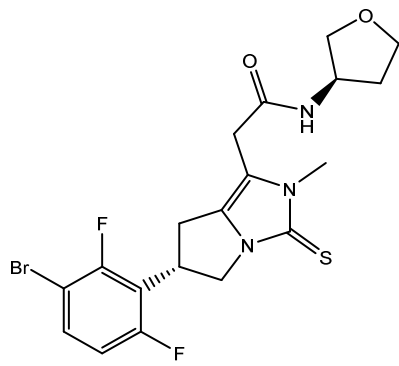
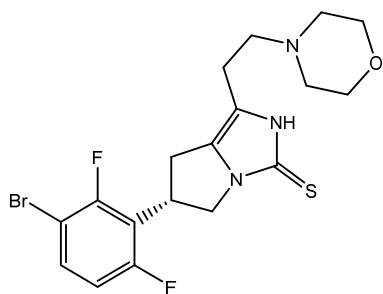


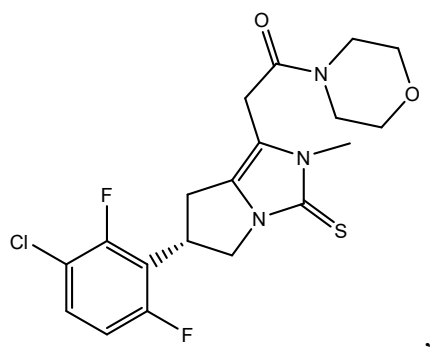
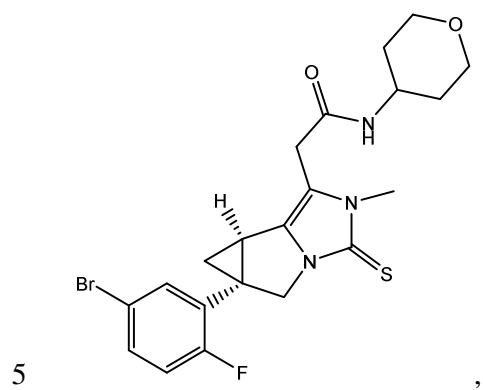
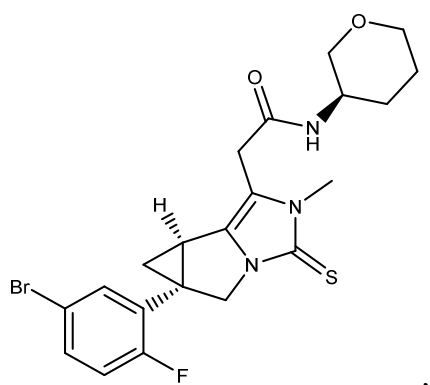
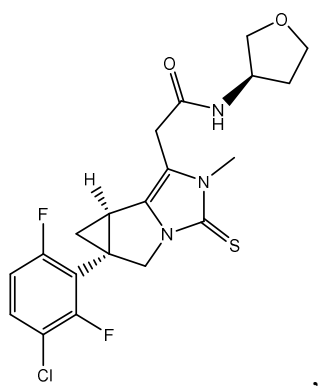
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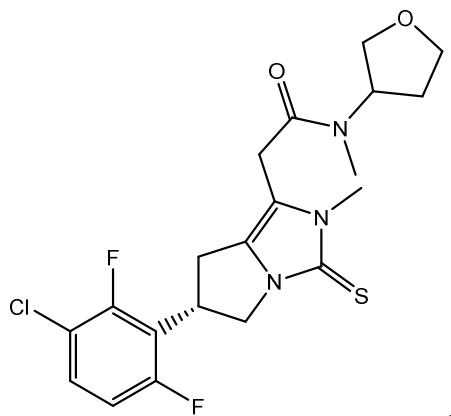
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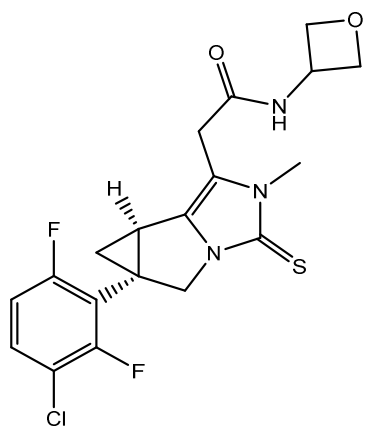
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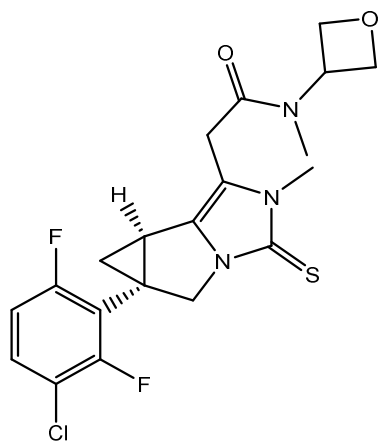




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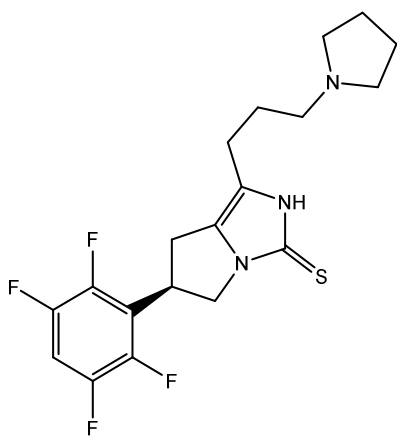


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, and



, or a pharmaceutically acceptable salt or solvate thereof.