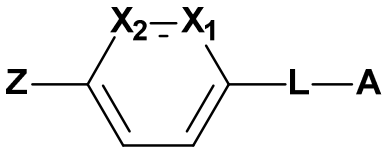
CLAIMS

1. A compound of formula I:



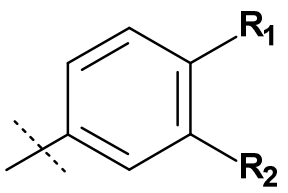
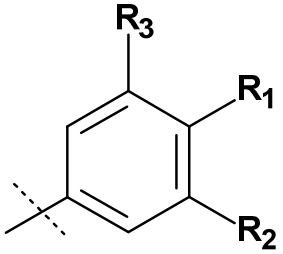
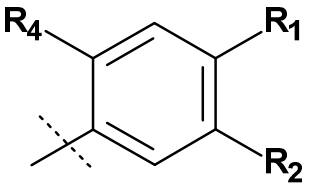
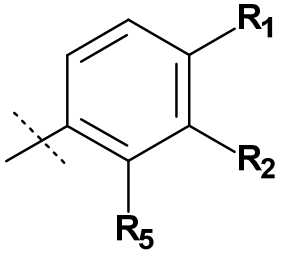
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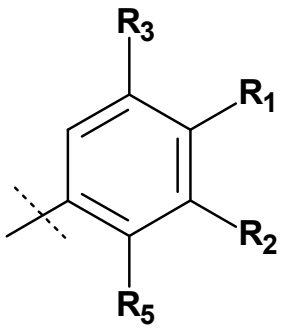
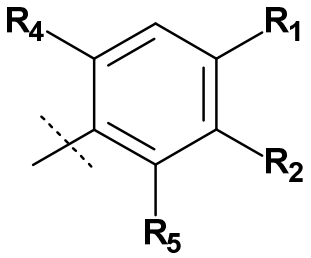
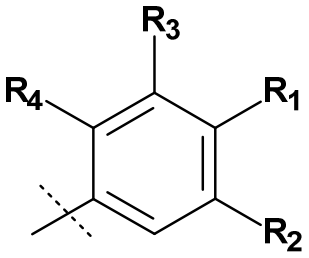
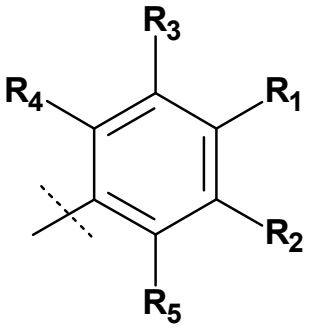
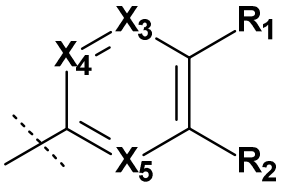
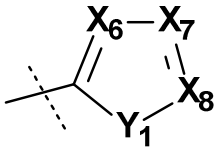
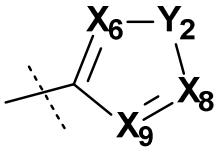
wherein:

X_1 and X_2 each independently represent N or CR_a

R_a independently represents H, NH_2, halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl and C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents);

A is selected from the group consisting of:

 ;	 ;
 ;	 ;

 ;	 ;
 ;	 ;
	 ; or
	

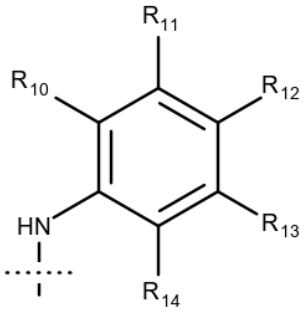
where:

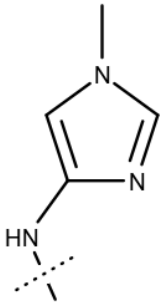
the dotted line represents the point of attachment to the rest of the molecule;

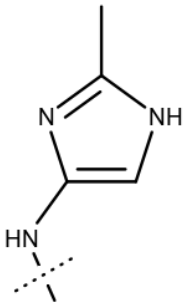
R_1 is selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, piperazine, methylpiperazine, ethylpiperazine, which latter seven groups are unsubstituted or substituted by one or more halo substituents, and where the piperazine, methylpiperazine and ethylpiperazine may be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

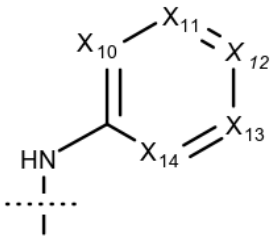
each R_2, and R_5 is independently selected from halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which latter four groups are unsubstituted or substituted by one or more halo substituents;

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 a group of the formula:





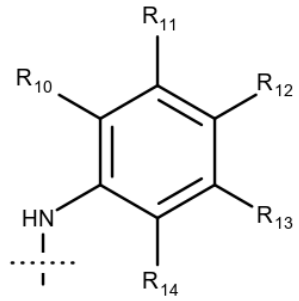
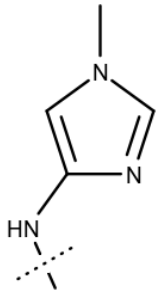
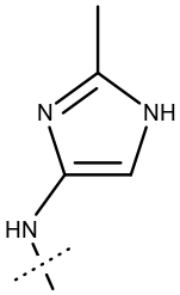
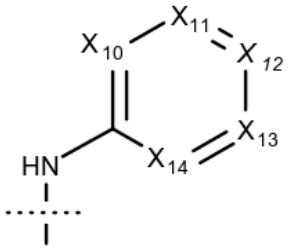




,

where R_{10} and R_{14} are each independently selected from H, F and Cl,
R_{11}, R_{12} and R_{13} are each independently selected from H, F, Cl and NH_2,
X_{10}, X_{11}, X_{12}, X_{13} and X_{14} are each independently selected from CH and 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_{10} to R_{14} and X_{10} to X_{14} are as defined above;

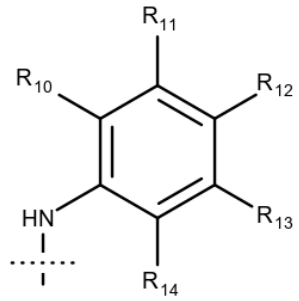
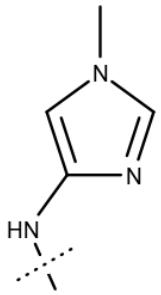
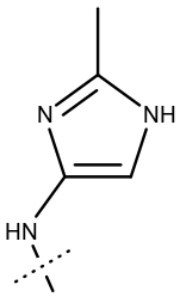
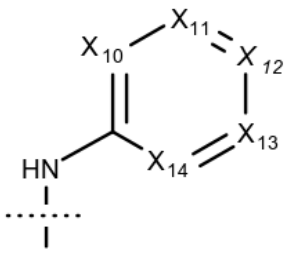
each X_8 and X_9 independently represents N, CH or CR_{6b}, where each R_{6b} is independently selected from C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl, C_{2-5} alkynyl, which four groups are unsubstituted or substituted by one or more halo substituents;

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:

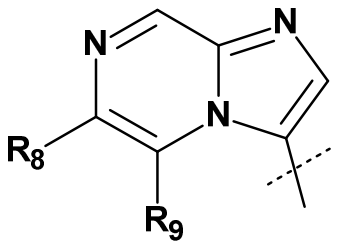
, where R_{10} to R_{14} and X_{10} to X_{14} are as defined above;

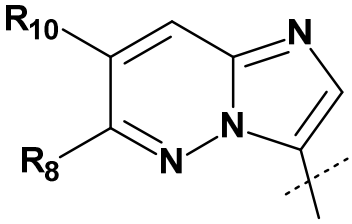
L is a linking group of the formula:

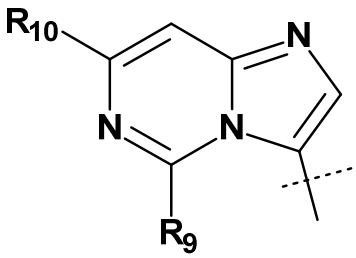
$-M-(CR_LR_M)_a-C(O)-NR_{7'}-$;
$-M-(CR_LR_M)_a-NR_{7'}-C(O)-$; or
$-M-C(O)-(CR_NR_O)-C(O)-M-$

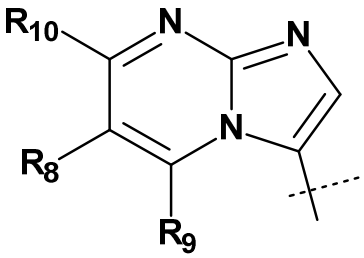
where M represents a covalent bond, O or NH;
R_L and R_M each independently represent H, methyl, ethyl, fluoro or chloro, or R_L and R_M together form a C_3 or C_4 cycloalkyl ring, carbonyl or thiocarbonyl group;
a represents 0 or 1;
$R_{7'}$ and $R_{7''}$ represent H or an optionally substituted alkyl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

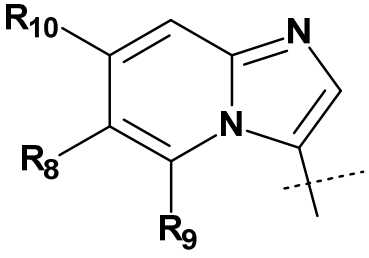
Z represents a heterocycle selected from the group consisting of:

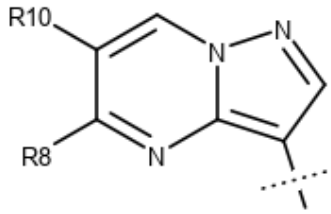
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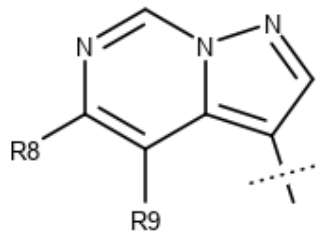
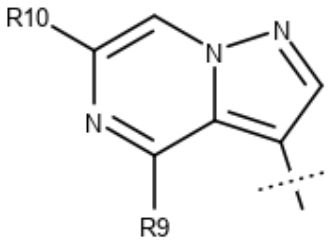
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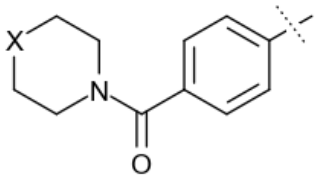
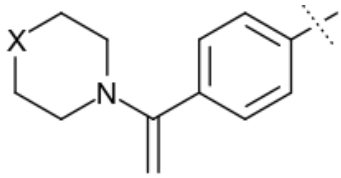
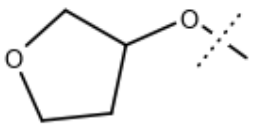
	

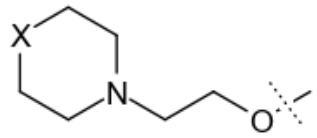
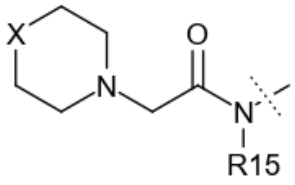
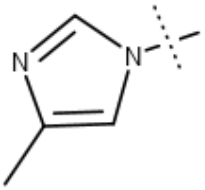
where:

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:

, , ,

, , or ;

where X represents O or NR_X;

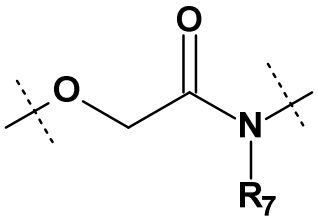
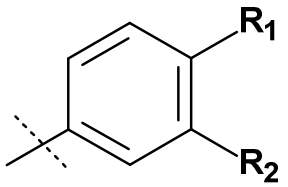
R_X represents H or C_{1-4} alkyl,

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, solvate or derivative thereof,

provided that when X_1 and X_2 are both CH, L is , and A is , then Z is not an optionally substituted heteroaryl selected from optionally substituted tetrazolyl or optionally substituted imidazopyridinyl.

2. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein R_a independently represents H, NH_2, F, Cl, or C_{1-3} alkyl, which C_{1-3} alkyl group is unsubstituted or substituted by one, two or three fluoro or chloro substituents,
optionally wherein R_a is H or F.

3. A compound according to claim 1, wherein X_1 is selected from N and CH, and X_2 is selected from CH and CF.

4. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative 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.

5. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein:
Y_1 and Y_2 independently represent O, NC_{1-3} alkyl or NH; and/or
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),
optionally wherein Y_1 and Y_2 independently represent O, NMe or NH, and/or
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.

6. A compound according to claim 4, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein each of R_1 to R_5 and R_6 independently represents methyl, trifluoromethyl, fluoro or chloro.

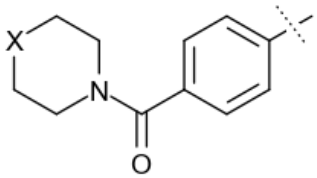
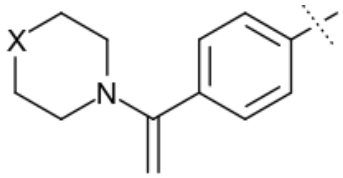
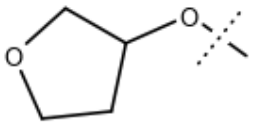
7. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein:

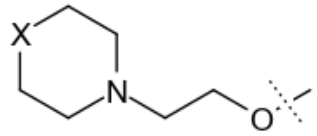
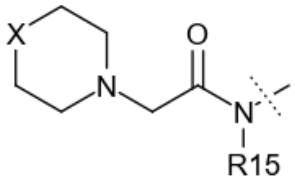
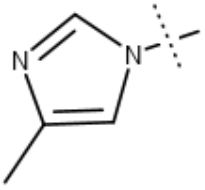
(a) each R_8 to R_{10} independently represents H, hydroxy, Me, C_{1-2} alkoxy (which is unsubstituted or substituted by one or more halo groups), $OC(O)R_{11}$, $C(O)OR_{12}$, C_2 to C_3 alkynyl (which is substituted by one or more halo groups), O-(C_{1-2} alkyleneyl)-O-C_{1-2} alkyl, or $NR_{13}R_{14}$,

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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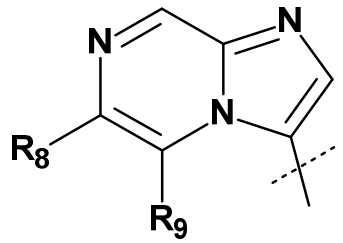
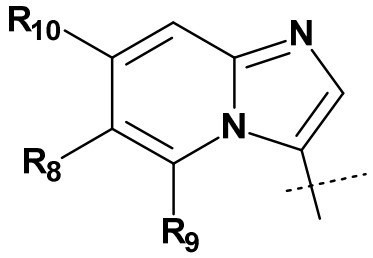

, 
, or 
;

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).

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

 ; and	 .

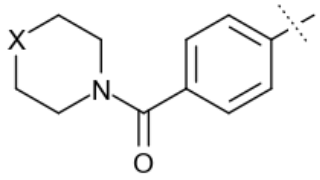
9. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein:

(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.

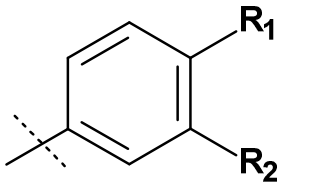
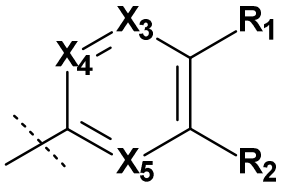
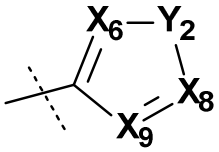
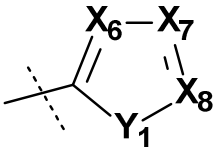
10. A compound according to claim 1, wherein:

R_9 and R_{10}, when present, are H, and/or

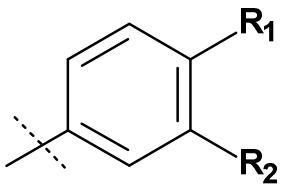
R_8 is selected from H and 

, where X is O or NH.

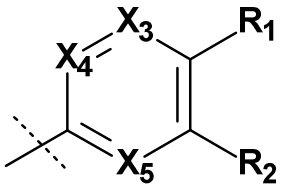
11. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein A is selected from the group consisting of:

 ;	 where only one of X_3 to X_5 is N;
 where only one of X_6, X_8 or X_9 is N; or	 where only one of X_6, X_7 or X_8 is N.

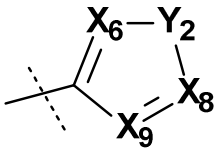
12. A compound according to claim 11, wherein A is selected from the group consisting of:



;



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, CH_3 and H,

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 and O.

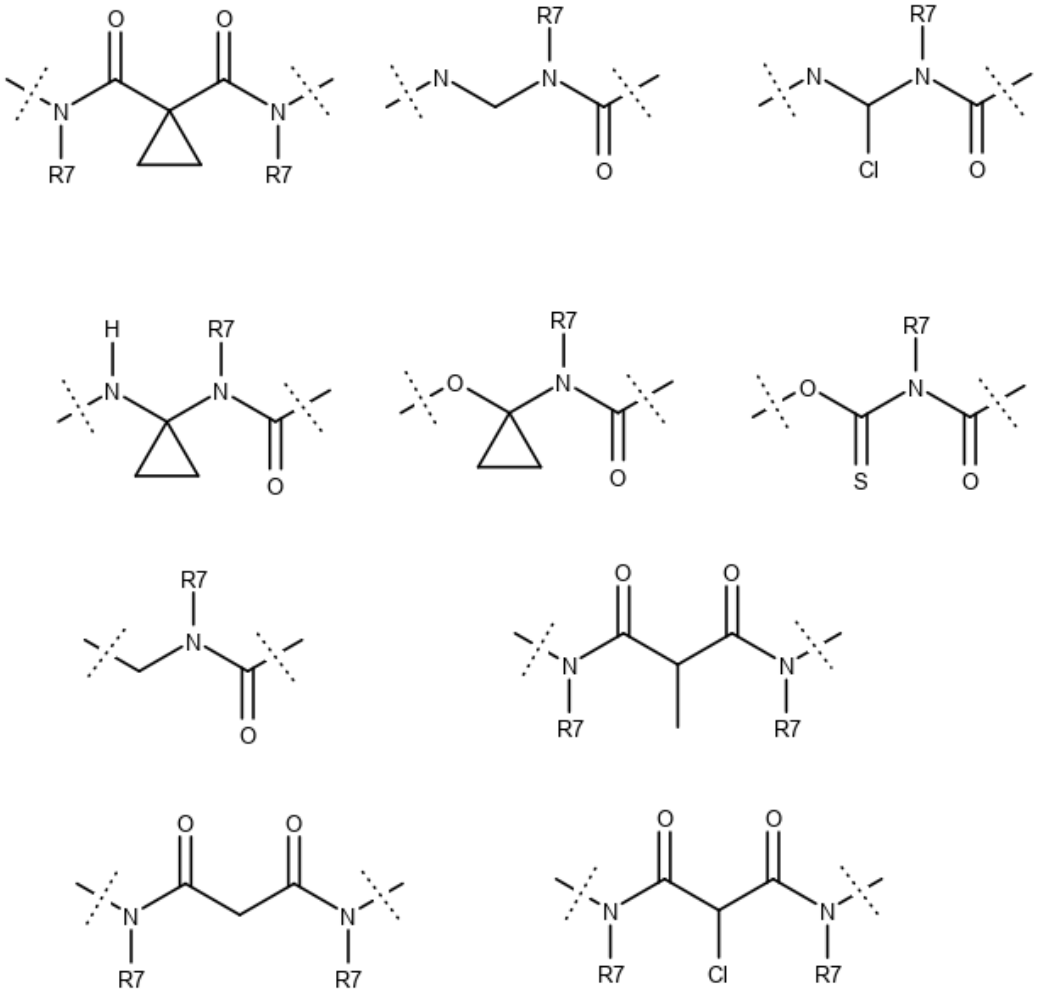
13. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein:

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

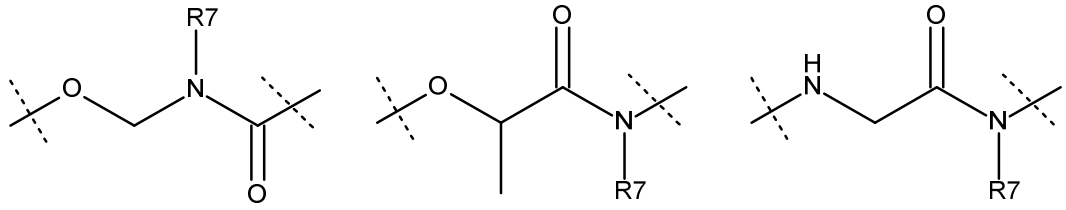
a represents 1.

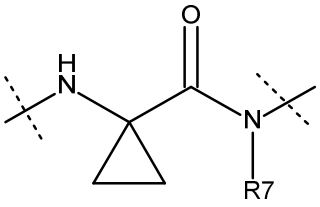
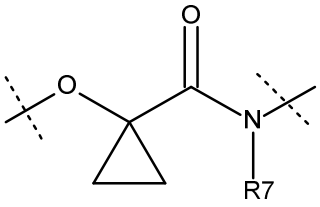
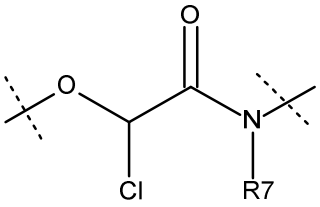
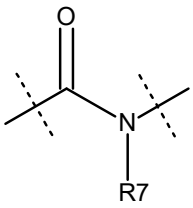
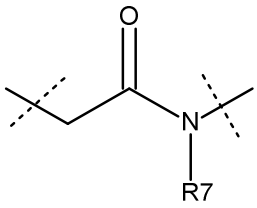
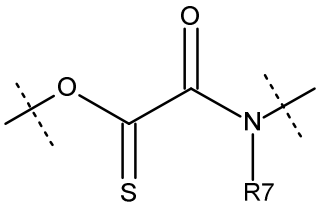
14. A compound according to claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein L is selected from:



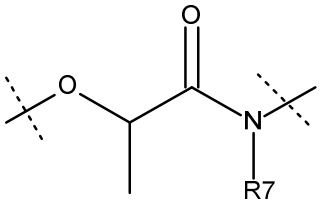
.

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

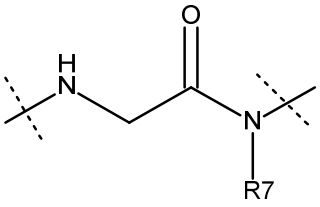


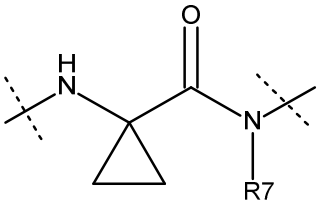
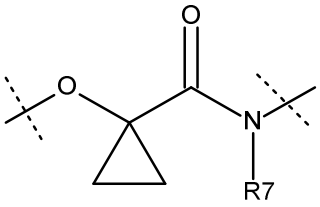
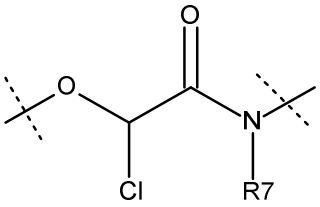
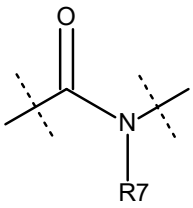
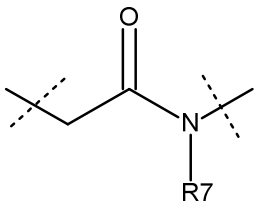
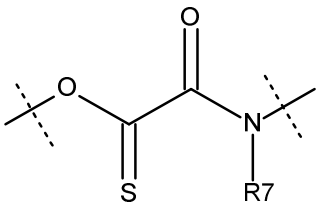







and ,



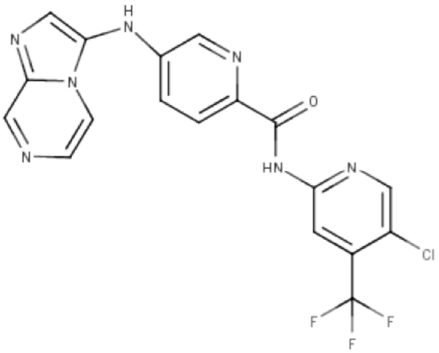
optionally wherein L is selected from

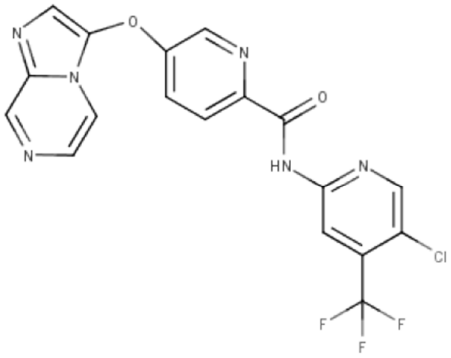


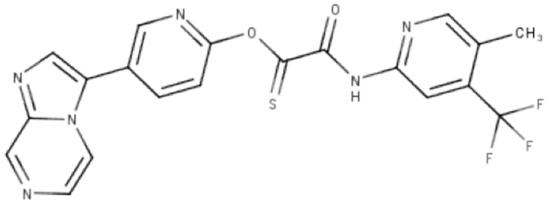







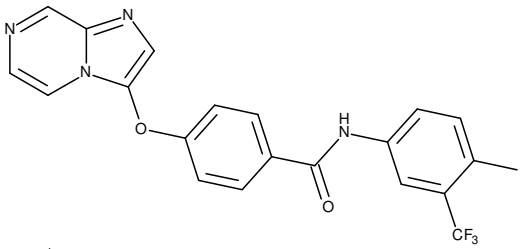
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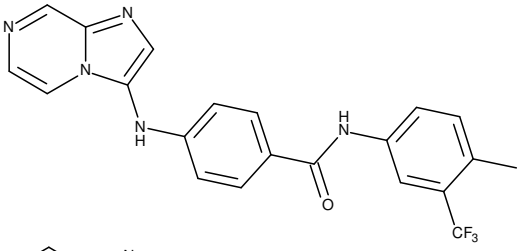
16. A compound according to claim 1 which is selected from

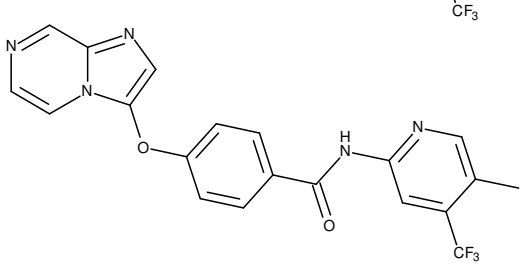


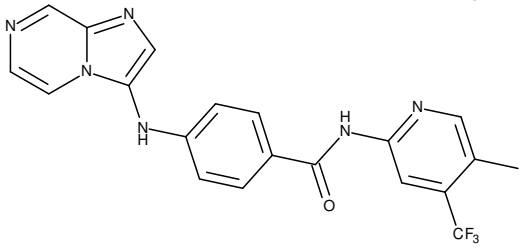


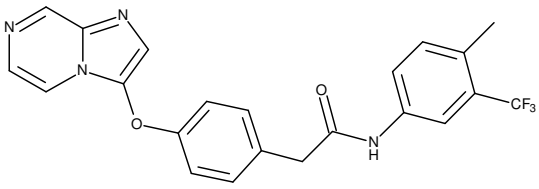


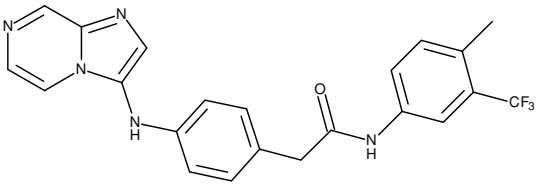


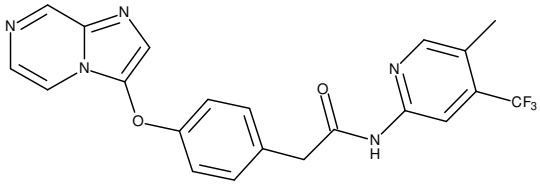


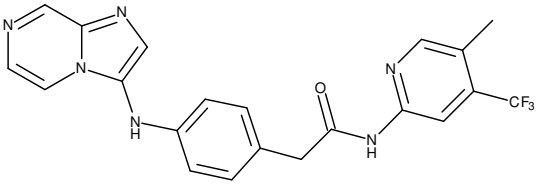


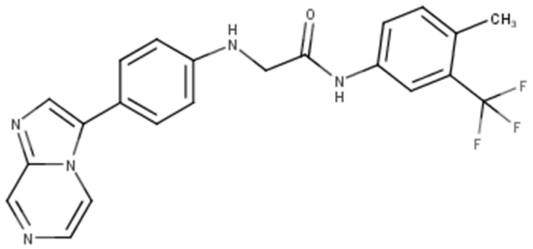


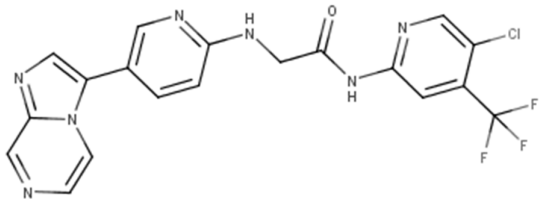


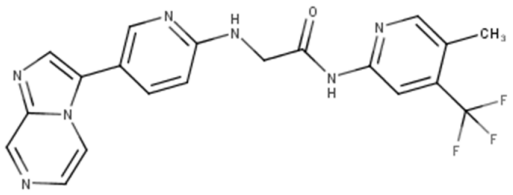


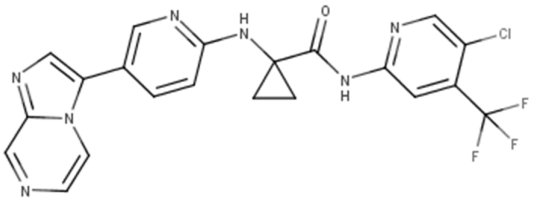


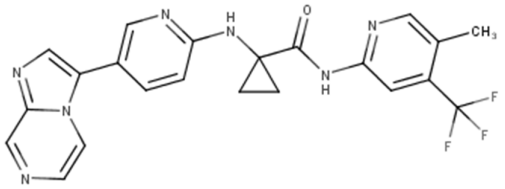


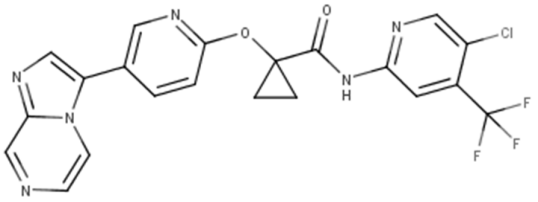


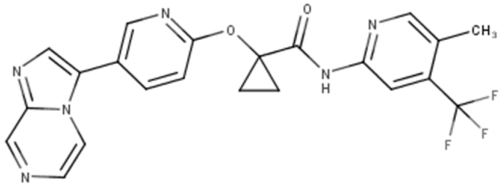


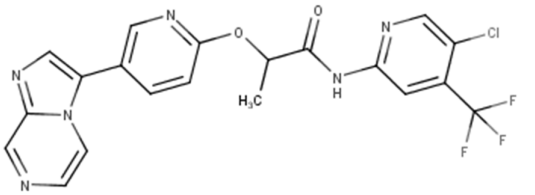


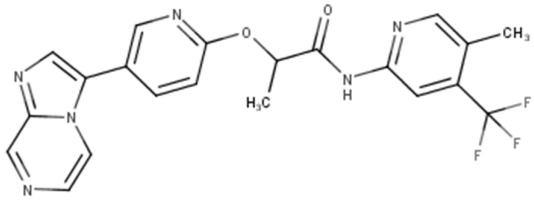


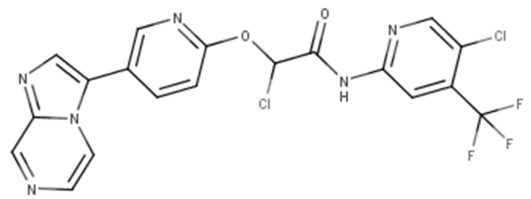


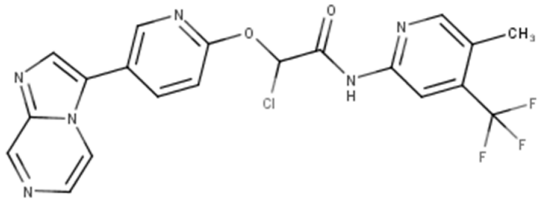


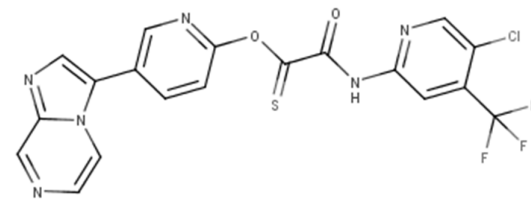


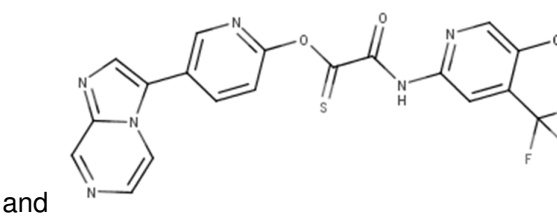












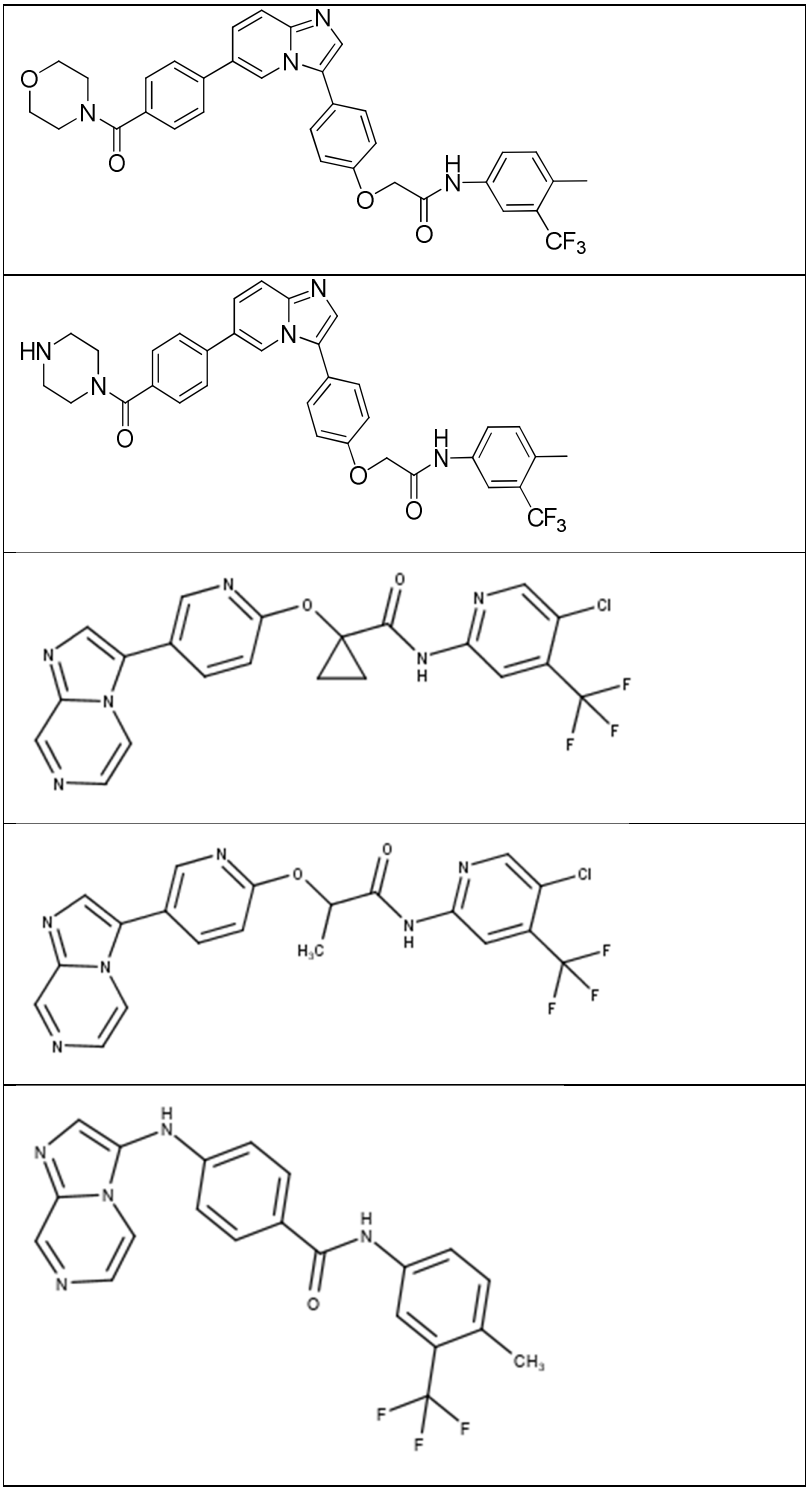
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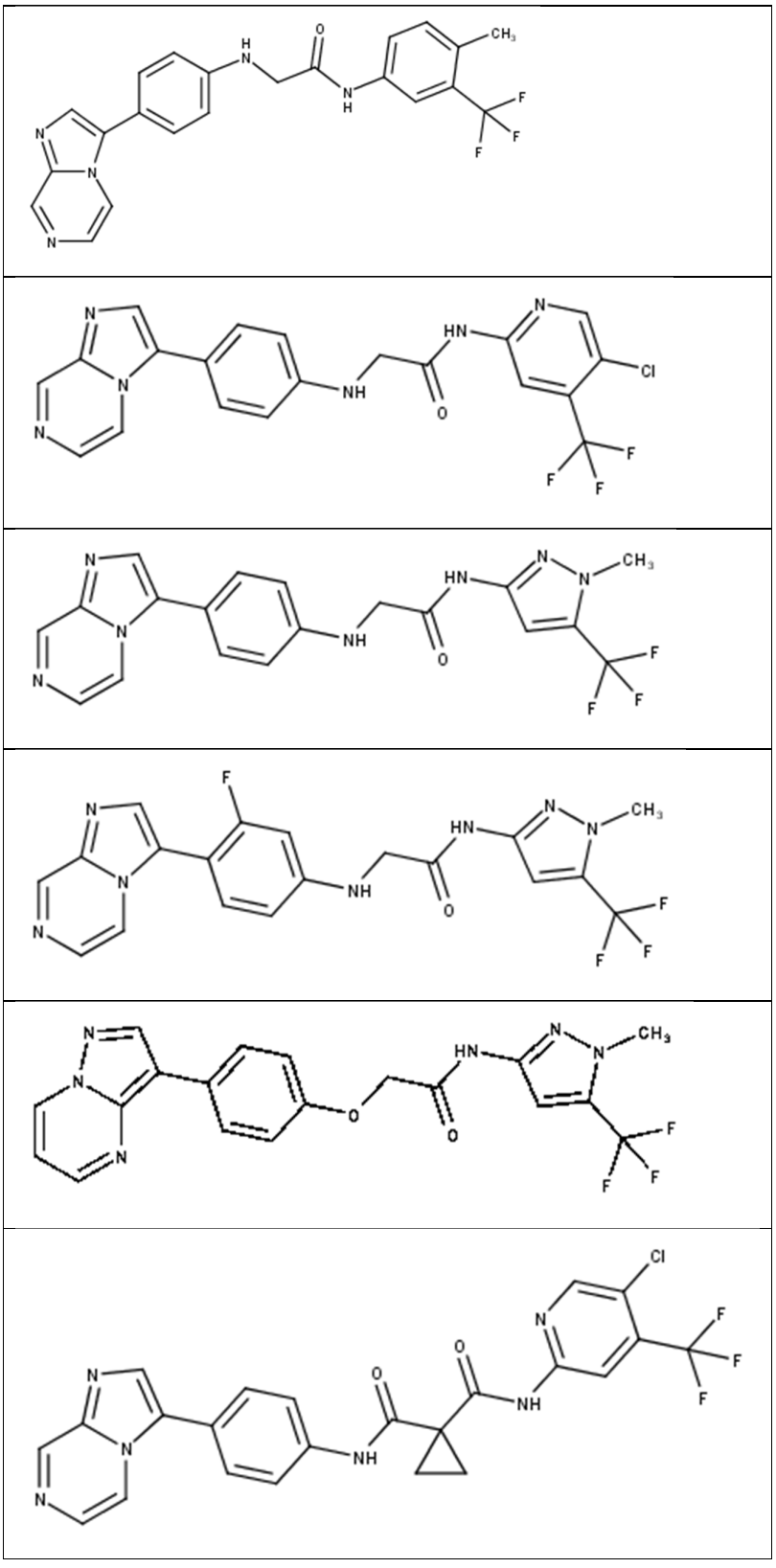
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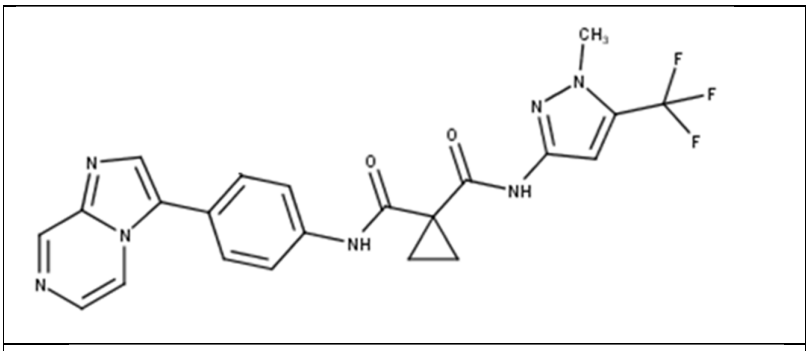
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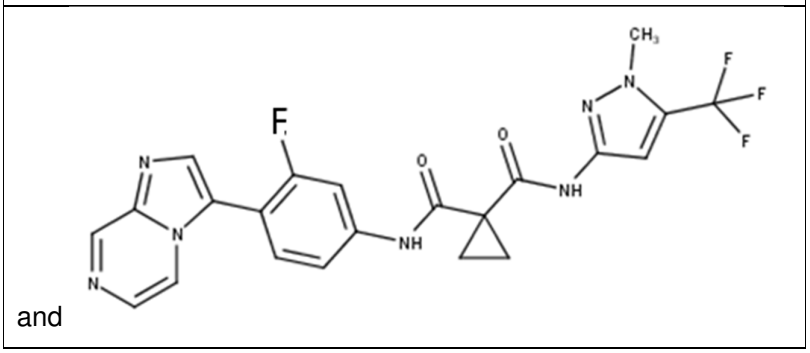
or a pharmaceutically acceptable or a salt, solvate or derivative thereof.

17. A compound according to claim 1, which is selected from:









and

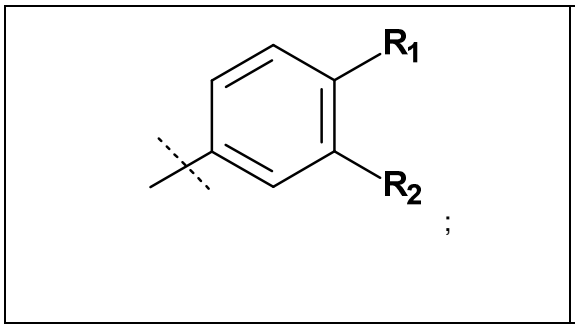
or a pharmaceutically acceptable salt, solvate or derivative thereof.

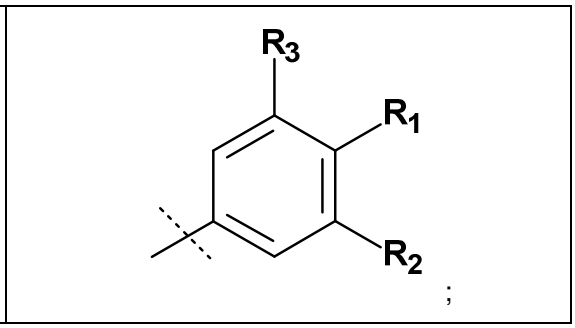
18. A compound according to Claim 1, or a pharmaceutically acceptable salt, solvate or derivative thereof, wherein:

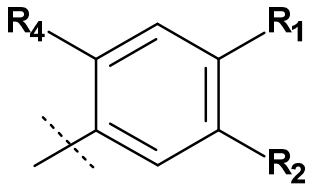
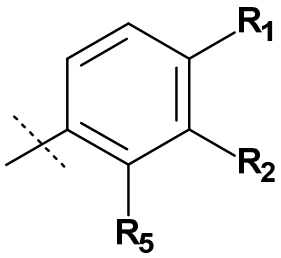
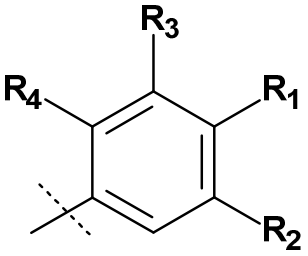
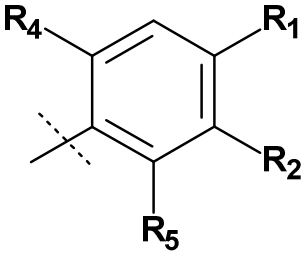
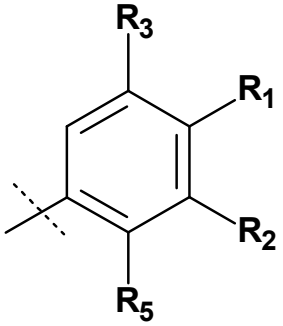
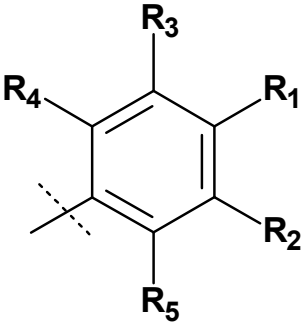
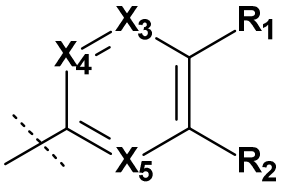
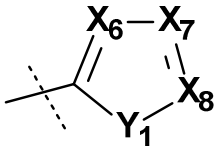
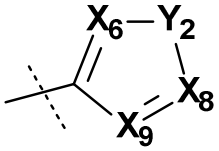
X_1 and X_2 each independently represent N or CR_a

R_a independently represents H, NH_2, halo, C_{1-5} alkyl, C_{1-5} alkoxy, C_{2-5} alkenyl and C_{2-5} alkynyl (which latter four groups are unsubstituted or substituted by one or more halo substituents);

A is selected from the group consisting of:





 ;	 ;
 ;	 ;
 ;	 ;
	 ; or
	

where:

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

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;

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 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;

Y_1 and Y_2 each independently represent NR_N, 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;

L is a linking group of the formula:

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

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

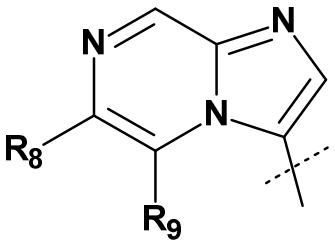
where M represents a covalent bond, O or NH;

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;

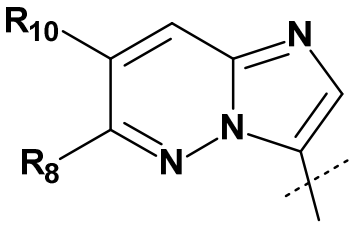
a represents 0 or 1;

R_7 and $R_{7'}$ represent H or an optionally substituted alkyl group;

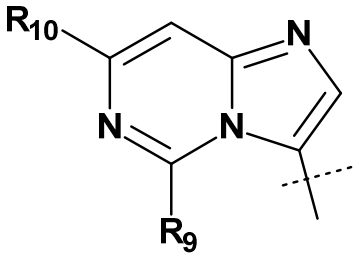
Z represents a heterocycle selected from the group consisting of:



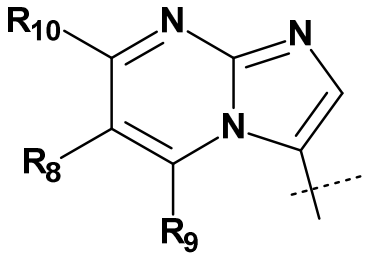
;



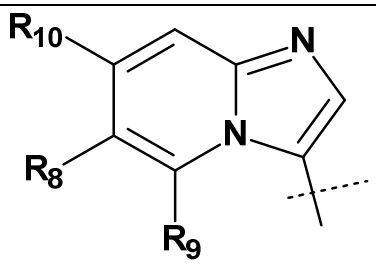
;



;



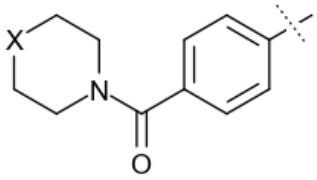
; and

 ;	

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;

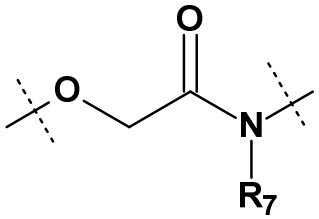
each of R_8 to R_{10} are independently selected from H, Me, C_1 to C_5 alkoxy which is unsubstituted or substituted by one or more halo groups, $OC(O)R_{11}$, $C(O)OR_{12}$, C_2 to C_5 alkynyl substituted by one or more halo groups or $NR_{13}R_{14}$, and one of R_8 to R_{10} may be a group of the formula

 ;

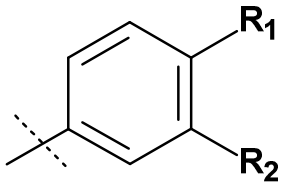
where X represents O or NH

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;



provided that when X_1 and X_2 are both CH, L is , and A is

 , then Z is not an optionally substituted heteroaryl selected from optionally substituted tetrazolyl or optionally substituted imidazopyridinyl.

19. Use of a compound of formula I as defined in claim 1, or a pharmaceutically acceptable salt, solvate or derivative 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.

20. A pharmaceutical composition comprising a compound of formula I as defined in claims 1 or a pharmaceutically acceptable salt, solvate or derivative thereof.