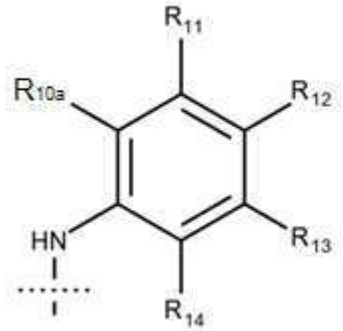
where:

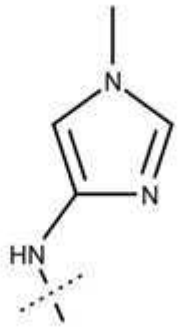
the dotted line represents the point of attachment to the rest of the molecule;

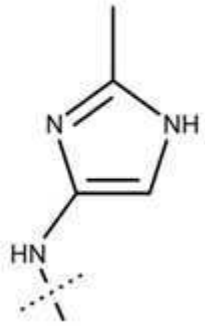
R_1 is selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, piperazine, methylpiperazine, ethylpiperazine, which latter seven groups are unsubstituted or substituted by one or more halo substituents, and where the piperazine, methylpiperazine and ethylpiperazine may be connected to the rest of moiety A *via* a carbon or nitrogen atom in the piperazine ring;

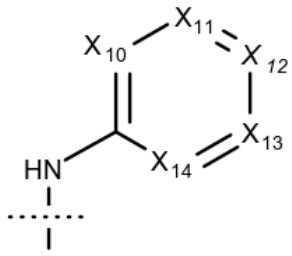
each R_2, and R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

each R_3 and R_4 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH, and/or a group of the formula:









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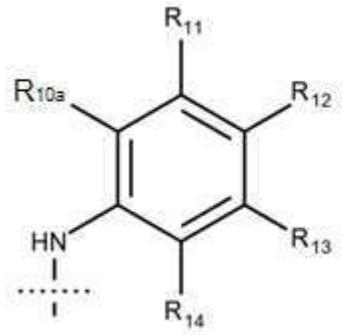
where R_{10a} and R_{14} are each independently selected from H, F and/or Cl,

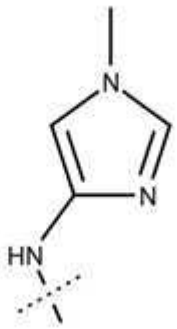
R_{11}, R_{12} and R_{13} are each independently selected from H, F, Cl and/or NH_2,

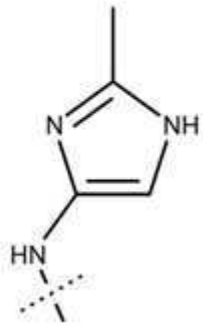
X_{10}, X_{11}, X_{12}, X_{13} and X_{14} are each independently selected from CH and/or N,

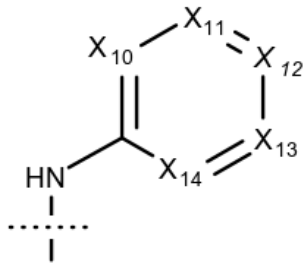
X_3 represents N, CH or CR_3, where R_3 is as defined above, X_4 represents N, CH or CR_4, where R_4 is as defined above, X_5 represents N, CH or CR_5, where R_5 is as defined above, provided that only one or two of X_3 to X_5 is N;

each X_6 and X_7 independently represents N, CH, CR_{6a}, where each R_{6a} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH or a group of the formula:









, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

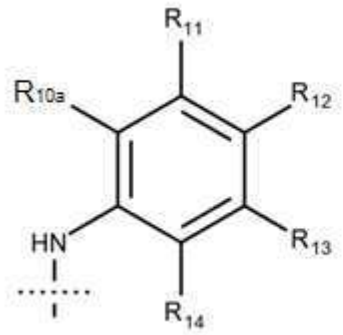
each X_8 and X_9 independently represents N, CH or CR_{6b}, where each R_{6b} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which four groups are unsubstituted or substituted by one or more halo substituents;

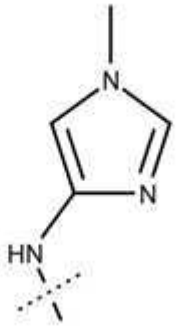
Y_1 represents NR_N, O or S;

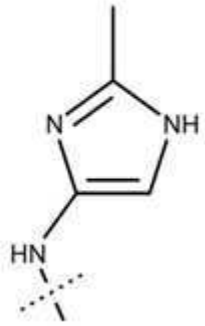
Y_2 represents NR_N, NR_Y O or S;

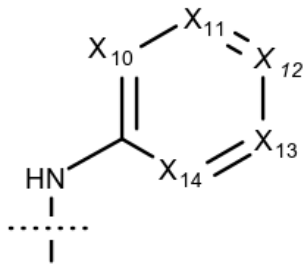
R_N represents H, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter three groups are unsubstituted or substituted by one or more halo substituents;

R_Y represents NH_2, OH or a group of the formula:









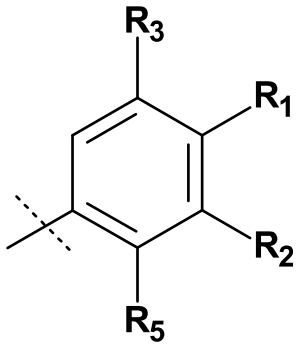
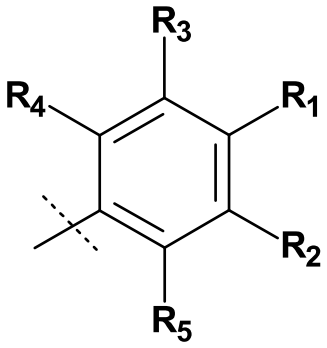
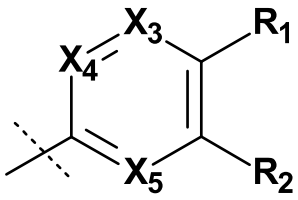
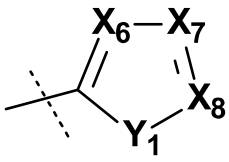
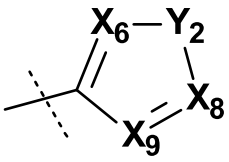
, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

L is a linking group of the formula:

$-M-(CR_LR_M)_a-C(O)-NR_7-$;
$-M-(CR_LR_M)_a-NR_{7'}-C(O)-$; or
$-M-C(O)-(CR_NR_O)-C(O)-M-$

where M represents a covalent bond, O or NH;
R_L and R_M each independently represent H, methyl, ethyl, fluoro or chloro, or R_L and R_M together form a C_3 or C_4 cycloalkyl ring, carbonyl or thiocarbonyl group;
a represents 0 or 1;
R_7 and $R_{7'}$ represent H or an optionally substituted alkyl group;
R_N and R_O each independently represent H, methyl, ethyl, fluoro or chloro, or R_N and R_O together form a C_3 or C_4 cycloalkyl ring;

Z represents a heterocycle selected from the group consisting of:

 ;	 ;
	 ; or
	

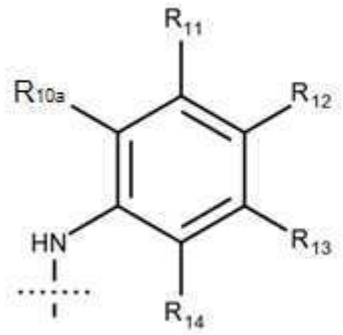
where:

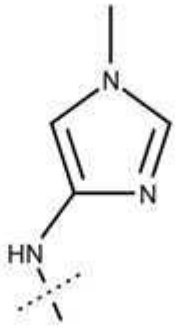
the dotted line represents the point of attachment to the rest of the molecule;

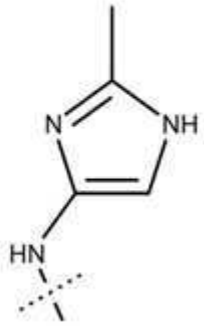
R_1 is selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, piperazine, methylpiperazine, ethylpiperazine, which latter seven groups are unsubstituted or substituted by one or more halo substituents, and where the piperazine, methylpiperazine and ethylpiperazine may be connected to the rest of moiety A *via* a carbon or nitrogen atom in the piperazine ring;

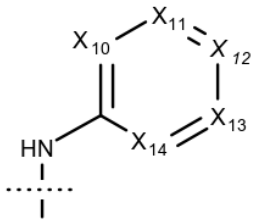
each R_2 and R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

each R_3 and R_4 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH, and/or a group of the formula:









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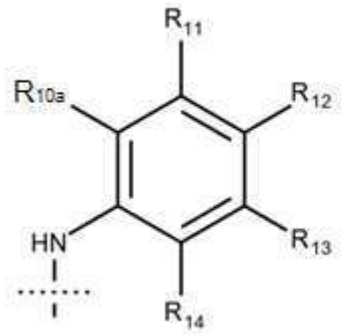
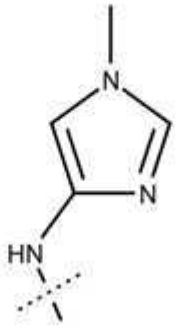
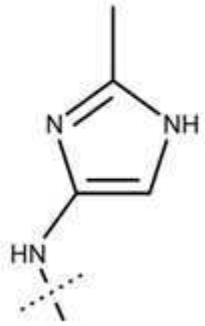
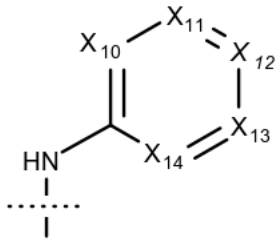
where R_{10a} and R_{14} are each independently selected from H, F and/or Cl,
R_{11}, R_{12} and R_{13} are each independently selected from H, F, Cl and/or NH_2,
X_{10}, X_{11}, X_{12}, X_{13} and X_{14} are each independently selected from CH and/or N,

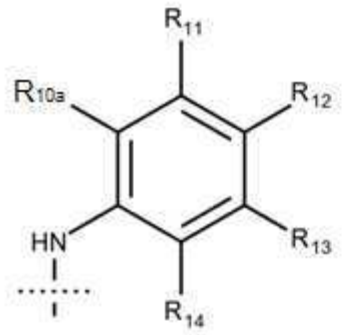
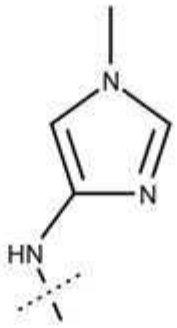
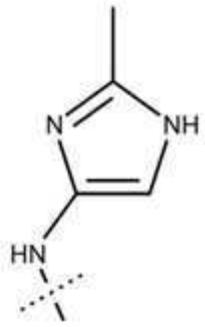
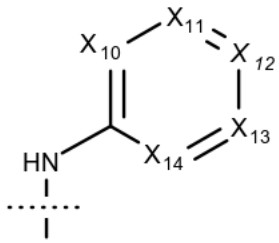
X_3 represents N, CH or CR_3, where R_3 is as defined above, X_4 represents N, CH or CR_4, where R_4 is as defined above, X_5 represents N, CH or CR_5, where R_5 is as defined above, provided that only one or two of X_3 to X_5 is N;
each X_6 and X_7 independently represents N, CH, CR_{6a}, where each R_{6a} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH or a group of the formula:

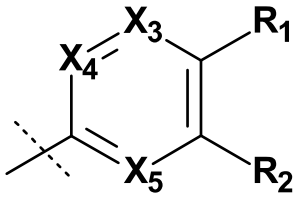
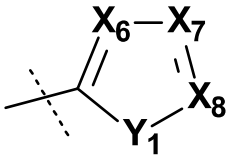
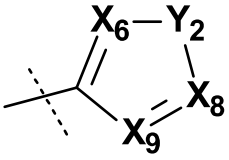
, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

each X_8 and X_9 independently represents N, CH or CR_{6b}, where each R_{6b} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which four groups are unsubstituted or substituted by one or more halo substituents;

Y_1 represents NR_N, O or S;
Y_2 represents NR_N, NR_Y O or S;
R_N represents H, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter three groups are unsubstituted or substituted by one or more halo substituents;
R_Y represents NH_2, OH or a group of the formula:

, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

	 ; or
	

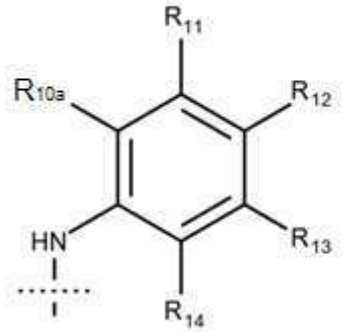
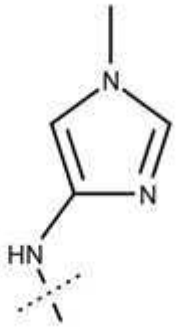
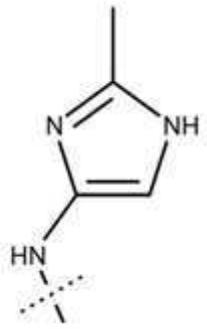
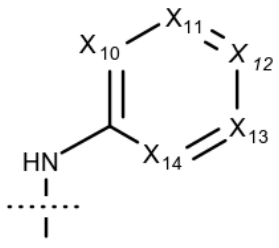
where for each moiety A:

the dotted line represents the point of attachment to the rest of the molecule;

R_1 is selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, piperazine, methylpiperazine, ethylpiperazine, which latter seven groups are unsubstituted or substituted by one or more halo substituents, and where the piperazine, methylpiperazine and ethylpiperazine may be connected to the rest of moiety A *via* a carbon or nitrogen atom in the piperazine ring;

each R_2 and R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

each R_3 and R_4 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH, and/or a group of the formula

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where R_{10a} and R_{14} are each independently selected from H, F and/or Cl,

R_{11}, R_{12} and R_{13} are each independently selected from H, F, Cl and/or NH_2,
X_{10}, X_{11}, X_{12}, X_{13} and X_{14} are each independently selected from CH and/or N.

In some embodiments of the invention, R_1 is selected from piperazine, methylpiperazine, and ethylpiperazine, each of which is unsubstituted or substituted by one or more halo substituents. In certain embodiments of the invention, R_1 is selected from piperazine, methylpiperazine, and ethylpiperazine.

In some embodiments of the invention each R_1 to R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents.

In some embodiments of the invention X_3 represents N, CH or CR_3, where R_3 is as defined above, X_4 represents N, CH or CR_4, where R_4 is as defined above, X_5 represents N, CH or CR_5, where R_5 is as defined above, provided that only one or two of X_3 to X_5 is N.

In some embodiments of the invention each X_6 to X_9 independently represents N, CH or CR_6, where each R_6 is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which four groups are unsubstituted or substituted by one or more halo substituents.

In some embodiments of the invention, each R_1 to R_5 independently represents halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{2-3} alkenyl and C_{2-3} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents). In some embodiments of the invention, each R_1 to R_5 independently represents fluoro, chloro, methyl or ethyl, which methyl and ethyl groups may be unsubstituted or substituted by one, two or three fluoro or chloro groups.

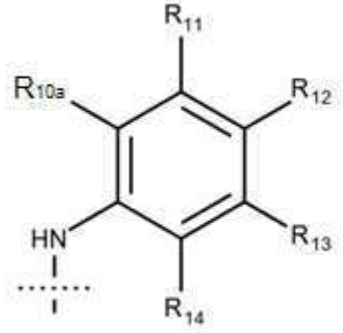
In some embodiments of the invention, each R_6 independently represents C_{1-3} alkyl, C_{1-3} alkoxy, C_{2-3} alkenyl and C_{2-3} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents. In some embodiments of the invention, each R_6 independently represents fluoro, chloro, methyl or ethyl, which methyl and ethyl groups may be unsubstituted or substituted by one, two or three fluoro or chloro groups.

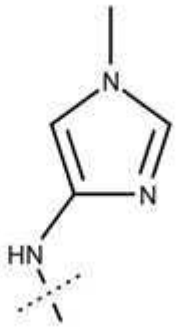
In some embodiments of the invention, each of R_1 to R_5 and R_6 independently represents methyl, trifluoromethyl, fluoro or chloro.

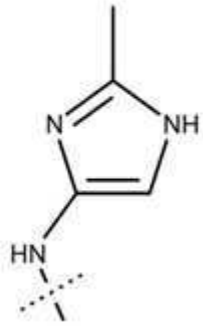
Y_1 represents NR_N, O or S;
Y_2 represents NR_N, NR_Y O or S;

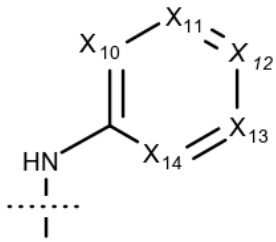
where R_N represents H, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter three groups are unsubstituted or substituted by one or more halo substituents;

R_Y represents NH_2, OH or a group of the formula:







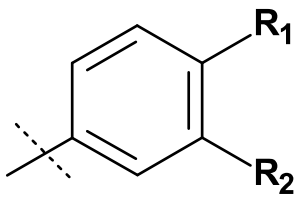
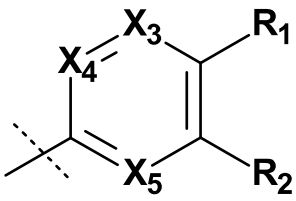
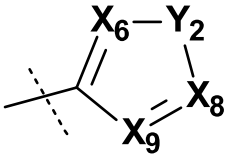
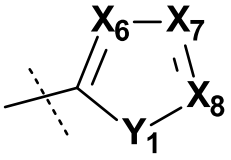


, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above.

In some embodiments of the invention Y_1 and Y_2 are not S.

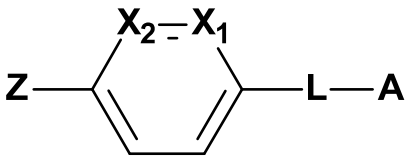
In some embodiments of the invention, Y_1 and Y_2 each independently represent NR_N, O or S, where R_N represents H, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter three groups are unsubstituted or substituted by one or more halo substituents. In some embodiments of the invention, Y_1 and Y_2 independently represent O, NC_{1-3} alkyl or NH. In some embodiments of the invention, Y_1 and Y_2 independently represent O, NMe or NH.

In some embodiments of the invention, A is selected from the group consisting of:

 ;	 where only one of X_3 to X_5 is N;
	

CLAIMS

1. A compound of formula I:

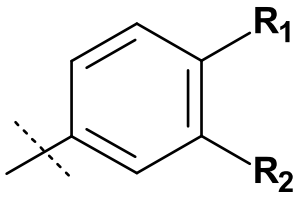
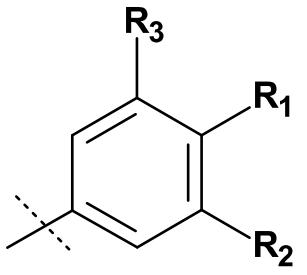
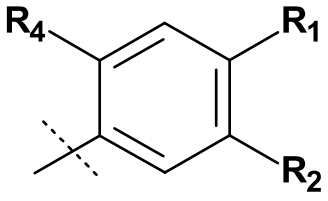
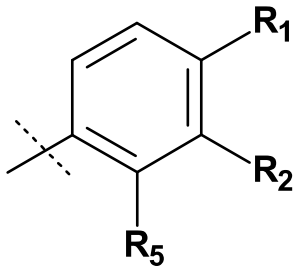
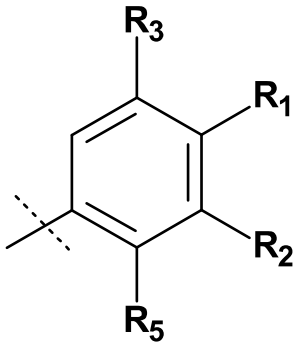
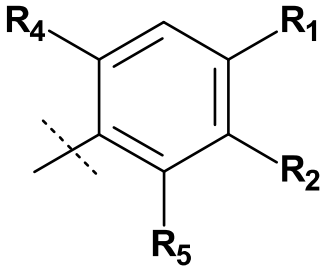


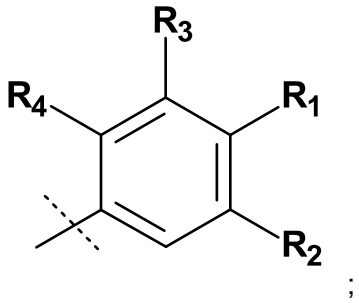
I

wherein:

X_1 is selected from N and CH, and X_2 is selected from CH and CF;

A is selected from the group consisting of:

 ;	 ;
 ;	 ;
 ;	 ;



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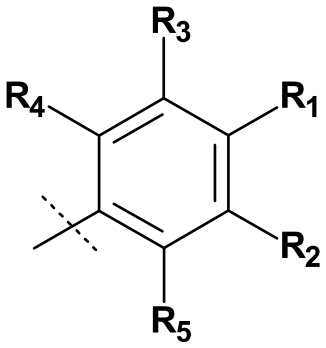

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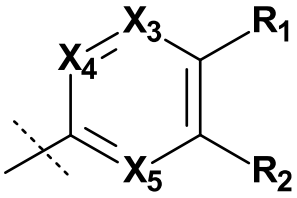

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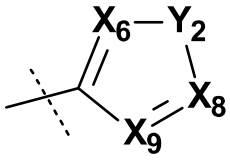


;

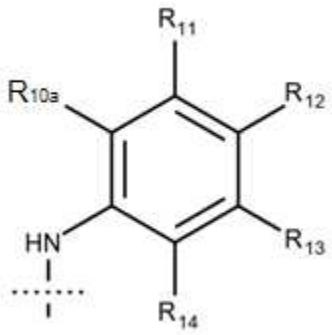
where:

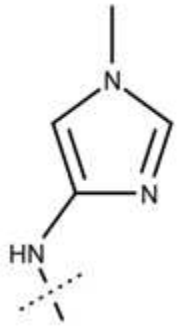
the dotted line represents the point of attachment to the rest of the molecule;

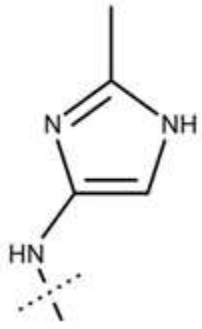
R_1 is selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

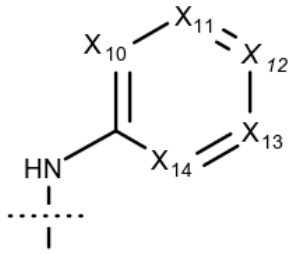
each R_2, and R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

each R_3 and R_4 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH, and/or a group of the formula:





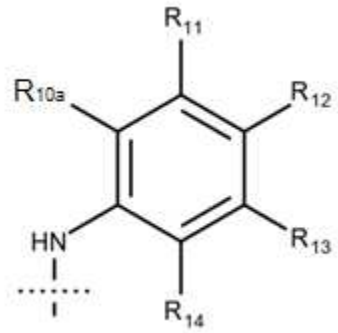


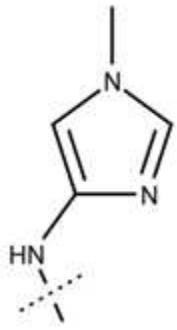


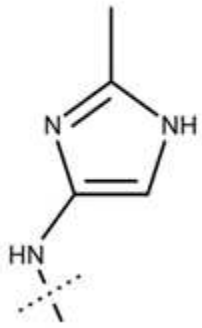
,

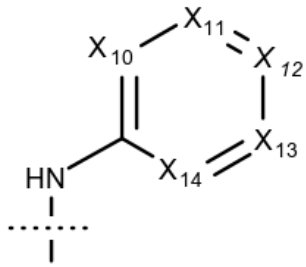
where R_{10a} and R_{14} are each independently selected from H, F, and/or Cl,
R_{11}, R_{12} and R_{13} are each independently selected from H, F, Cl and/or NH_2,
X_{10}, X_{11}, X_{12}, X_{13} and X_{14} are each independently selected from CH and/or N,

X_3 represents N, CH or CR_3, where R_3 is as defined above, X_4 represents N, CH or CR_4, where R_4 is as defined above, X_5 represents N, CH or CR_5, where R_5 is as defined above, provided that only one or two of X_3 to X_5 is N;
each X_6 and X_7 independently represents N, CH, CR_{6a}, where each R_{6a} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents), NH_2, OH or a group of the formula:









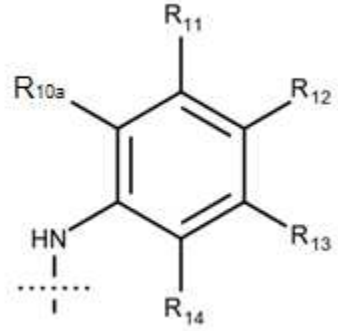
, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

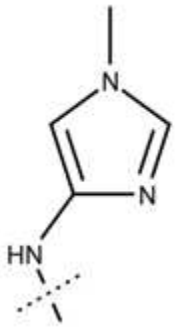
each X_8 and X_9 independently represents N, CH or CR_{6b}, where each R_{6b} is independently selected from C_{1-3} alkyl, C_{1-3} alkoxy, C_{2-3} alkenyl and C_{2-3} alkynyl, which four groups are unsubstituted or substituted by one or more halo substituents;

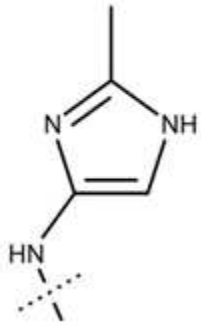
Y_2 represents NR_N, or NR_Y;

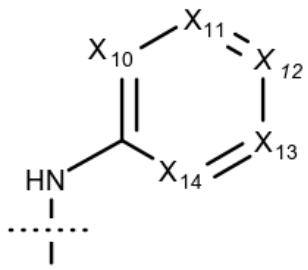
R_N represents H, C_{1-5} alkyl, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter three groups are unsubstituted or substituted by one or more halo substituents;

R_Y represents NH_2, OH or a group of the formula:









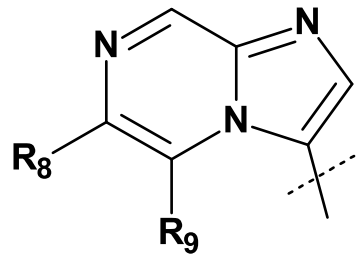
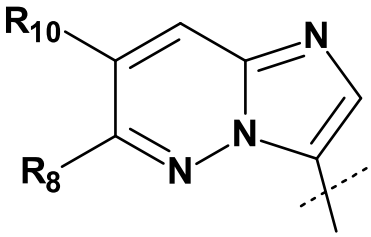
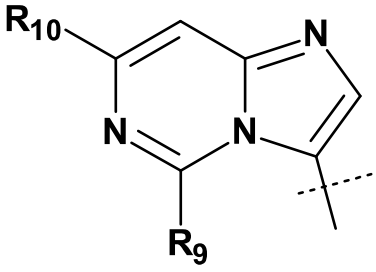
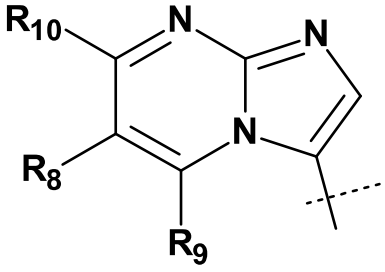
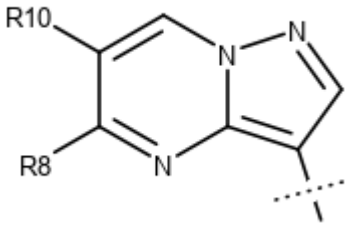
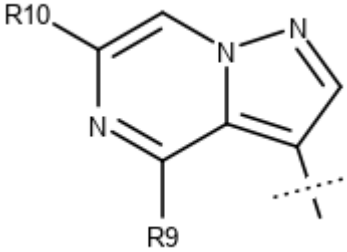
, where R_{10a} to R_{14} and X_{10} to X_{14} are as defined above;

L is a linking group of the formula:

-M-$(CR_LR_M)_a$-C(O)-NR_7-;
-M-$(CR_LR_M)_a$-$NR_{7'}$-C(O)-; or
-M-C(O)-(CR_NR_O)-C(O)-M-

where M represents a covalent bond, O or NH;
R_L and R_M each independently represent H, methyl, ethyl, fluoro or chloro, or R_L and R_M together form a C_3 or C_4 cycloalkyl ring, carbonyl or thiocarbonyl group;
a represents 0 or 1;
R_7 and $R_{7'}$ represent H or an optionally substituted alkyl group;
R_N and R_O each independently represent H, methyl, ethyl, fluoro or chloro, or R_N and R_O together form a C_3 or C_4 cycloalkyl ring;

Z represents a heterocycle selected from the group consisting of:

 ;	 ;
 ;	 ;
 ;	 ;or
	

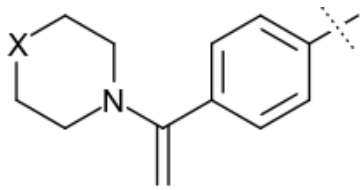
where:

the dotted line represents the point of attachment to the rest of the molecule, and Z is attached to the rest of the molecule *via* a covalent bond, or *via* a -O- or –NH- group;

each of R_8 to R_{10} are independently selected from H, hydroxy, C_1 to C_5 alkyl, C_1 to C_5 alkoxy (which latter two groups are unsubstituted or substituted by one or more halo groups),

$OC(O)R_{11}$, $C(O)OR_{12}$, C_2 to C_5 alkynyl (which is unsubstituted or substituted by one or more halo groups) or $NR_{13}R_{14}$, and O-(C_{1-4} alkyleneyl)-O-C_{1-4} alkyl,

and one of R_8 to R_{10} may be a group of the formula:



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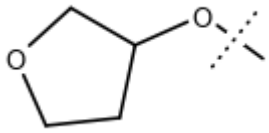

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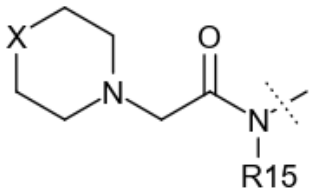

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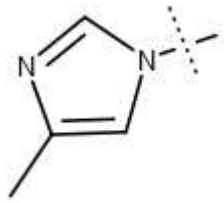


;

where X represents O or NR_X;

R_X represents H or C_{1-4} alkyl,

R_{11} and R_{12} each independently represent, at each occurrence, optionally substituted alkyl;

R_{13} and R_{14} each independently represent, at each occurrence, H or optionally substituted alkyl;

R_{15} represents H or C_{1-2} alkyl; or

a pharmaceutically acceptable salt or solvate thereof.

2. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein:

each R_1 to R_5 independently represents halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{2-3} alkenyl and C_{2-3} alkynyl (which four groups are unsubstituted or substituted by one or more halo substituents), optionally wherein each R_1 to R_5 independently represents fluoro, chloro, methyl or ethyl, which methyl and ethyl groups may be unsubstituted or substituted by one, two or three fluoro or chloro groups.

3. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein:

Y_2 independently represent NC_{1-3} alkyl or NH;

optionally wherein Y_2 independently represent NMe or NH, and/or

R_{6a} R_{6b} independently represents methyl or ethyl, which methyl and ethyl groups may be unsubstituted or substituted by one, two or three fluoro or chloro groups.

4. A compound according to claim 2, or a pharmaceutically acceptable salt or solvate thereof, wherein each of R_1 to R_5, R_{6a} and R_{6b} independently represents methyl, trifluoromethyl, fluoro or chloro.

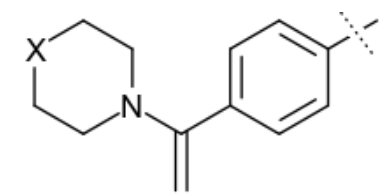
5. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein:

(a) each R_8 to R_{10} independently represents H, hydroxy, Me, C_{1-2} alkoxy (which is unsubstituted or substituted by one or more halo groups), $OC(O)R_{11}$, $C(O)OR_{12}$, C_2 to C_3 alkynyl (which is substituted by one or more halo groups), O-(C_{1-2} alkyleneyl)-O-C_{1-2} alkyl, or $NR_{13}R_{14}$,

R_{11} and R_{12} each independently represent methyl or ethyl,

R_{13} and R_{14} each independently represent H, methyl or ethyl; or

(b) one of R_8 to R_{10} represents a group of the formula



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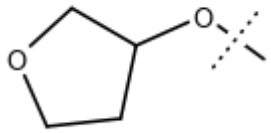

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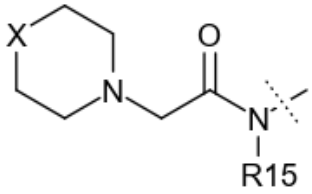

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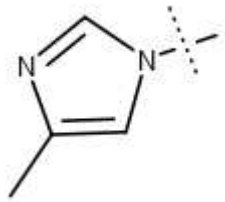


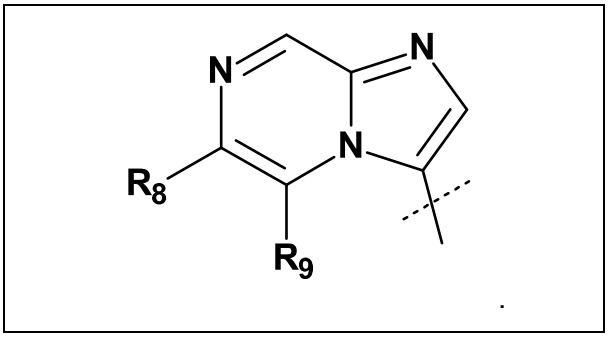
;

where X represents O, or NH, or N-C_{1-2} alkyl,

R_{15} represents methyl,

and the remaining two of R_8 to R_{10} are as defined in part (a).

6. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein Z represents a heterocycle selected from:



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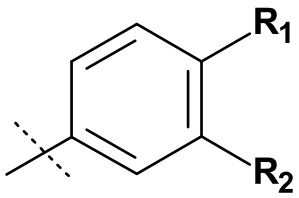
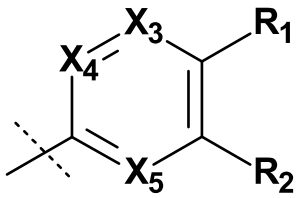
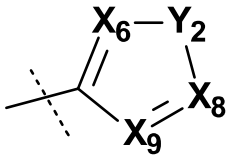
7. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein:

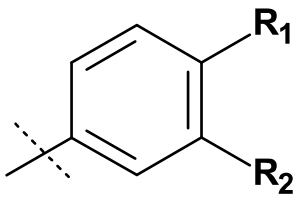
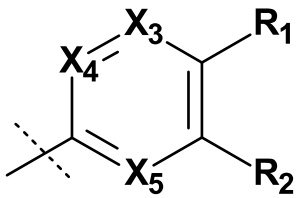
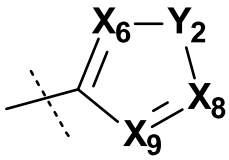
(a) when any of R_8 to R_{10} is a C_1 to C_5 alkyl group, it is an unsubstituted methyl group; and/or

(b) when any of R_8 to R_{10} is a C_2 to C_5 alkynyl group, it is a C_2 to C_5 alkynyl group which is substituted by one or more halo groups.

8. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein A is selected from the group consisting of:

 ;	 where only one of X_3 to X_5 is N; or
 where only one of X_6, X_8 or X_9 is N.	

9. A compound according to claim 9, wherein when A is selected from the group consisting of:

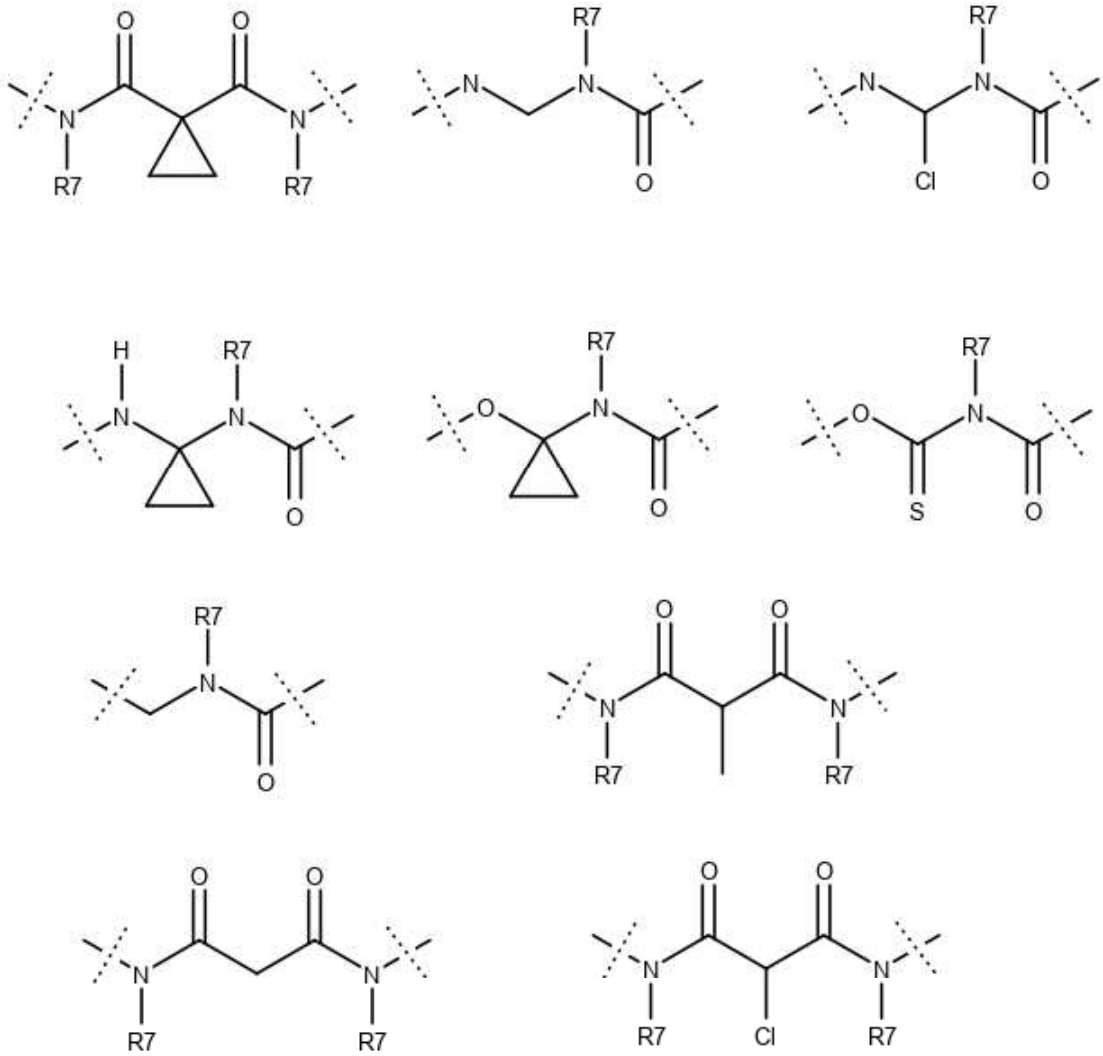
 ;	 where only one of X_3 to X_5 is N;
	

where only one of X_6, X_8 or X_9 is N;

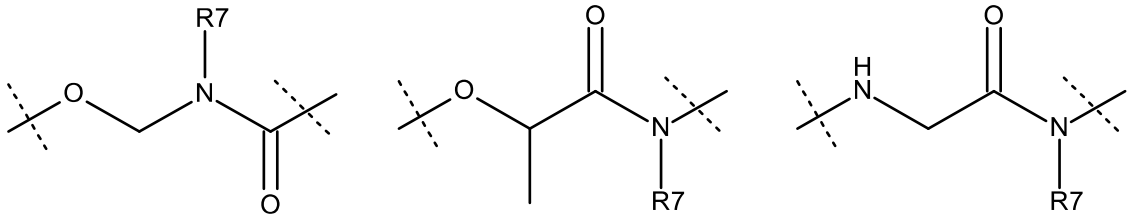
and where when present:
R_1 is selected from Cl and CH_3,
R_2 is CF_3,
X_3 and X_5 are CH,
X_4 is N,
X_6 is N,
X_8 and X_9 are CH,
Y_2 is selected from N-CH_3.

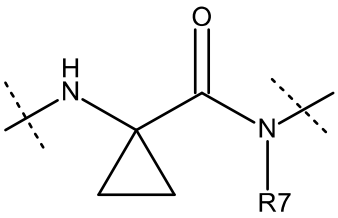
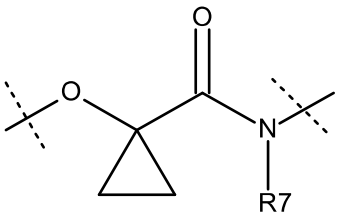
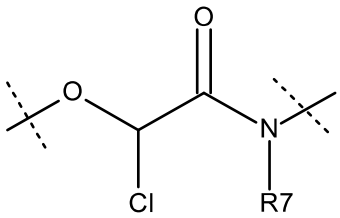
10. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein:
M represents O or NH; and/or
R_L and R_M each independently represent H, methyl or chloro, or R_L and R_M together represent thiocarbonyl or cyclopropyl; and/or
a represents 1.

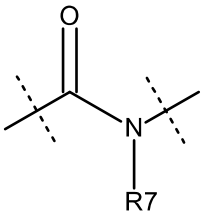
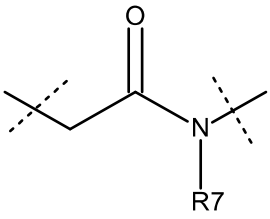
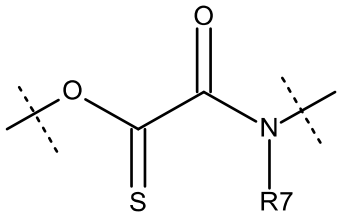
11. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein L is selected from:



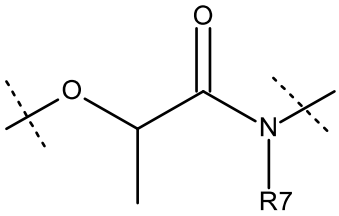
12. A compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein L is selected from:



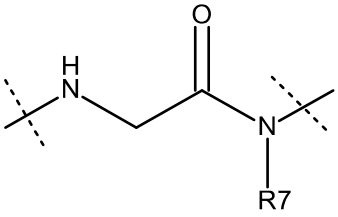




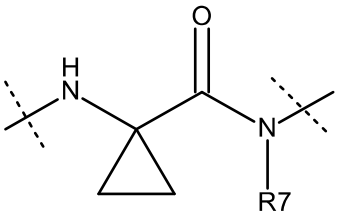
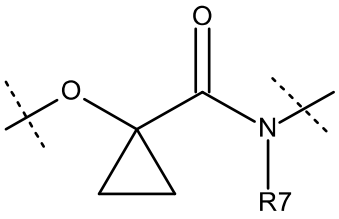
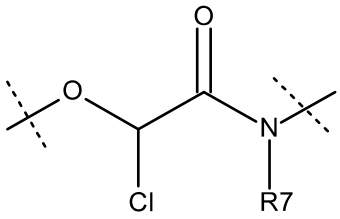




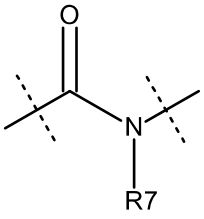
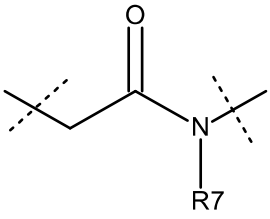
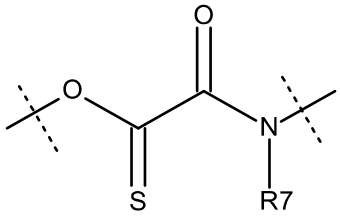
and ,



optionally wherein L is selected from

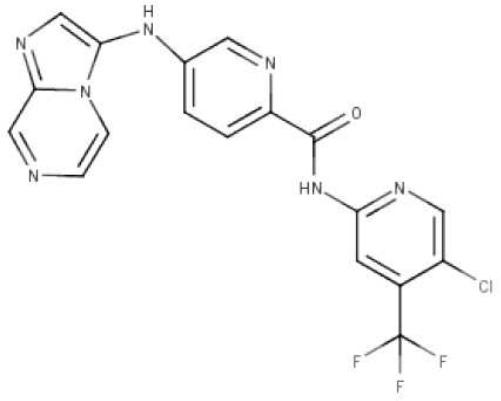


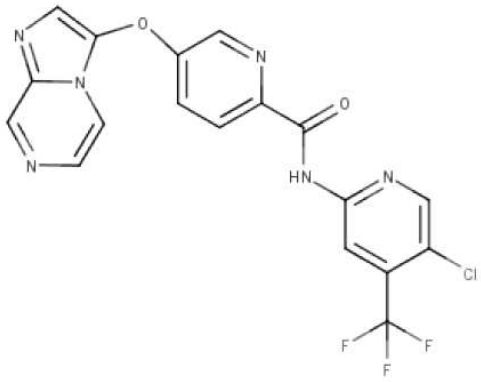




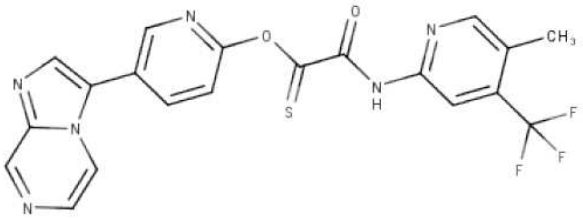




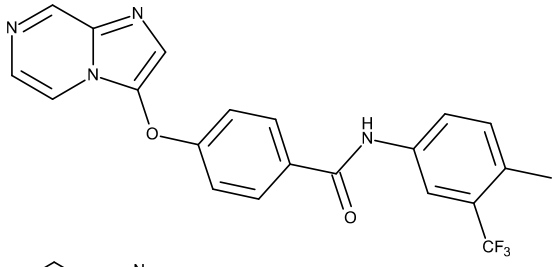
and .

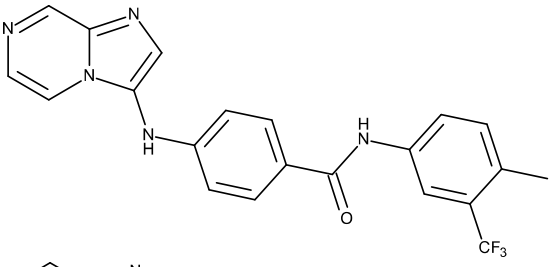
13. A compound according to claim 1 which is selected from

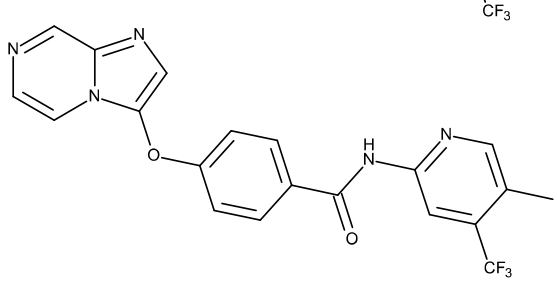


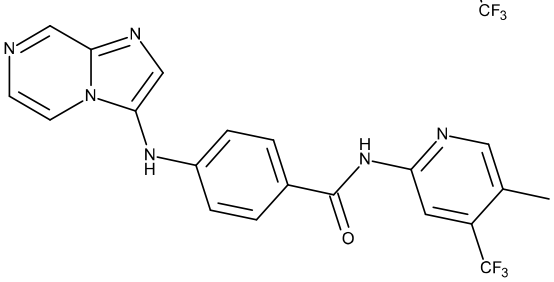


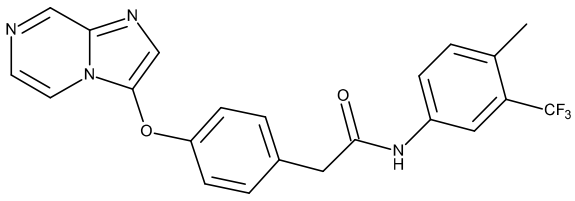


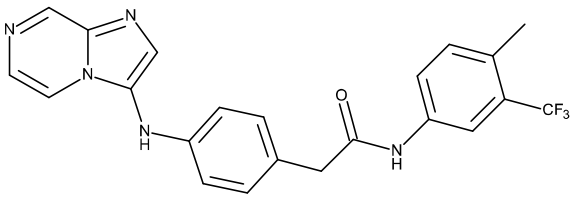


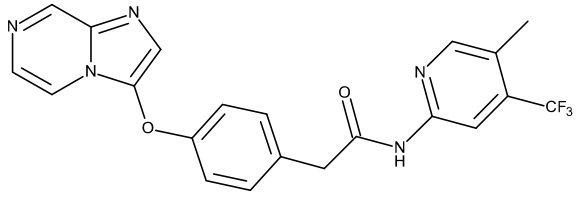


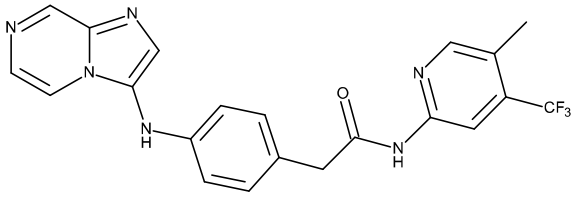


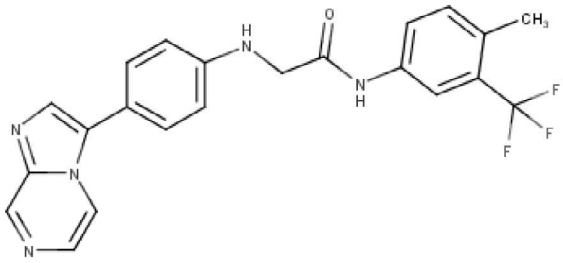


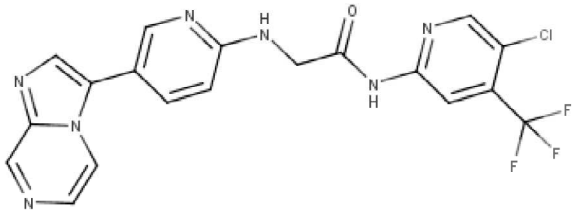


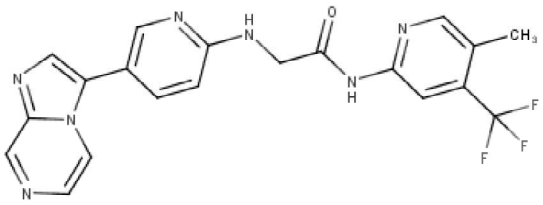


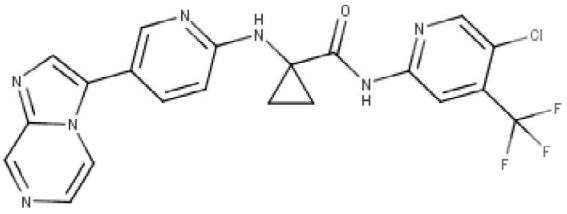


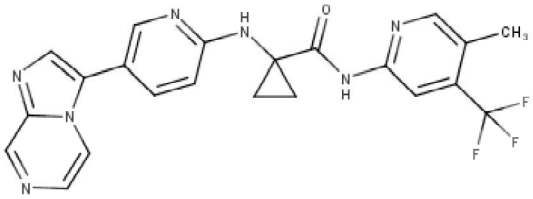


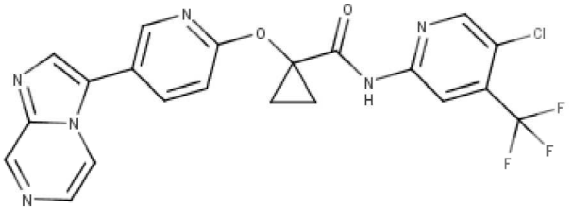


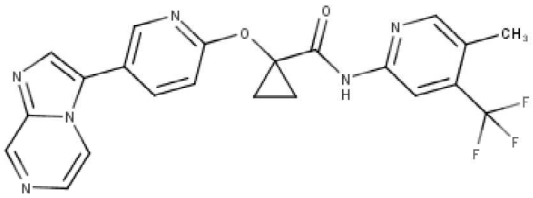


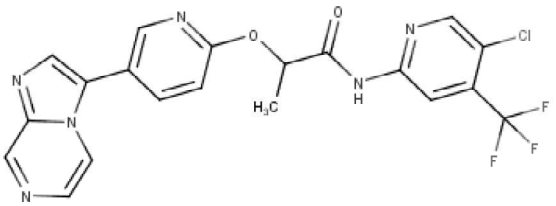


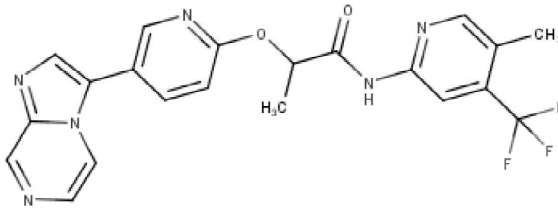


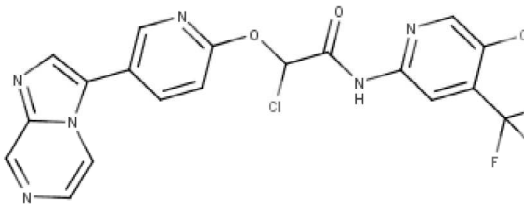


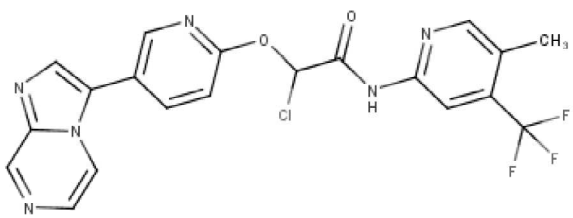


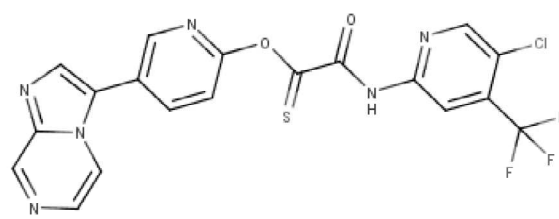


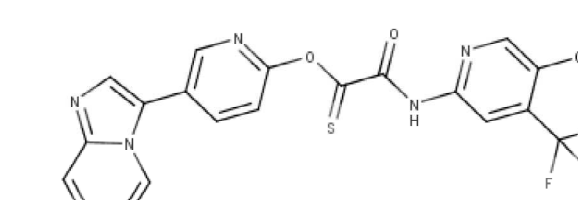












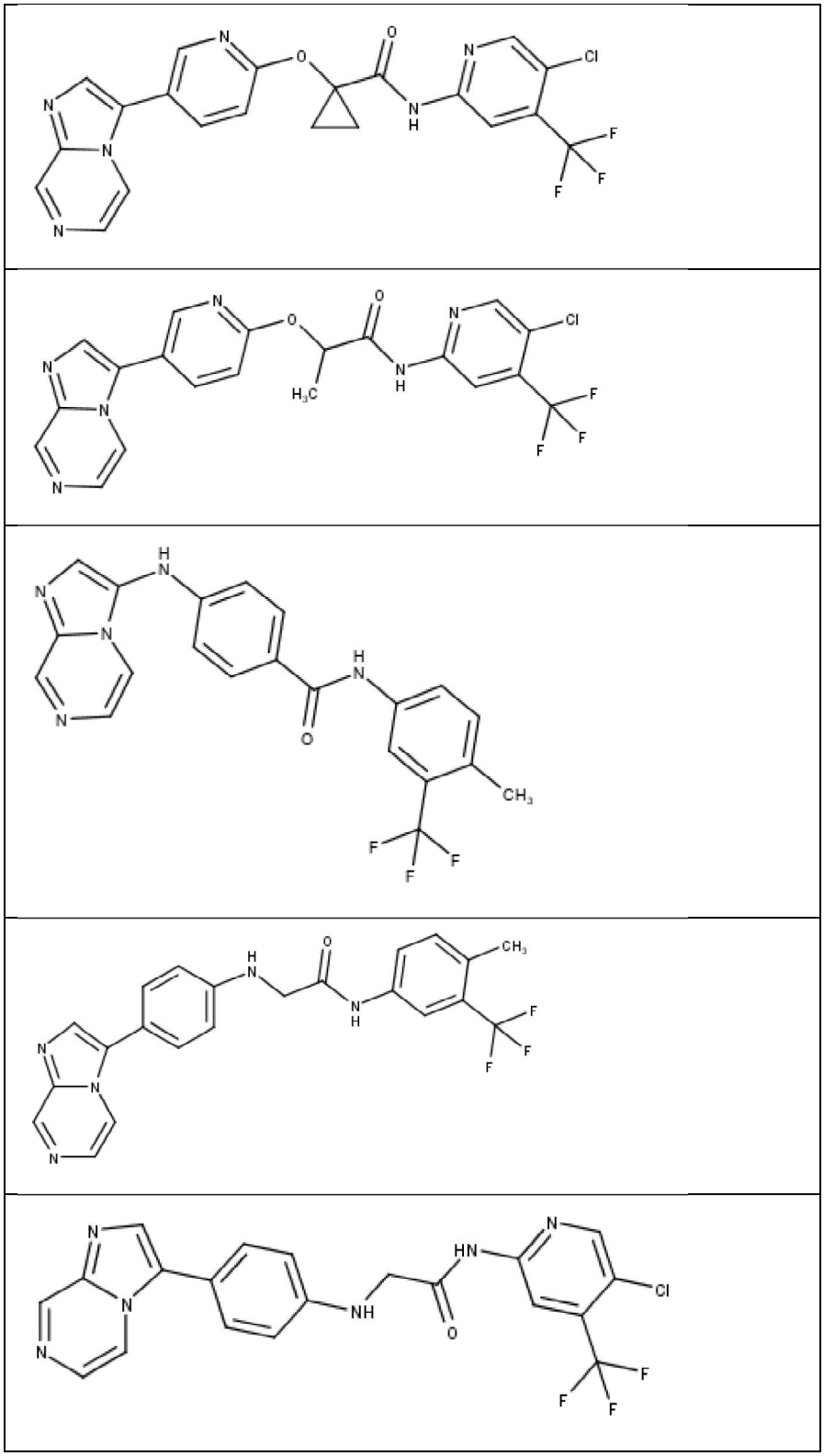
,

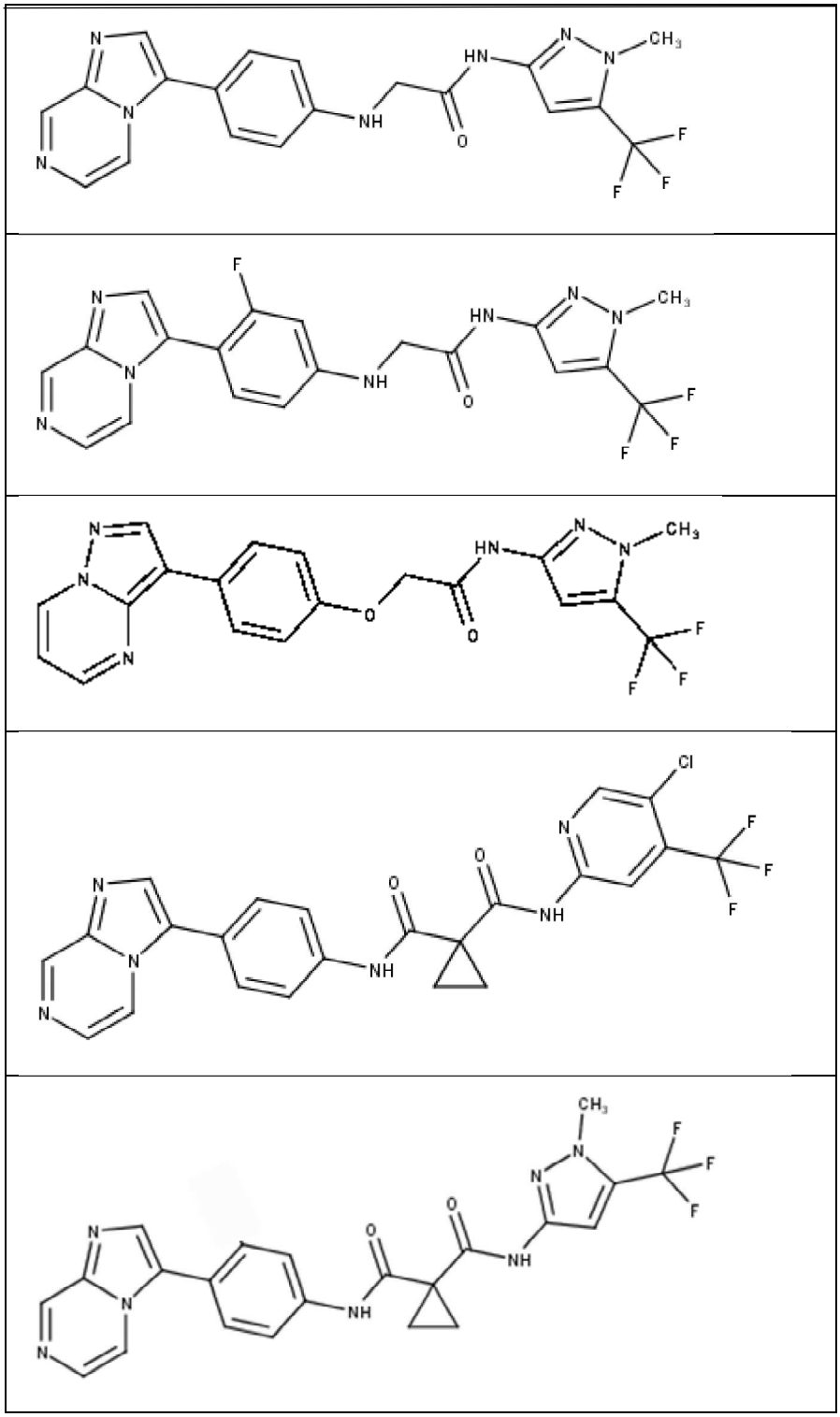
and

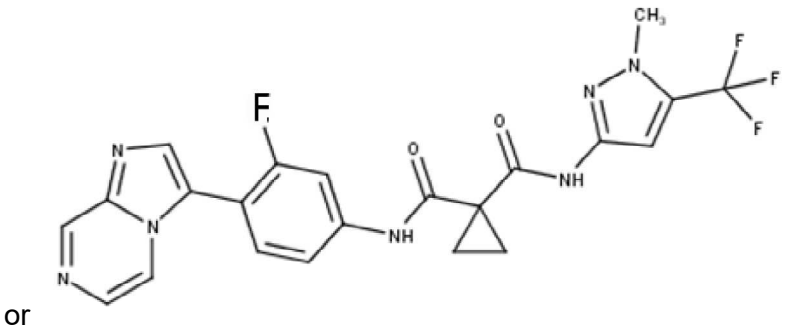
,

or a pharmaceutically acceptable or a salt or solvate thereof.

14. A compound according to Claim 1, which is selected from:







or

or a pharmaceutically acceptable salt or solvate thereof.

15. Use of a compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof in the preparation of a medicament for treating one or more of cancer (e.g. prostate cancer, colon cancer, rectal cancer, colorectal cancer, acute myeloid leukaemia or chronic myelomonocytic leukaemia) and angiogenesis.

16. A pharmaceutical composition comprising a compound of formula I as defined in claim 1 or a pharmaceutically acceptable salt or solvate thereof.