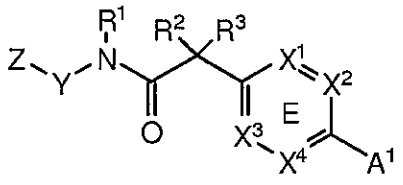
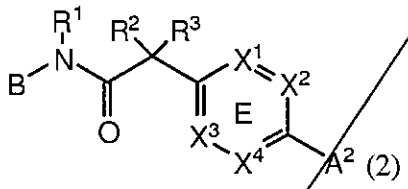
Claims

1. A compound having Formula (1) or (2):

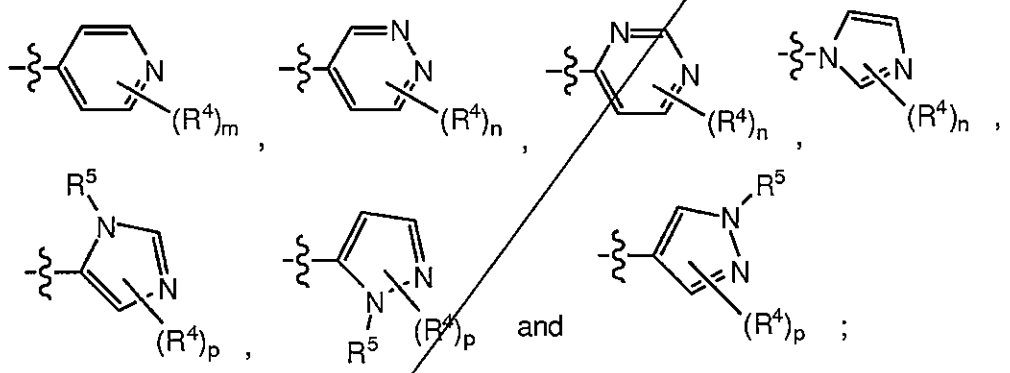

(1)


(2)

or a physiologically acceptable salt thereof, wherein:

ring E is an optionally substituted aryl or heteroaryl;

A^1 and A^2 are independently a C_{1-5}heterocycle, quinolinyl, or a heteroaryl selected from the group



wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-LC(O)R^{10}$;

B is benzothiazolyl, quinolinyl or isoquinolinyl, each of which is optionally substituted with 1-3 R^6 groups;

X^1, X^2, X^3 and X^4 are independently CR^7 or N;

Y is phenyl or a 5-6 membered heteroaryl containing 1-2 heteroatoms selected from N, O and S;

Z is aryl, C_{1-5} heterocycle, or a 5-6 membered heteroaryl containing 1-2 heteroatoms selected from N, O and S;

each Y and Z are optionally substituted with 1-3 R^6 groups;

R^1 and R^5 are independently H or C_{1-6} alkyl;

R^2 and R^3 are independently H, C_{1-6} alkyl or halo;

R^4 is halo, cyano, C_{1-6}alkoxy, or a C_{1-6} alkyl optionally substituted with halo, alkoxy or amino;

R^6 is hydrogen, halo, C_{1-6}alkoxy, $-S(O)_2R^{10}$, $-C(O)OR^{10}$, $-C(O)R^{10}$, $-C(O)NR^8R^9$, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which can be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; halo, CN, -L-W, NR^8R^9, -L-$C(O)R^{10}$, -L-$C(O)OR^{10}$, -L-$C(O)NR^8R^9$, OR^{10}; -L-$S(O)_2R^{10}$ or –L-$S(O)_2NR^8R^9$;

R^7 is H, halo, C_{1-6} alkoxy, -L-$S(O)_2R^{10}$, C_{1-6} alkyl optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; NR^8R^9, -L-$C(O)R^{10}$, -L-$C(O)NR^8R^9$, OR^{10}; -L-$S(O)_2R^{10}$ or –L-$S(O)_2NR^8R^9$;

R^8 and R^9 are independently H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; or R^8 and R^9 together with the atoms to which they are attached may form a ring;

R^{10} is H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano;

L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

W is C_{3-7}cycloalkyl, C_{1-5}heterocycle, aryl or heteroaryl;

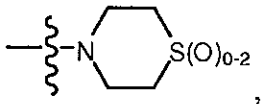
m is 0-4;

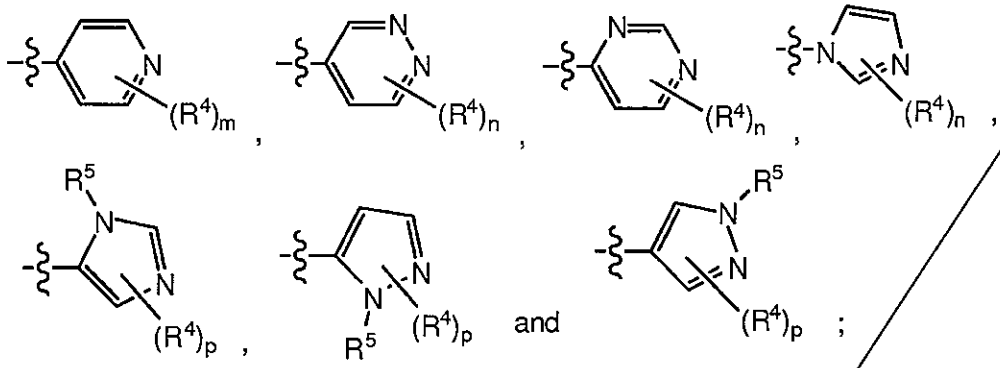
n is 0-3; and

p is 0-2.

2. The compound of claim 1, wherein Y is phenyl, thiazolyl, pyridinyl, pyridazinyl, pyrimidinyl or pyrazinyl, each of which is optionally substituted with 1-2 R^6 groups and R^6 is as defined in claim 1.

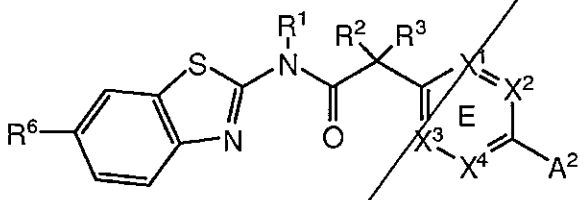
3. The compound of claim 1, wherein Z is phenyl, pyridinyl, pyridazine, pyrimidine, pyrazine, piperazinyl, piperidinyl, morpholinyl, pyrazole or 1,2,3,6-tetrahydropyridine, each of which is optionally substituted with 1-2 R^6 groups and R^6 is as defined in claim 1.

4. The compound of claim 1, wherein A^1 and A^2 are independently morpholinyl, piperazinyl, quinolinyl, , or a heteroaryl selected from the group:



wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-C(O)CH_3$; R^4 and n are as defined in claim 1.

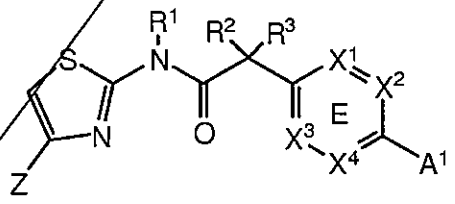
5. The compound of claim 1, wherein said compound is of Formula (3):



(3)

wherein R^1, R^2, R^3, X^1, X^2, X^3, X^4, A^2 and R^6 are as defined in claim 1.

6. The compound of claim 1, wherein said compound is of Formula (4):



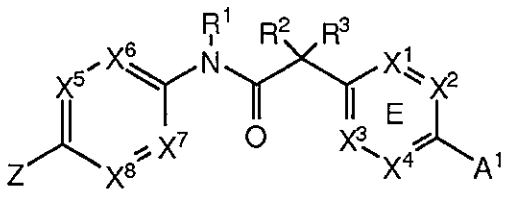
(4)

wherein R^1, R^2, R^3, X^1, X^2, X^3, X^4, A^1 and Z are as defined in claim 1.

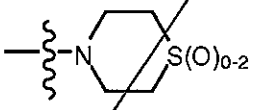
7. The compound of any one of claims 1-6, wherein ring E is phenyl, pyridyl or pyrimidinyl, each of which optionally substituted with R^7.

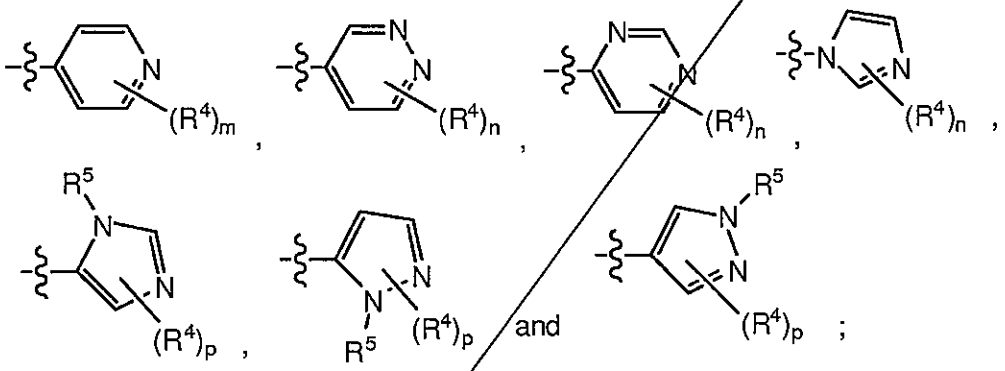
8. The compound of any one of claims 1-6, wherein R^7 is H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl.

9. The compound of claim 1, wherein said compound is of Formula (5):



(5)

wherein A^1 is piperazinyl substituted with $-C(O)CH_3$,  or selected from:



ring E is phenyl or one of X^1, X^2, X^3 and X^4 is N and the others are CR^7;

one of X^5, X^6, X^7 and X^8 is N and the others are CR^{11};

Z is a 6-membered heterocycle or a 6-membered heteroaryl, each containing 1-2 nitrogen heteroatoms and each of which is optionally substituted with 1-2 R^6 groups;

R^1, R^2 and R^3 are H or C_{1-6} alkyl;

R^4 and R^6 are independently hydrogen, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, $-C(O)NR^8R^9$, -L-$C(O)R^{10}$, -L-$C(O)OR^{10}$, C_{1-6} alkyl optionally substituted with halo, C_{2-6} alkenyl or C_{2-6} alkynyl;

R^{10} is C_{1-6} alkyl or -L-W;

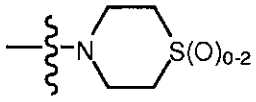
L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

W is C_{3-7}cycloalkyl;

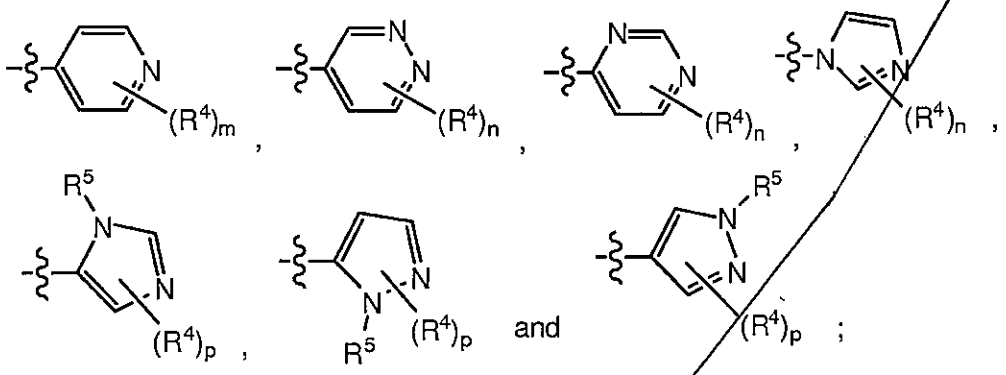
R^7 and R^{11} are independently H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl; and

m and n are independently 0-2.

10. The compound of claim 9, wherein A^1 is piperazinyl substituted with $-C(O)CH_3$,



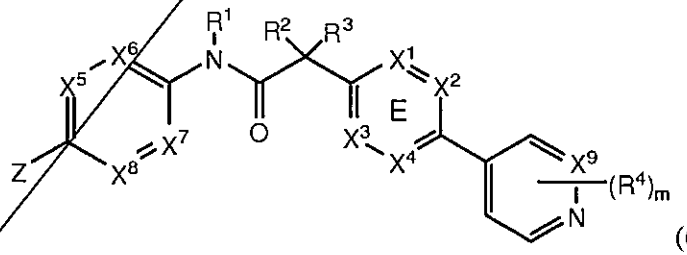
or selected from:



and m is 0-1.

11. The compound of claim 9, wherein one of X^1, X^2, X^3 and X^4 is N and the others are CR^7.

12. The compound of claim 1, wherein said compound is of Formula (6):



(6)

wherein X^1, X^2, X^3 and X^4 is selected from N and CR_7;

one of X^5, X^6, X^7 and X^8 is N and the others are CH;

X^9 is selected from N and CH;

Z is selected from phenyl, pyrazinyl, pyridinyl, pyridazinyl and piperazinyl; wherein each phenyl, pyrazinyl, pyridinyl, pyridazinyl or piperazinyl of Z is optionally substituted with an R^6 group;

R^1, R^2 and R^3 are hydrogen;

m is 1;

R^4 is selected from hydrogen, halo, difluoromethyl, trifluoromethyl and methyl;

R^6 is selected from hydrogen, halo and $-C(O)R^{10}$; wherein R^{10} is methyl; and

R^7 is selected from hydrogen, halo, cyano, methyl and trifluoromethyl.

13. The compound of any one of claims 1-12, wherein R^1, R^2 and R^3 are H.

14. The compound of any one of claims 1-12, wherein R^4 and R^6 are independently selected from hydrogen, halo, methyl, trifluoromethyl and $-C(O)CH_3$.

15. The compound of claim 1 selected from: tert-butyl 4-(5-{2-[4-(2-methylpyridin-4-yl)phenyl]acetamido}pyridin-2-yl)-1,2,3,6-tetrahydropyridine-1-carboxylate; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[6-(morpholin-4-yl)pyridin-3-yl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[4-(quinolin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[6-(quinolin-4-yl)pyridin-3-yl]acetamide; N-(6-methanesulfonyl-1,3-benzothiazol-2-yl)-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(6-fluoro-1,3-benzothiazol-2-yl)-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(1,3-benzothiazol-2-yl)-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[6-(pyridin-4-yl)pyridin-3-yl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[3-methyl-4-(2-methylpyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[4-(2-methylpyrimidin-4-yl)phenyl]acetamide; N-[4-(pyridin-2-yl)-1,3-thiazol-2-yl]-2-[4-(pyridin-4-yl)phenyl]acetamide; N-[4-(pyridin-4-yl)-1,3-thiazol-2-yl]-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[2-methyl-4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(4-phenyl-1,3-thiazol-2-yl)acetamide; N-(isoquinolin-3-yl)-2-[4-(pyridin-4-yl)phenyl]acetamide; N-(6-fluoro-1,3-

benzothiazol-2-yl)-2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; 2-[4-(pyridin-4-yl)phenyl]-N-(quinolin-2-yl)acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[5-(2-methylpyridin-4-yl)pyrimidin-2-yl]acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[5-(2-methylpyridin-4-yl)pyridin-2-yl]acetamide; 2-[3-methyl-4-(2-methylpyridin-4-yl)phenyl]-N-(4-phenyl-1,3-thiazol-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(4-phenyl-1,3-thiazol-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(5-phenylpyridin-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(4-phenylpyridin-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[6-(trifluoromethoxy)-1,3-benzothiazol-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(5-phenyl-1,3-thiazol-2-yl)acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-2-[4-(2-methoxypyridin-4-yl)phenyl]acetamide; 2-[4-(2-ethylpyridin-4-yl)phenyl]-N-(6-methoxy-1,3-benzothiazol-2-yl)acetamide; 2-[2-methyl-4-(2-methylpyridin-4-yl)phenyl]-N-(4-phenyl-1,3-thiazol-2-yl)acetamide; N-[4-(4-methoxyphenyl)-1,3-thiazol-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[4-(4-fluorophenyl)-1,3-thiazol-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[4-(3,4-difluorophenyl)-1,3-thiazol-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(6-phenylpyridin-3-yl)acetamide; N-(5-phenylpyridin-2-yl)-2-[4-(pyridazin-4-yl)phenyl]acetamide; N-[5-(4-methylphenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[5-(3-methoxyphenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[5-(2-methoxyphenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[5-(4-methoxyphenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(5-phenylpyrazin-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridin-2-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl]-N-(4-phenyl-1,3-thiazol-2-yl)acetamide; N-[5-(3-methylphenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl]-N-(5-phenylpyridin-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridin-3-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridin-4-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(6-phenylpyridazin-3-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(4-phenylphenyl)acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(5-phenylpyridin-2-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(2-phenylpyrimidin-5-yl)acetamide; 2-[4-(1H-imidazol-1-yl)phenyl]-N-(5-phenylpyridin-2-yl)acetamide; N-(6-phenylpyridin-3-yl)-2-[4-(pyridazin-4-yl)phenyl]acetamide; N-[5-(4-fluorophenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-

yl)phenyl]acetamide; N-[5-(3-fluorophenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[5-(4-ethylpiperazin-1-yl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]pyridin-2-yl}-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[4-(pyridin-3-yl)phenyl]acetamide; N-(6-fluoro-1,3-benzothiazol-2-yl)-2-[4-(pyridazin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-(5-phenylpyrimidin-2-yl)acetamide; N-(6-methoxy-1,3-benzothiazol-2-yl)-N-methyl-2-[4-(pyridin-4-yl)phenyl]acetamide; 2-[4-(pyridazin-4-yl)phenyl]-N-[4-(pyridin-3-yl)phenyl]acetamide; N-(6-phenylpyridazin-3-yl)-2-[4-(pyridazin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(1H-pyrazol-4-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyrazin-2-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyrimidin-5-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[4-(pyridazin-4-yl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(1,2,3,6-tetrahydropyridin-4-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridazin-3-yl)pyridin-2-yl]acetamide; 2-[5-methyl-6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(6-phenylpyridin-3-yl)acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridazin-4-yl)pyridin-2-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[6-(morpholin-4-yl)pyridin-3-yl]acetamide; N-[5-(3-fluorophenyl)pyridin-2-yl]-2-[5-methyl-6-(pyridazin-4-yl)pyridin-3-yl]acetamide; 2-[3-methyl-4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridin-2-yl)pyridin-2-yl]acetamide; 2-[3-methyl-4-(pyridazin-4-yl)phenyl]-N-[5-(pyridin-2-yl)pyridin-2-yl]acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-[5-(pyridazin-3-yl)pyridin-2-yl]acetamide; N-[5-(pyridazin-3-yl)pyridin-2-yl]-2-[6-(pyridazin-4-yl)pyridin-3-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl]-N-[5-(pyrazin-2-yl)pyridin-2-yl]acetamide; N-[5-(3-fluorophenyl)pyridin-2-yl]-2-[5-methyl-6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; N-[5-(3-fluorophenyl)pyridin-2-yl]-2-[4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[5-(pyridazin-4-yl)pyridin-2-yl]acetamide; N-[5-(3-fluorophenyl)pyridin-2-yl]-2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[6-(pyridazin-4-yl)pyridin-3-yl]acetamide; 2-[5-methyl-6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-[5-(pyrazin-2-yl)pyridin-2-yl]acetamide; 2-[5-methyl-6-(pyridazin-4-yl)pyridin-3-yl]-N-(6-phenylpyridin-3-yl)acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(6-phenylpyridin-3-yl)acetamide; N-(6-phenylpyridin-3-yl)-2-[6-(pyridazin-4-yl)pyridin-3-yl]acetamide; N-[6-(1-acetyl-1,2,3,6-

tetrahydropyridin-4-yl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; methyl 4-(5-{2-[4-(2-methylpyridin-4-yl)phenyl]acetamido}pyridin-2-yl)-1,2,3,6-tetrahydropyridine-1-carboxylate; N-[6-(1-methanesulfonyl-1,2,3,6-tetrahydropyridin-4-yl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[6-(1-methylpiperidin-4-yl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; 2-[5-methyl-6-(pyridazin-4-yl)pyridin-3-yl]-N-[5-(pyridin-2-yl)pyridin-2-yl]acetamide; 2-[6-(pyridazin-4-yl)pyridin-3-yl]-N-[5-(pyridin-2-yl)pyridin-2-yl]acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(5-phenylpyrimidin-2-yl)acetamide; N-[5-(3-fluorophenyl)pyrimidin-2-yl]-2-[6-(pyridazin-4-yl)pyridin-3-yl]acetamide; ethyl 4-(5-{2-[4-(2-methylpyridin-4-yl)phenyl]acetamido}pyridin-2-yl)-1,2,3,6-tetrahydropyridine-1-carboxylate; propan-2-yl 4-(5-{2-[4-(2-methylpyridin-4-yl)phenyl]acetamido}pyridin-2-yl)-1,2,3,6-tetrahydropyridine-1-carboxylate; 1-methylcyclopropyl 4-(5-{2-[4-(2-methylpyridin-4-yl)phenyl]acetamido}pyridin-2-yl)-1,2,3,6-tetrahydropyridine-1-carboxylate; 2-[4-(2-methylpyridin-4-yl)phenyl]-N-[6-(1,2,3,6-tetrahydropyridin-4-yl)pyridin-3-yl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[5-methyl-6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[5-methyl-6-(pyridazin-4-yl)pyridin-3-yl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[4-(pyridazin-4-yl)-3-(trifluoromethyl)phenyl]acetamide; N-[6-(1-methyl-1,2,3,6-tetrahydropyridin-4-yl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[6-(1-ethyl-1,2,3,6-tetrahydropyridin-4-yl)pyridin-3-yl]-2-[4-(2-methylpyridin-4-yl)phenyl]acetamide; N-[6-(3-fluorophenyl)pyridin-3-yl]-2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]acetamide; N-(6-phenylpyridazin-3-yl)-2-[6-(pyridazin-4-yl)pyridin-3-yl]acetamide; 2-[6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(6-phenylpyridazin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(2,3'-bipyridin-6'-yl)-2-(4-(pyridazin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; N-(5-(pyridazin-3-yl)pyridin-2-yl)-2-(4-(pyridazin-4-yl)phenyl)acetamide; N-(5-(3-fluorophenyl)pyridin-2-yl)-2-(6-(pyridazin-4-yl)pyridin-3-yl)acetamide; N-(6-(3-fluorophenyl)pyridin-3-yl)-2-(6-(pyridazin-4-yl)pyridin-3-yl)acetamide; N-(6-(1-(2-amino-2-oxoethyl)-1,2,3,6-tetrahydropyridin-4-yl)pyridin-3-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(6-(3-fluorophenyl)pyridin-3-yl)-2-(4-(pyridazin-4-yl)phenyl)acetamide; N-(5-(pyrazin-2-yl)pyridin-2-yl)-2-(4-(pyridazin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; tert-butyl 4-(5-(2-(4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-2-yl)piperazine-1-carboxylate; N-(5-(3-fluorophenyl)pyridin-2-yl)-

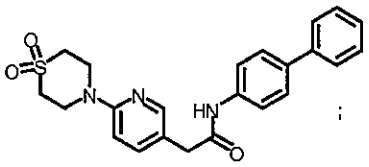
2-(4-(pyridazin-4-yl)phenyl)acetamide; N-(2,3'-bipyridin-6'-yl)-2-(4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; N-(5-(pyridazin-3-yl)pyridin-2-yl)-2-(4-(pyridazin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; N-(2-(3-fluorophenyl)pyrimidin-5-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(2,3'-bipyridin-6'-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; tert-butyl 4-(6-(2-(4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; N-(2,3'-bipyridin-6'-yl)-2-(2'-methyl-2,4'-bipyridin-5-yl)acetamide; N-(6-(1-acetylpiperidin-4-yl)pyridin-3-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(2'-methyl-2,4'-bipyridin-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(pyrazin-2-yl)pyridin-2-yl)-2-(6-(pyridazin-4-yl)pyridin-3-yl)acetamide; 2-(5-methyl-6-(pyridazin-4-yl)pyridin-3-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; methyl 4-(6-(2-(4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; 2-(3-methyl-4-(pyridazin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(3-methyl-4-(pyridazin-4-yl)phenyl)-N-(5-(pyridazin-4-yl)pyridin-2-yl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(5-(pyridazin-4-yl)pyridin-2-yl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(6-(pyridazin-4-yl)pyridin-3-yl)acetamide; 2-(3-methyl-4-(pyridazin-4-yl)phenyl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; tert-butyl 4-(6-(2-(4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-3-yl)piperidine-1-carboxylate; 2-(3-methyl-4-(pyridazin-4-yl)phenyl)-N-(6-(pyridazin-4-yl)pyridin-3-yl)acetamide; 2-(6-(4-acetylpiperazin-1-yl)pyridin-3-yl)-N-(5-(3-fluorophenyl)pyridin-2-yl)acetamide; 2-(4-(2-methylpyridin-4-yl)phenyl)-N-(5-(3-oxopiperazin-1-yl)pyridin-2-yl)acetamide; 4-(6-(2-(4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-3-yl)piperazine-1-carboxamide; N-(5-(4-methyl-1H-imidazol-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(4-(4-methyl-1H-imidazol-1-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; 2-(5-methyl-6-(pyridazin-4-yl)pyridin-3-yl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; 2-(5-methyl-6-(pyridazin-4-yl)pyridin-3-yl)-N-(5-(pyridazin-4-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; N-(5-((3S,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(4-(1-acetylpiperidin-4-yl)phenyl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(6-(4-(2-hydroxyethyl)piperazin-1-yl)pyridin-3-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(6-(3-fluorophenyl)pyridin-3-yl)-2-(5-methyl-6-(pyridazin-4-yl)pyridin-3-yl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-

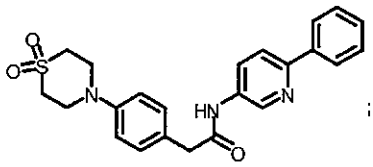
N-(4-(pyrazin-2-yl)phenyl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(4-(pyridazin-3-yl)phenyl)acetamide; 2-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)-5-(pyrazin-2-yl)pyridine 1-oxide; 2',3-dimethyl-5-(2-oxo-2-(5-(pyrazin-2-yl)pyridin-2-ylamino)ethyl)-2,4'-bipyridine 1'-oxide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(6-(pyrazin-2-yl)pyridin-3-yl)acetamide; N-(5-(4-isobutyrylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-methyl-4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(6-(4-acetylpiperazin-1-yl)pyridin-3-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; (R)-N-(6-(4-acetyl-3-methylpiperazin-1-yl)pyridin-3-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; (S)-N-(6-(4-acetyl-3-methylpiperazin-1-yl)pyridin-3-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; (S)-N-(6-(4-acetyl-3-methylpiperazin-1-yl)pyridin-3-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; (R)-N-(6-(4-acetyl-3-methylpiperazin-1-yl)pyridin-3-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; N-(5-((3S,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)pyridin-2-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; methyl 4-(6-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; methyl 4-(6-(2-(3-methyl-4-(2-methylpyridin-4-yl)phenyl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-fluoro-4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-chloro-4-(2-methylpyridin-4-yl)phenyl)acetamide; ethyl 4-(6-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; 2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(2',3-dimethyl-2,4'-bipyridin-5-yl)-N-(5-(4-propionylpiperazin-1-yl)pyridin-2-yl)acetamide; N-(5-(4-(cyanomethyl)piperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-cyanopiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-chloropyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-fluoropyridin-4-yl)phenyl)acetamide; 2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)-N-(6-(pyrazin-2-yl)pyridin-3-yl)acetamide; 2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-methoxy-4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-

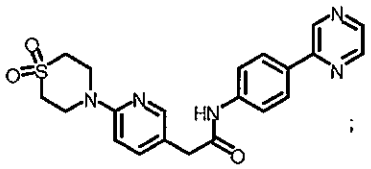
2-(3-chloro-2'-methyl-2,4'-bipyridin-5-yl)acetamide; (S)-N-(5-(4-acetyl-3-methylpiperazin-1-yl)pyridin-2-yl)-2-(3-cyano-4-(2-methylpyridin-4-yl)phenyl)acetamide; (R)-N-(5-(4-acetyl-3-methylpiperazin-1-yl)pyridin-2-yl)-2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamide; isopropyl 4-(6-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)pyridin-3-yl)piperazine-1-carboxylate; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-cyano-2'-methyl-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-3-(trifluoromethyl)-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2-fluoro-5-methyl-4-(2-methylpyridin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyrimidin-4-yl)-3-(trifluoromethyl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-fluoro-3-methyl-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2',3-difluoro-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-methylpyrimidin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(5-fluoropyrimidin-4-yl)phenyl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-3-(methylsulfonyl)-2,4'-bipyridin-5-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(6-methylpyrimidin-4-yl)phenyl)acetamide; 2-(2'-fluoro-3-methyl-2,4'-bipyridin-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(2-(difluoromethyl)pyridin-4-yl)phenyl)acetamide; N-(6-(4-acetylpiperazin-1-yl)pyridin-3-yl)-2-(4-(2-(difluoromethyl)pyridin-4-yl)phenyl)acetamide; 2-(4-(2-(difluoromethyl)pyridin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-(5-fluoropyrimidin-4-yl)-3-methylphenyl)acetamide; 2-(2',3-difluoro-2,4'-bipyridin-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(3-cyano-4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-fluoro-4-(2-fluoropyridin-4-yl)phenyl)acetamide; 2-(2'-fluoro-2,4'-bipyridin-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-fluoro-2,4'-bipyridin-5-yl)acetamide; 2-(2',3-difluoro-2,4'-bipyridin-5-yl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-cyano-4-(2-fluoropyridin-4-yl)phenyl)acetamide; 2-(3-fluoro-4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; 2-(3-fluoro-4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; 2-(3-cyano-4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide; 2-(4-(2-fluoropyridin-4-yl)phenyl)-N-(5-(pyridazin-3-

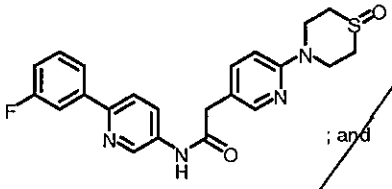
yl)pyridin-2-yl)acetamide; and 2-(2'-fluoro-3-methyl-2,4'-bipyridin-5-yl)-N-(5-(pyridazin-3-yl)pyridin-2-yl)acetamide, or a physiogically acceptable salt thereof.

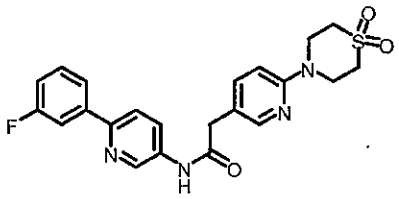
16. The compound of claim 1 selected from:


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; and


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17. A compound selected from: N-(6-methoxybenzo[d]thiazol-2-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridazin-4-yl)phenyl)acetamide; 2-(3-(2-methoxypyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyridazin-3-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyrazin-2-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-(pyrazin-2-yl)pyridin-3-yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-6-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-2,4'-bipyridin-4-

yl)acetamide; and N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2-cyano-2'-methyl-3,4'-bipyridin-5-yl)acetamide, or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-17 and a physiologically acceptable carrier.

19. A method for inhibiting Wnt signaling in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 1-17, or a pharmaceutical composition thereof.

20. A method for inhibiting a Porcupine gene in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 1-17, or a pharmaceutical composition thereof.

21. A method for treating a Wnt-mediated disorder in a mammal suffering therefrom, comprising administering to the mammal a therapeutically effective amount of a compound of any one of claims 1-17, or a pharmaceutical composition thereof, and optionally in combination with a second therapeutic agent.

22. The method of claim 21, wherein said disorder is keloids, fibrosis, proteinuria, kidney graft rejection, osteoarthritis, Parkinson's disease, cystoid macular edema, retinopathy, macular degeneration or a cell proliferative disorder associated with aberrant Wnt signaling activity.

23. The method of claim 22, wherein said disorder is keloids, fibrosis, proteinuria or a cell proliferative disorder.

24. The method of claim 22, wherein said disorder is fibrosis selected from skin fibrosis, idiopathic pulmonary fibrosis, renal interstitial fibrosis and liver fibrosis.

25. The method of claim 22, wherein said disorder is a cell proliferative disorder selected from the group colorectal cancer, breast cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, non-small cell lung cancer, gastric cancer,

pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilm's tumor, basal cell carcinoma, melanoma, head and neck cancer, cervical cancer and prostate cancer.

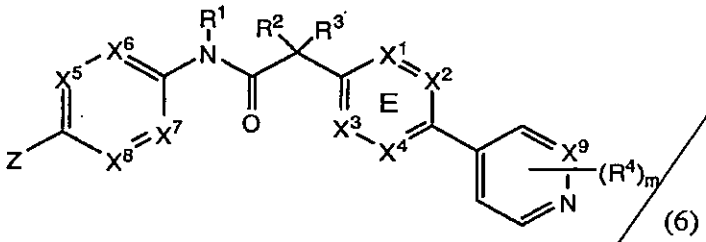
26. The method of claim 22, wherein said disorder is retinopathy selected from diabetic retinopathy and retinopathy of prematurity.

27. The use of a compound of any one of claims 1-17, or a pharmaceutical composition thereof, for inhibiting Wnt signaling.

28. The use of a compound of any one of claims 1-17, or a pharmaceutical composition thereof, for the manufacture of a medicament for treating a Wnt-mediated disorder.

Claims

1. A compound having Formula (6):



(6)

or a physiologically acceptable salt thereof, wherein:

wherein X^1, X^2, X^3 and X^4 is selected from N and CR^7;

one of X^5, X^6, X^7 and X^8 is N and the others are CH;

X^9 is selected from N and CH;

Z is selected from phenyl, pyrazinyl, pyridinyl, pyridazinyl and piperazinyl; wherein each phenyl, pyrazinyl, pyridinyl, pyridazinyl or piperazinyl of Z is optionally substituted with an R^6 group;

R^1, R^2 and R^3 are hydrogen;

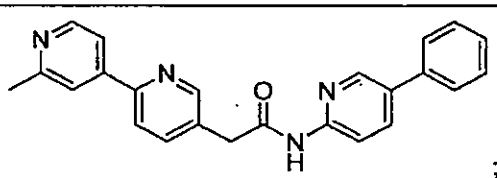
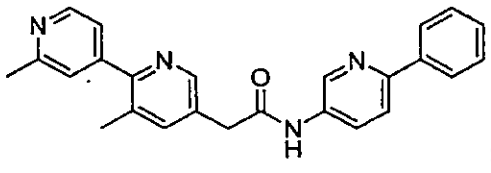
m is 1;

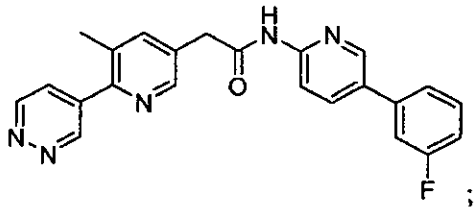
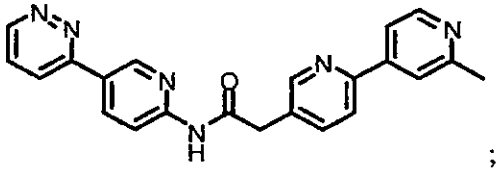
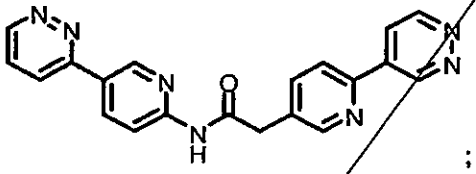
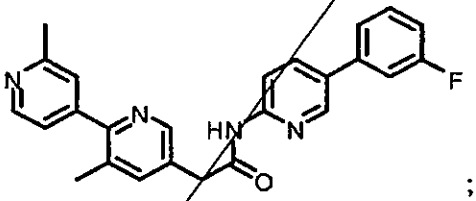
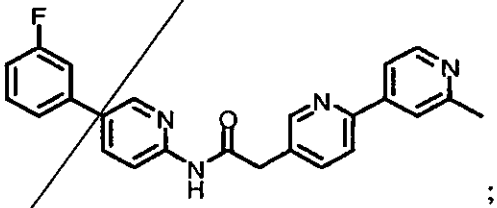
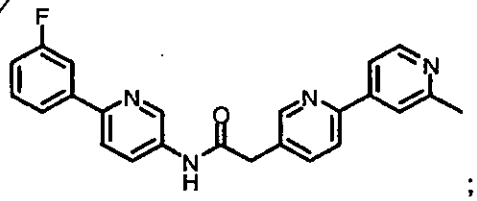
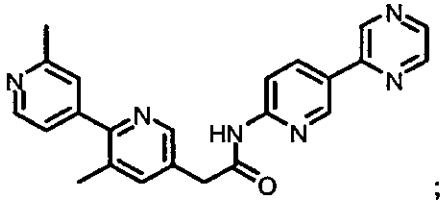
R^4 is selected from hydrogen, halo, difluoromethyl, trifluoromethyl and methyl;

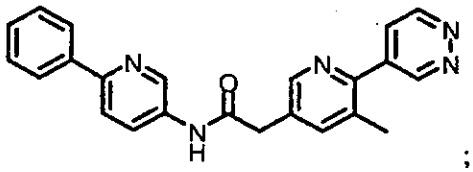
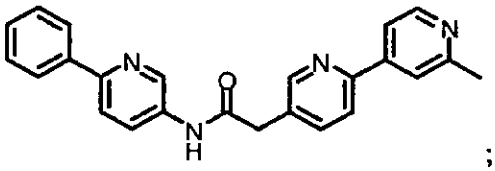
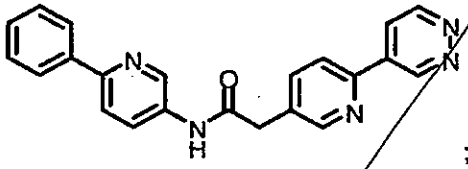
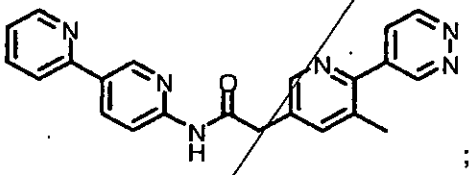
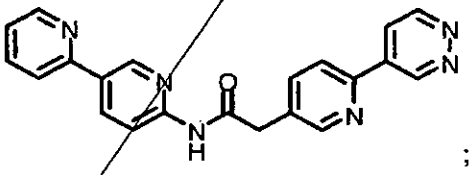
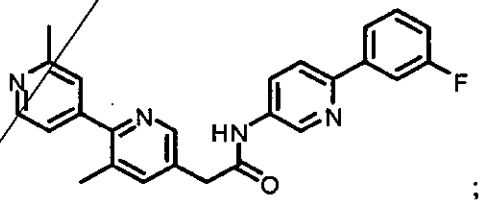
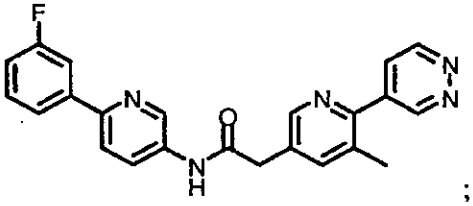
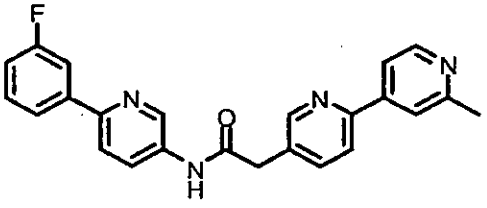
R^6 is selected from hydrogen, halo and $-C(O)R^{10}$; wherein R^{10} is methyl; and

R^7 is selected from hydrogen, halo, cyano, methyl and trifluoromethyl.

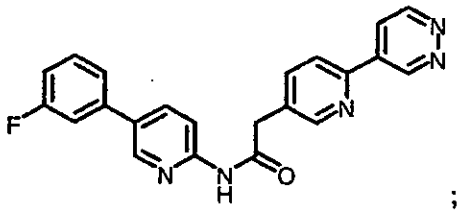
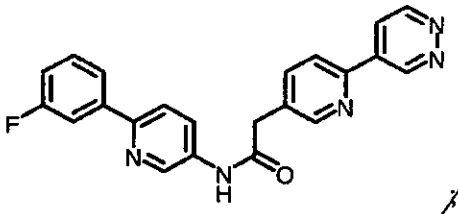
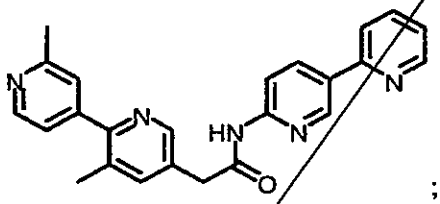
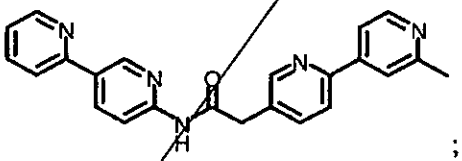
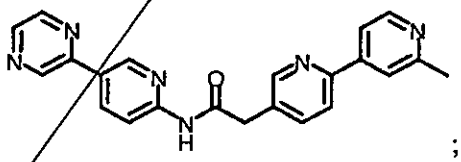
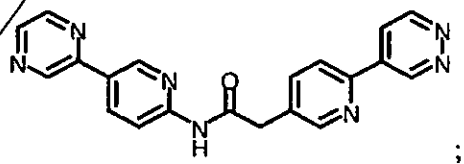
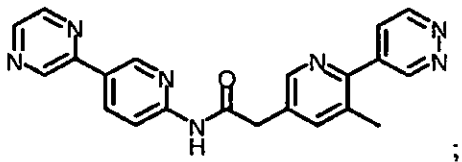
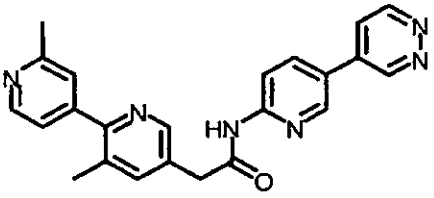
2. The compound of claim 1, wherein said compound is selected from

51	 ;
71	 ;

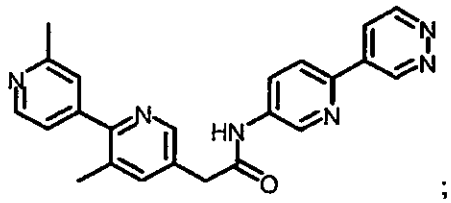
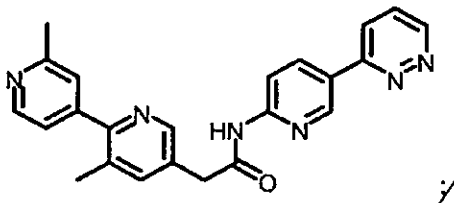
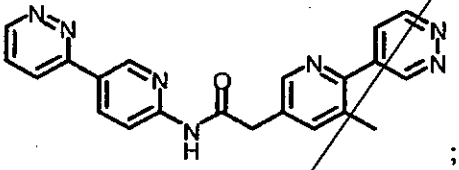
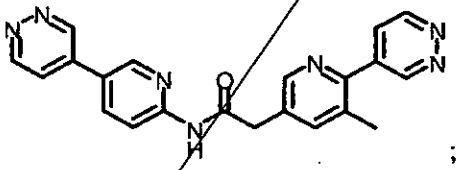
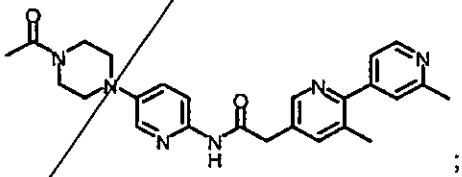
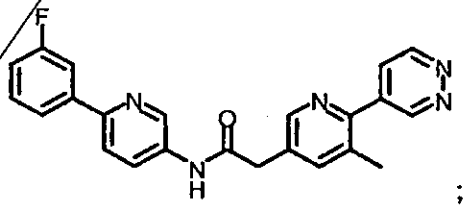
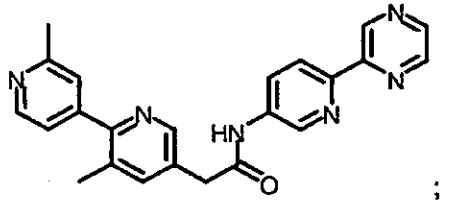
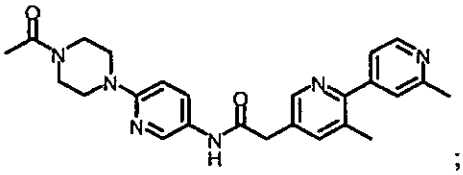
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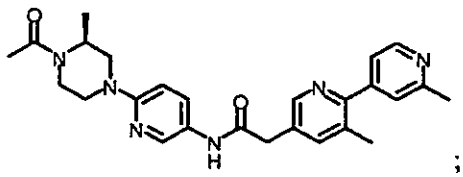
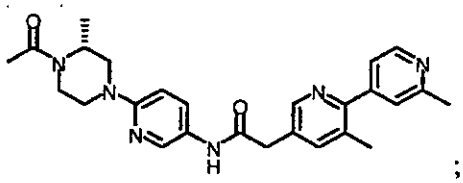
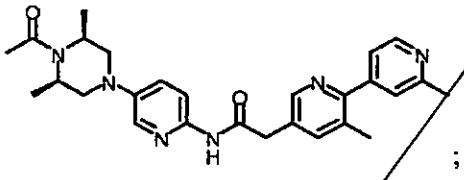
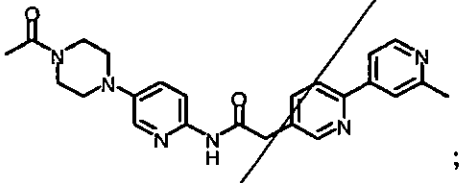
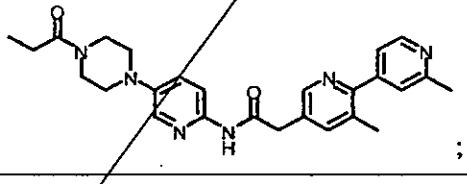
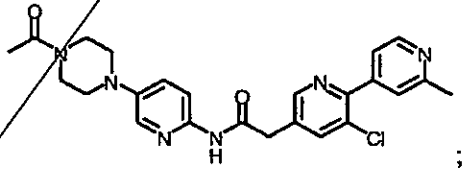
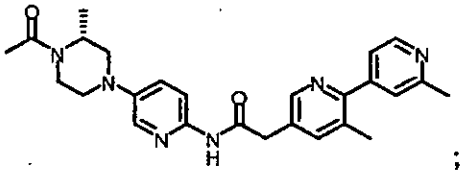
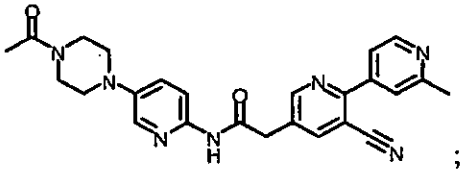
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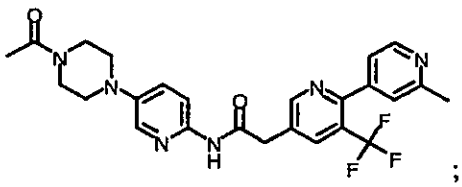
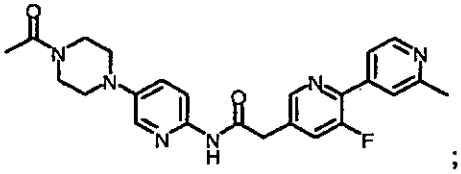
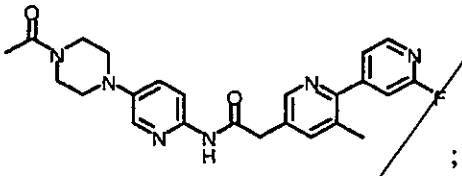
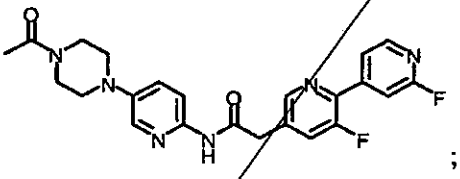
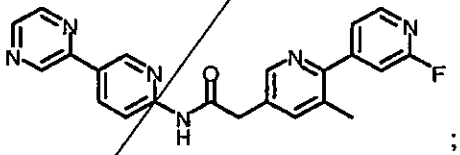
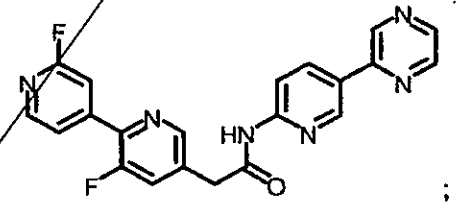
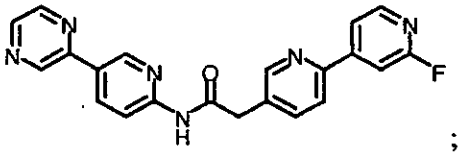
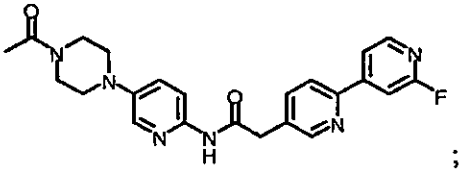
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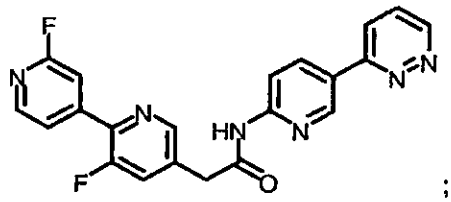
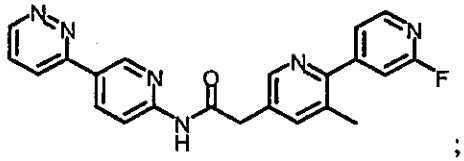
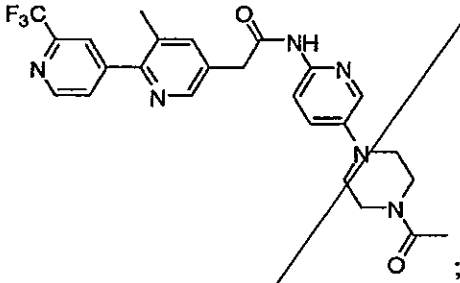
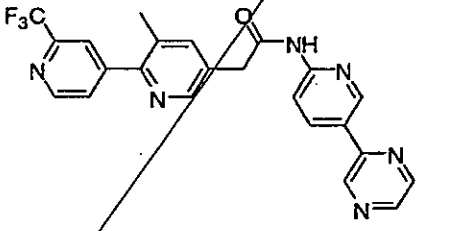
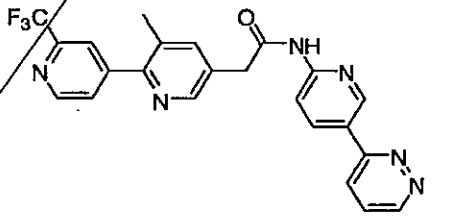
AMENDED SHEET (ARTICLE 19)

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AMENDED SHEET (ARTICLE 19)

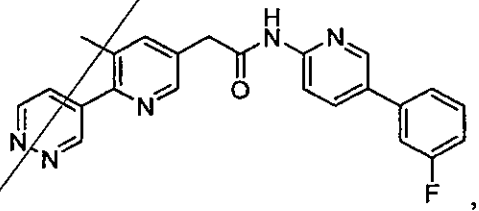
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AMENDED SHEET (ARTICLE 19)

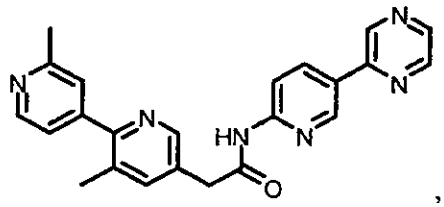
210	 ;
221	 ;
222	 ;
223	 ;
224	 ;

or a physiologically acceptable salt thereof.

3. The compound of claim 1, wherein said compound is

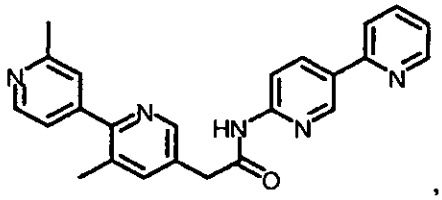
 , or a physiologically acceptable salt thereof.

4. The compound of claim 1, wherein said compound is



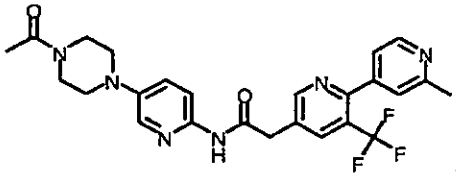
, or a physiologically acceptable salt thereof.

5. The compound of claim 1, wherein said compound is



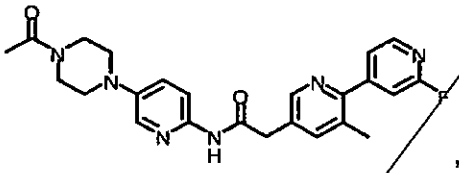
, or a physiologically acceptable salt thereof.

6. The compound of claim 1, wherein said compound is



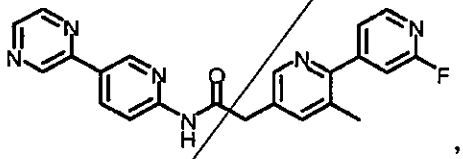
, or a physiologically acceptable salt thereof.

7. The compound of claim 1, wherein said compound is



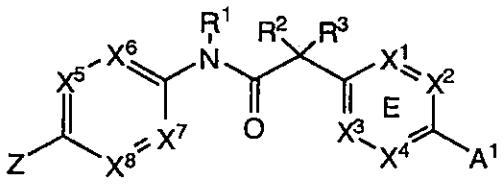
, or a physiologically acceptable salt thereof.

8. The compound of claim 1, wherein said compound is



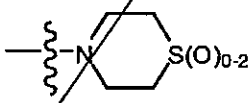
, or a physiologically acceptable salt thereof.

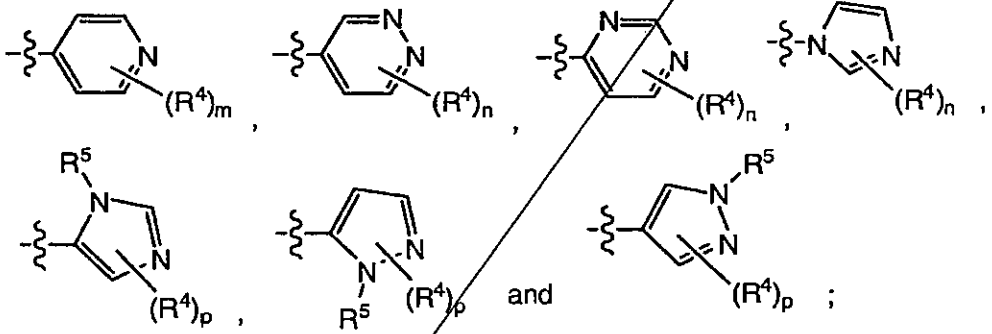
9. A compound having Formula (5):



(5)

or a physiologically acceptable salt thereof, wherein:

wherein A^1 is piperazinyl substituted with $-C(O)CH_3$,  or selected from:



ring E is phenyl or one of X^1, X^2, X^3 and X^4 is N and the others are CR^7;

one of X^5, X^6, X^7 and X^8 is N and the others are CR^{11};

Z is a 6-membered heterocycle or a 6-membered heteroaryl, each containing 1-2 nitrogen heteroatoms and each of which is optionally substituted with 1-2 R^6 groups;

R^1, R^2 and R^3 are H;

R^4 and R^6 are independently hydrogen, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, $-C(O)NR^8R^9$, -L-$C(O)R^{10}$, -L-$C(O)OR^{10}$, C_{1-6} alkyl optionally substituted with halo, C_{2-6} alkenyl or C_{2-6} alkynyl;

R^5 is H or C_{1-6} alkyl;

L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

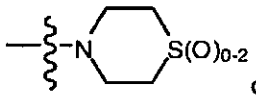
W is C_{3-7}cycloalkyl;

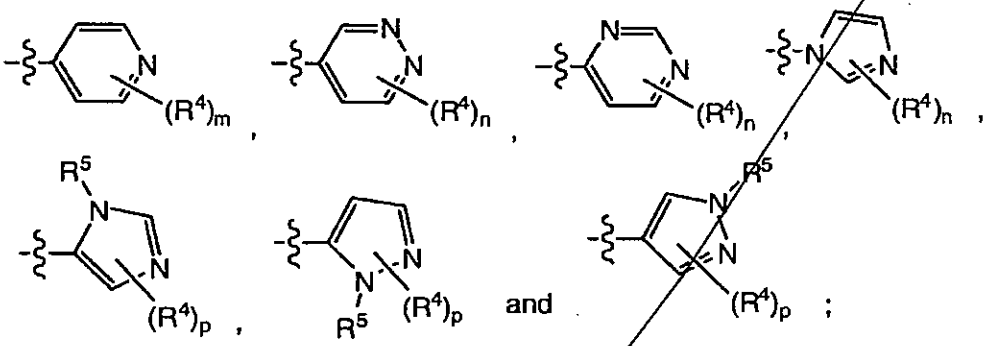
R^7 and R^{11} are independently H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl;

R^8 and R^9 are independently H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; or R^8 and R^9 together with the atoms to which they are attached may form a ring;

R^{10} is C_{1-6} alkyl or -L-W; and

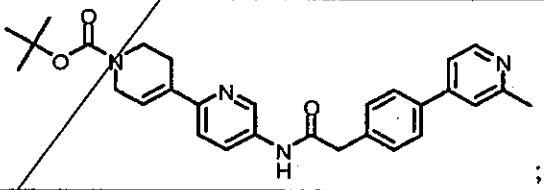
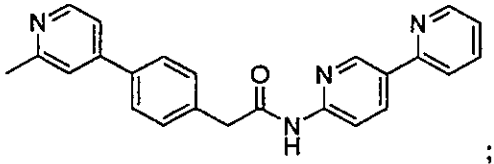
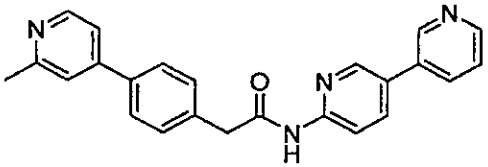
m, n and p are independently 0-2.

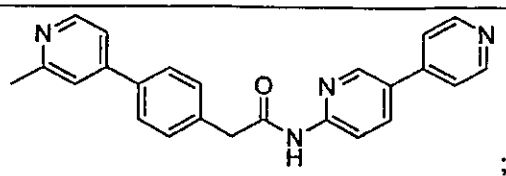
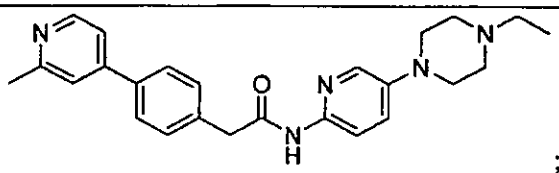
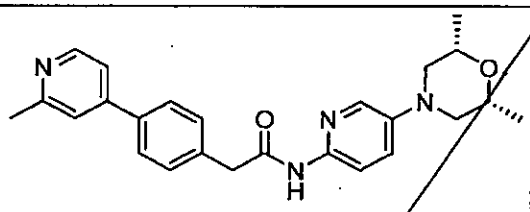
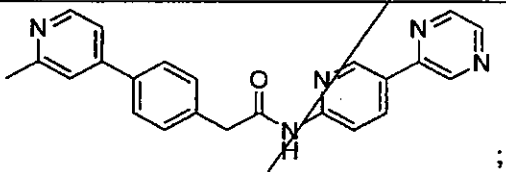
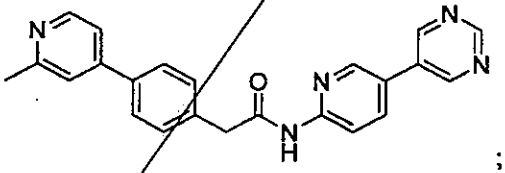
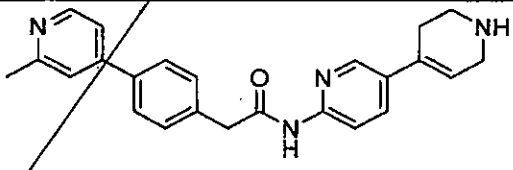
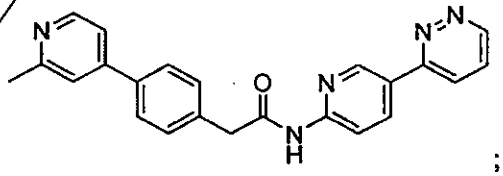
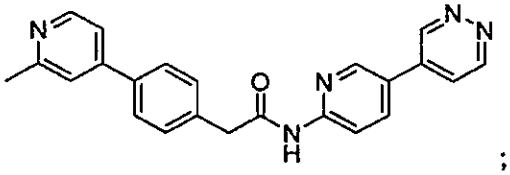
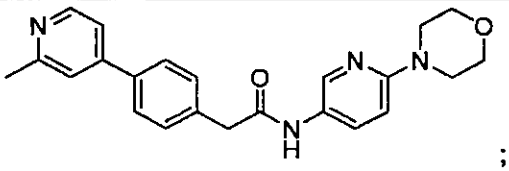
10. The compound of claim 9, wherein A^1 is piperazinyl substituted with –$C(O)CH_3$,  or selected from:



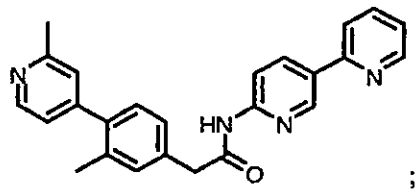
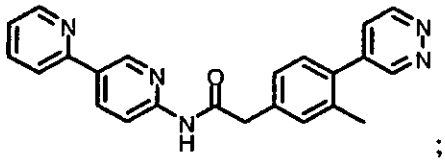
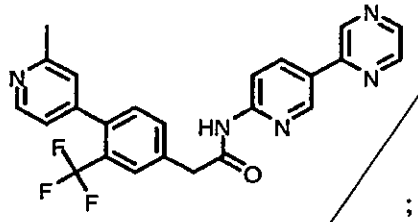
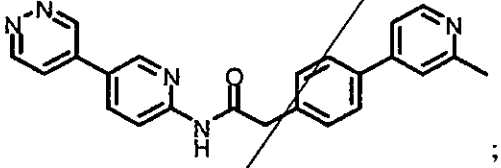
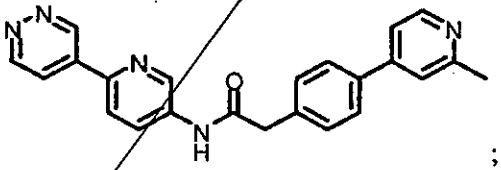
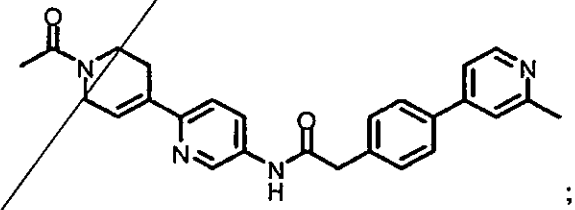
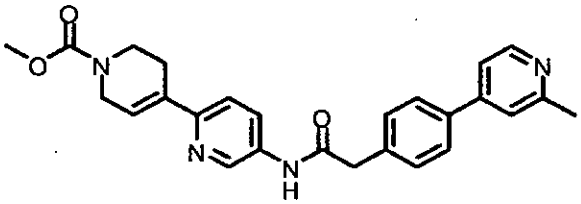
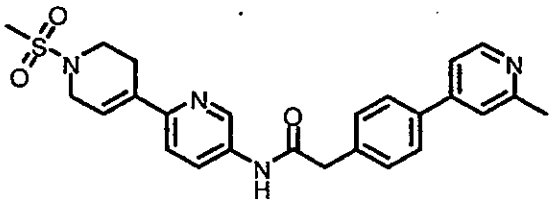
and m is 0-1.

11. The compound of any one of claims 9-10, wherein said compound is selected from:

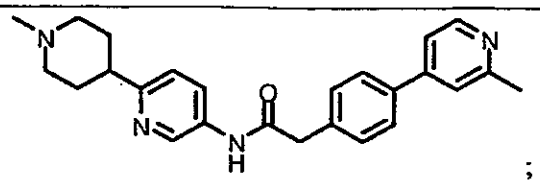
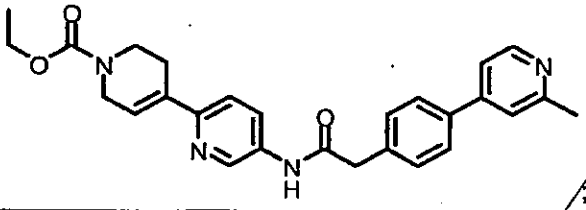
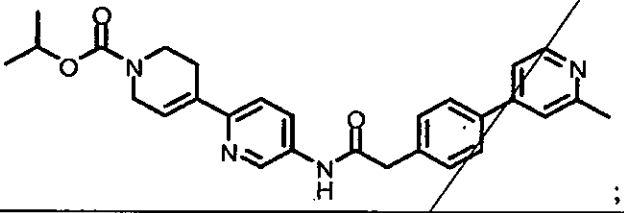
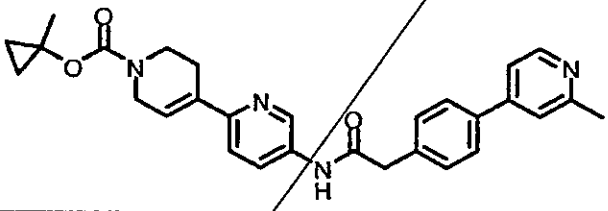
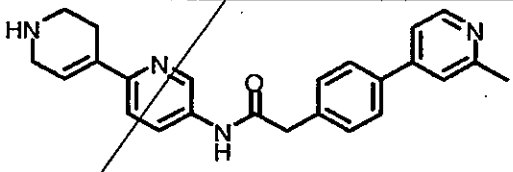
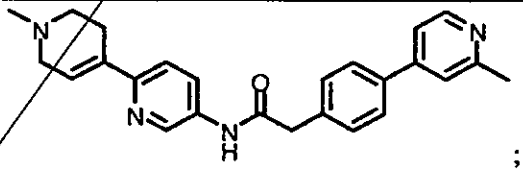
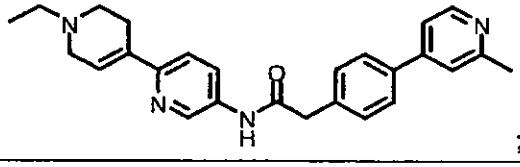
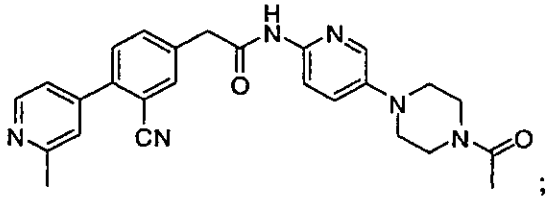
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47	 ;

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72	 ;
73	 ;

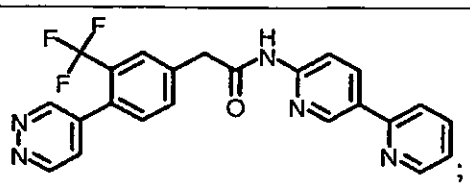
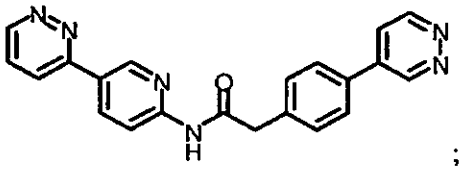
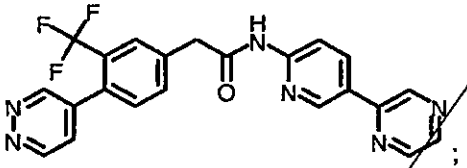
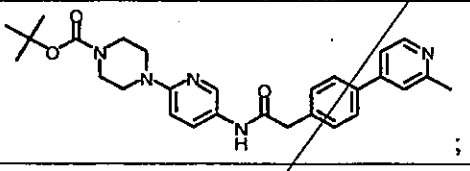
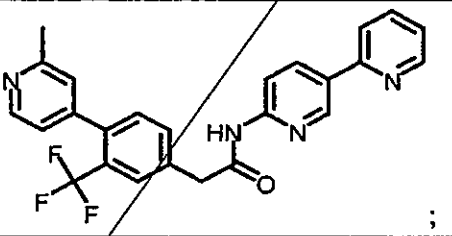
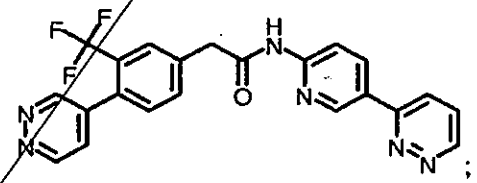
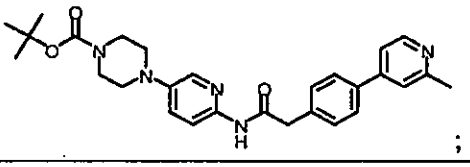
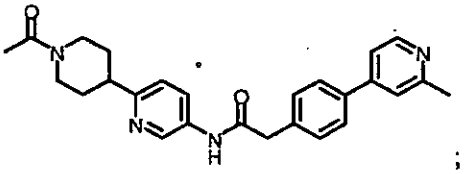
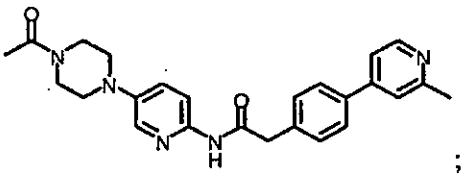
AMENDED SHEET (ARTICLE 19)

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91	 ;
92	 ;

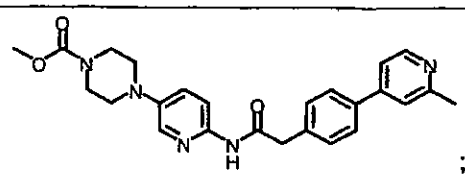
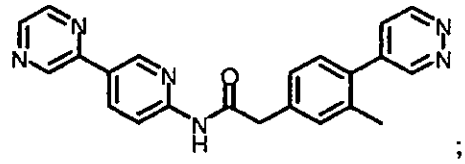
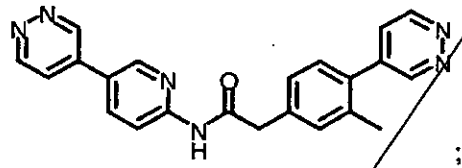
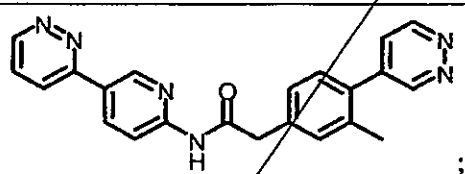
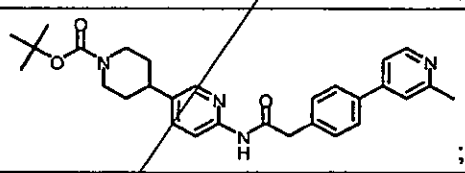
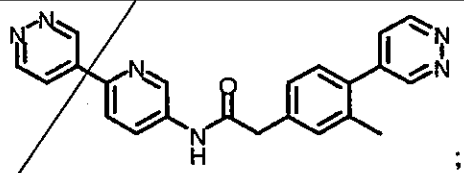
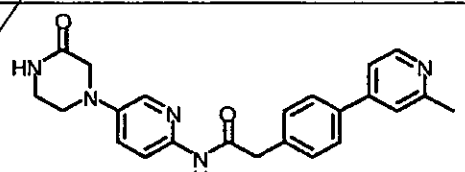
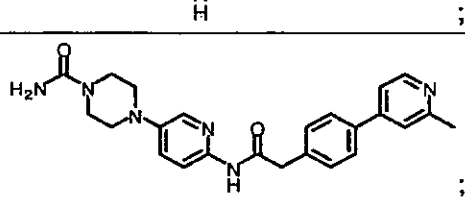
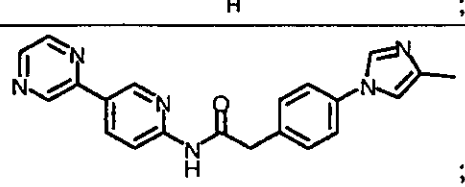
AMENDED SHEET (ARTICLE 19)

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106	 ;
107	 ;
111	 ;

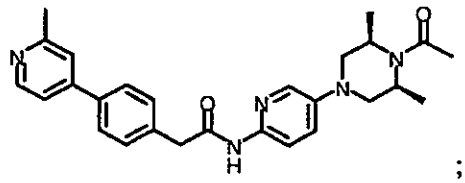
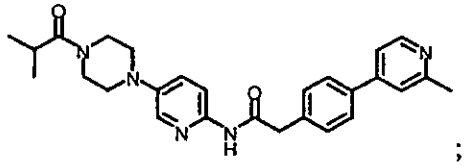
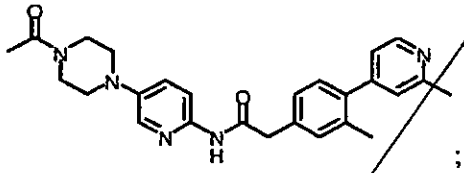
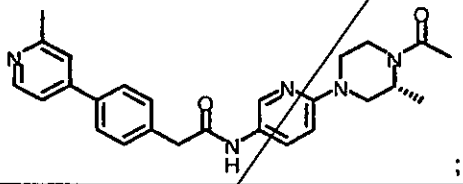
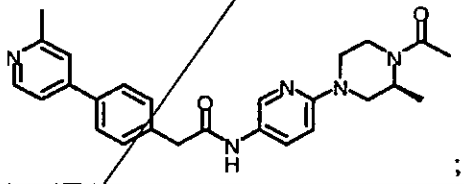
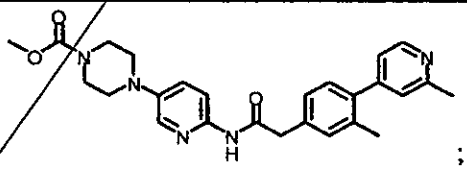
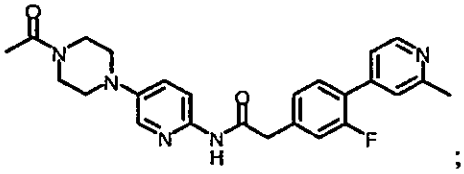
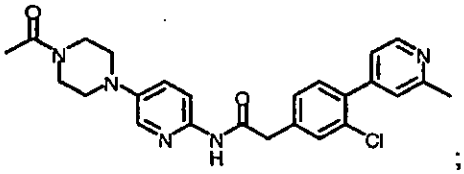
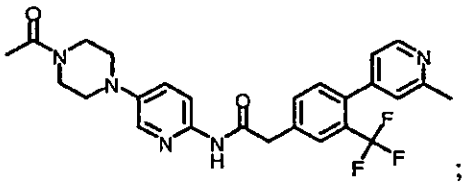
AMENDED SHEET (ARTICLE 19)

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121	 ;
122	 ;
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127	 ;
131	 ;

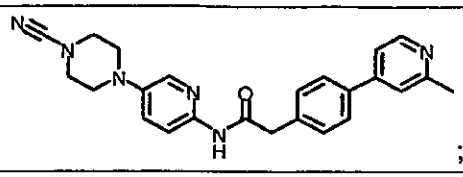
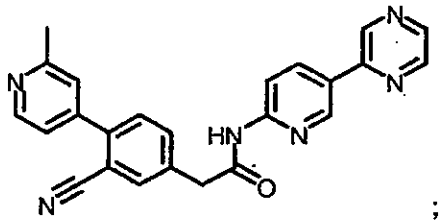
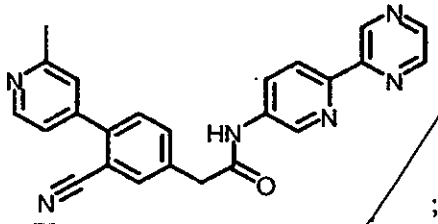
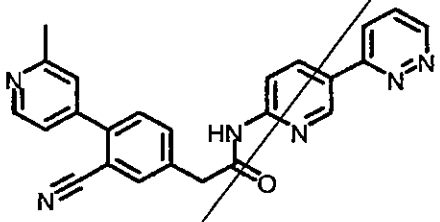
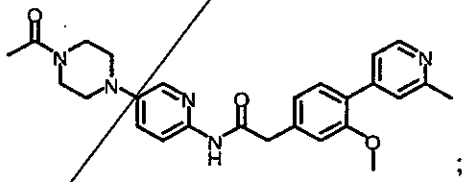
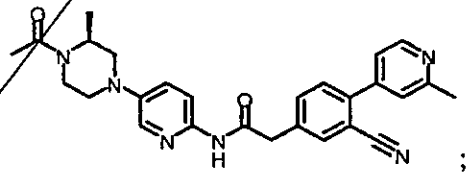
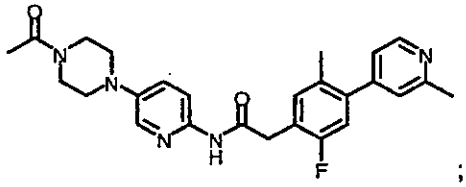
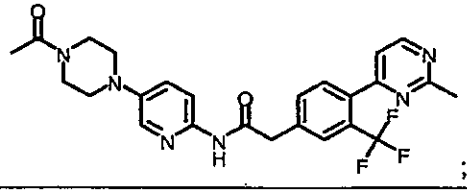
AMENDED SHEET (ARTICLE 19)

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139	 ;
141	 ;
142	 ;
144	 ;

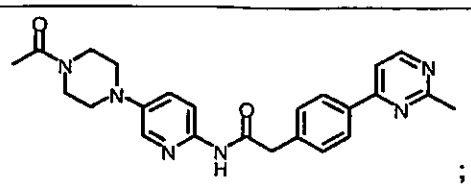
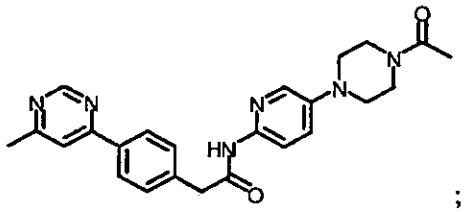
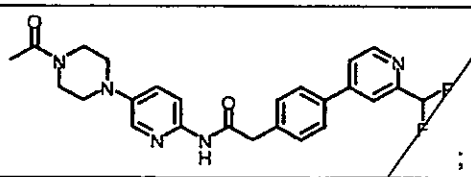
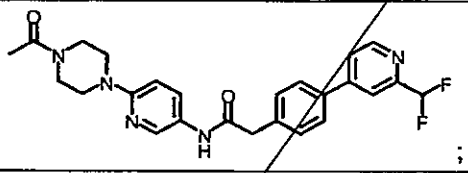
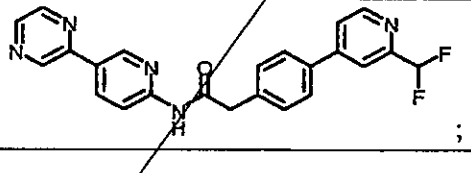
AMENDED SHEET (ARTICLE 19)

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159	 ;
161	 ;
162	 ;
167	 ;
168	 ;
170	 ;
172	 ;

AMENDED SHEET (ARTICLE 19)

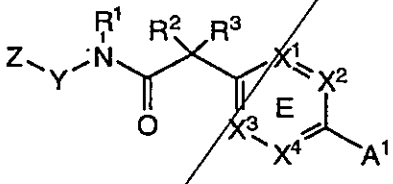
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191	 ;
192	 ;

AMENDED SHEET (ARTICLE 19)

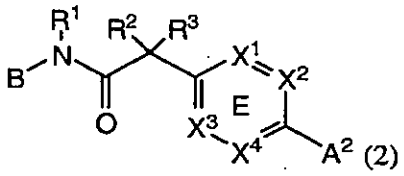
195	 ;
198	 ;
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203	 ;

or a physiologically acceptable salt thereof.

12. A compound having Formula (1) or (2):



(1)

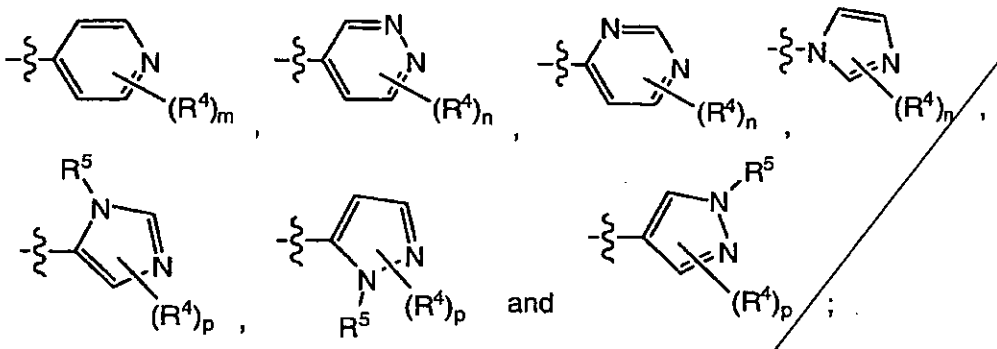


(2)

or a physiologically acceptable salt thereof, wherein:

ring E is an optionally substituted aryl or heteroaryl;

A^1 and A^2 are independently a C_{1-5}heterocycle, quinolinyl, or a heteroaryl selected from the group



wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-LC(O)R^{10}$;

B is benzothiazolyl, quinolinyl or isoquinolinyl, each of which is optionally substituted with 1-3 R^6 groups;

X^1, X^2, X^3 and X^4 are independently CR^7 or N;

Y is phenyl, thiazolyl, pyridinyl, pyridazinyl, pyrimidinyl or pyrazinyl, each of which is optionally substituted with 1-2 R^6 groups;

Z is aryl, C_{1-5} heterocycle, or a 5-6 membered heteroaryl containing 1-2 heteroatoms selected from N, O and S;

each Y and Z are optionally substituted with 1-3 R^6 groups;

R^1 and R^5 are independently H or C_{1-6} alkyl;

R^2 and R^3 are independently H, C_{1-6} alkyl or halo;

R^4 is halo, cyano, C_{1-6}alkoxy, or a C_{1-6} alkyl optionally substituted with halo, alkoxy or amino;

R^6 is hydrogen, halo, C_{1-6}alkoxy, $-S(O)_2R^{10}$, $-C(O)OR^{10}$, $-C(O)R^{10}$, $-C(O)NR^8R^9$, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which can be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; halo, CN, -L-W, NR^8R^9, -L-$C(O)R^{10}$, -L-$C(O)OR^{10}$, -L-$C(O)NR^8R^9$, OR^{10}; -L-$S(O)_2R^{10}$ or $-L$-$S(O)_2NR^8R^9$;

R^7 is H, halo, C_{1-6} alkoxy, -L-$S(O)_2R^{10}$, C_{1-6} alkyl optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; NR^8R^9, -L-$C(O)R^{10}$, -L-$C(O)NR^8R^9$, OR^{10}; -L-$S(O)_2R^{10}$ or $-L$-$S(O)_2NR^8R^9$;

R^8 and R^9 are independently H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; or R^8 and R^9 together with the atoms to which they are attached may form a ring;

R^{10} is H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano;

L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

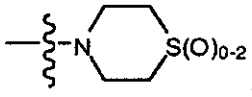
W is C_{3-7}cycloalkyl, C_{1-5}heterocycle, aryl or heteroaryl;

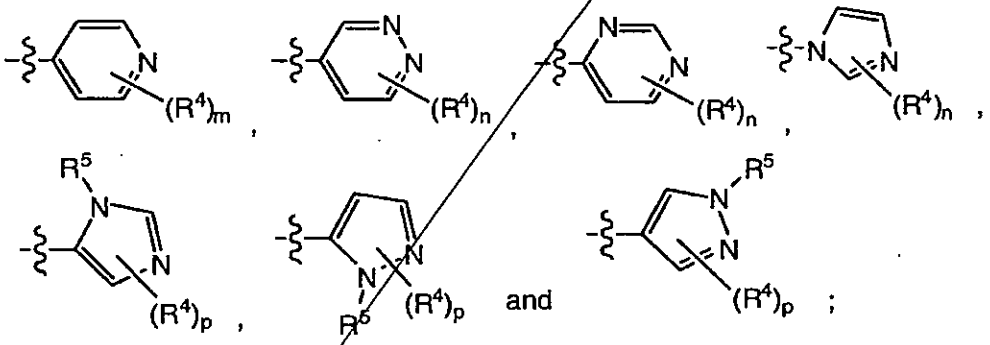
m is 0-4;

n is 0-3; and

p is 0-2.

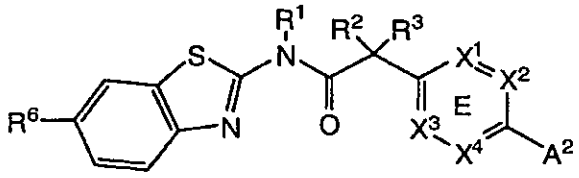
13. The compound of claim 12, wherein Z is phenyl, pyridinyl, pyridazine, pyrimidine, pyrazine, piperazinyl, piperidinyl, morpholinyl, pyrazole or 1,2,3,6-tetrahydropyridine, each of which is optionally substituted with 1-2 R^6 groups and R^6 is as defined in claim 1.

14. The compound of claim 12, wherein A^1 and A^2 are independently morpholinyl, piperazinyl, quinolinyl, , or a heteroaryl selected from the group:

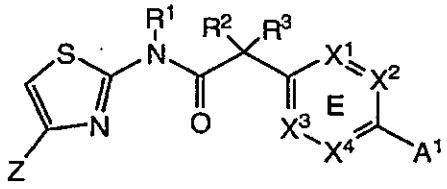


wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-C(O)CH_3$; R^4 and n are as defined in claim 1.

15. The compound of claim 12, wherein said compound is of Formula (3) or Formula (4):



(3)



(4)

wherein R^1, R^2, R^3, X^1, X^2, X^3, X^4, A^1, A^2, Z and R^6 are as defined in claim 1.

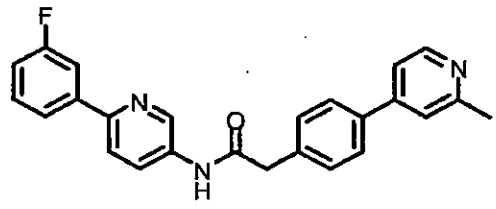
16. The compound of any one of claims 12-15, wherein ring E is phenyl, pyridyl or pyrimidinyl, each of which optionally substituted with R^7.

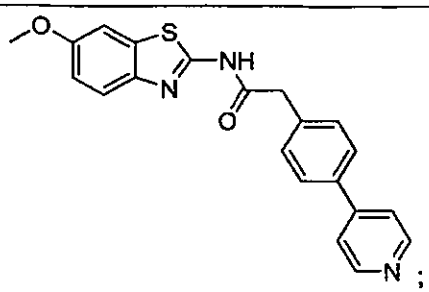
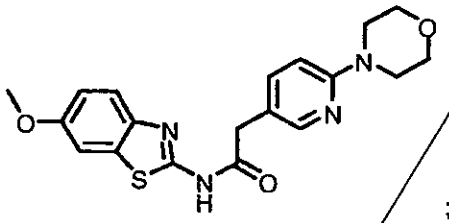
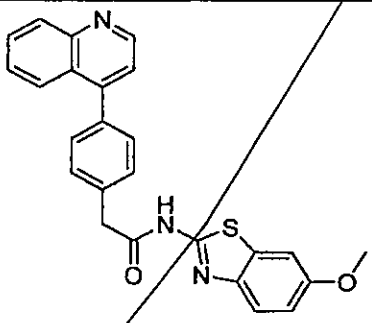
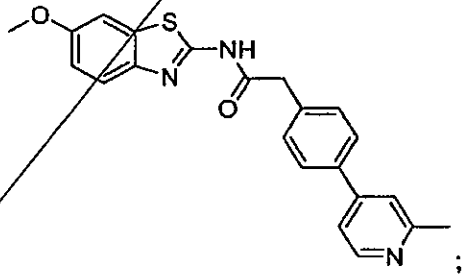
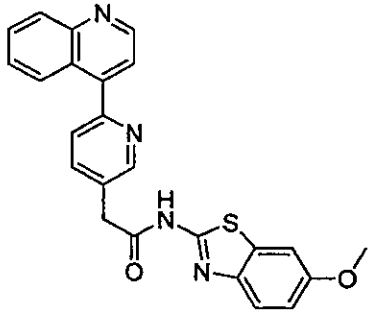
17. The compound of any one of claims 12-15, wherein R^7 is H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl.

18. The compound of any one of claims 12-15, wherein R^1, R^2 and R^3 are H.

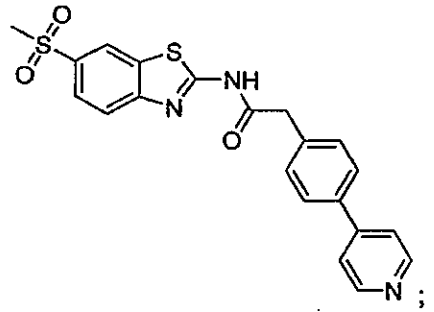
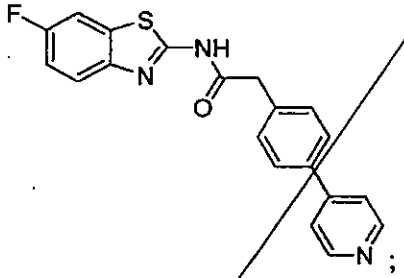
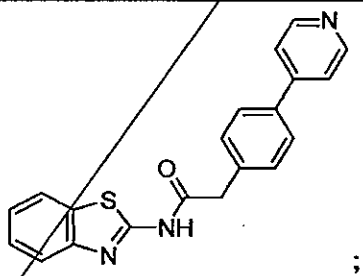
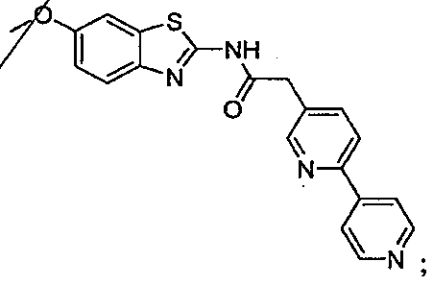
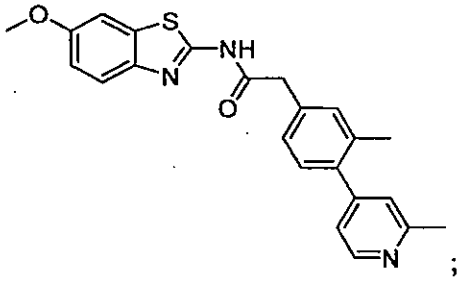
19. The compound of any one of claims 12-15, wherein R^4 and R^6 are independently selected from hydrogen, halo, methyl, trifluoromethyl and $-C(O)CH_3$.

20. The compound of any one of claims 12-19, wherein said compound is selected from:

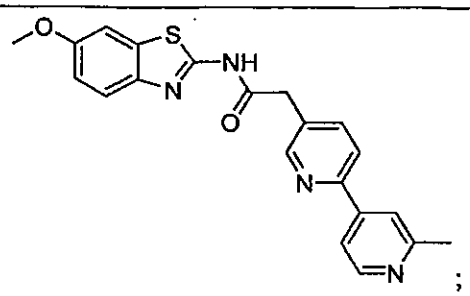
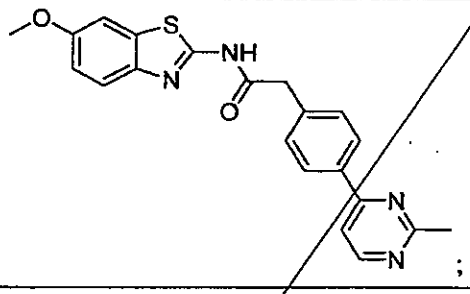
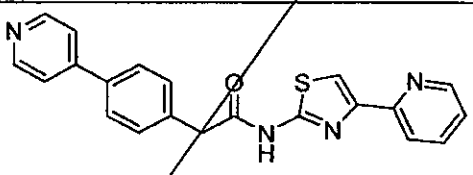
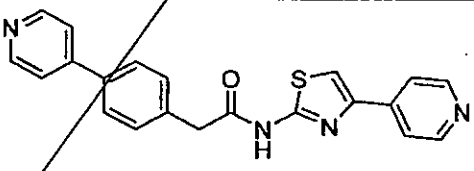
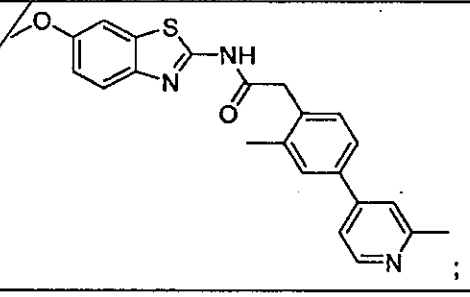
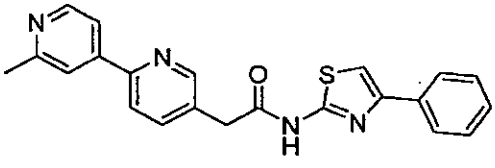
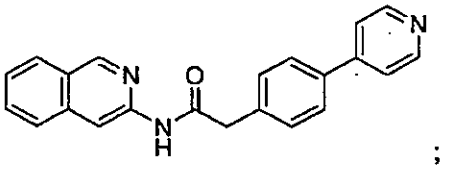
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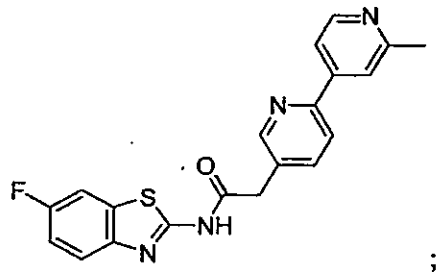
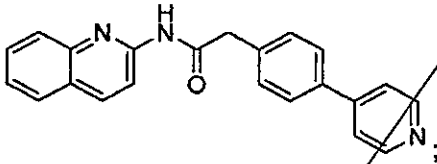
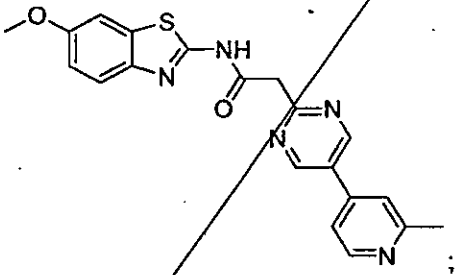
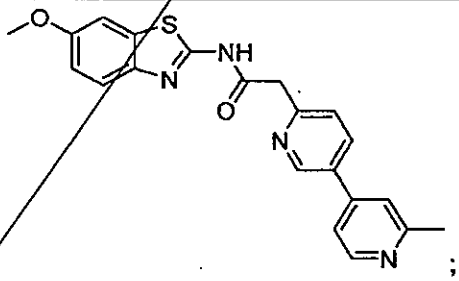
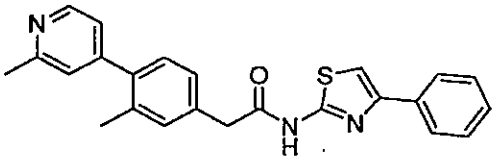
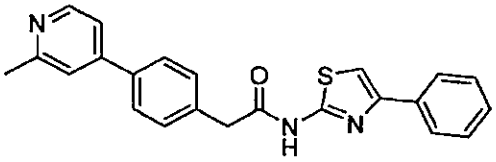
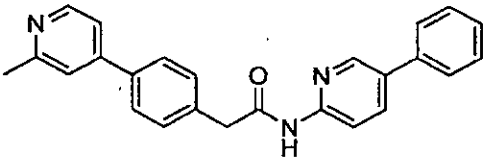
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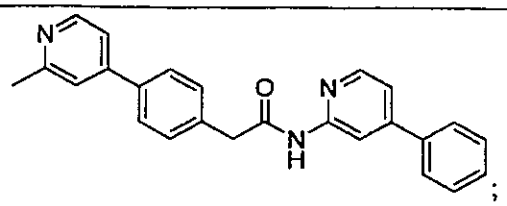
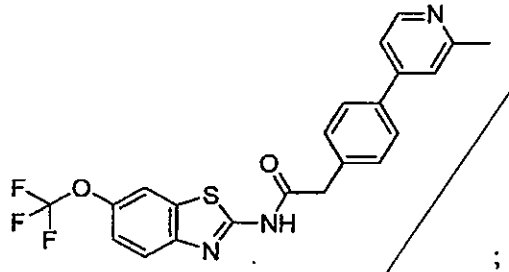
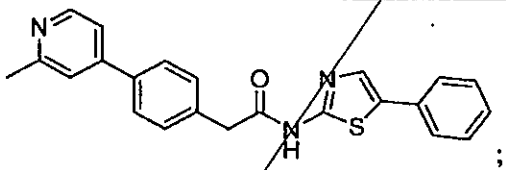
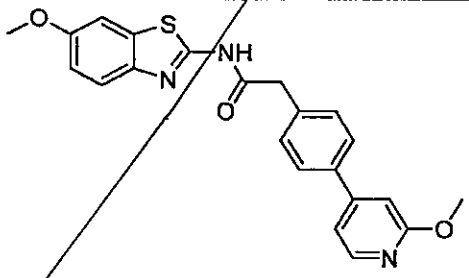
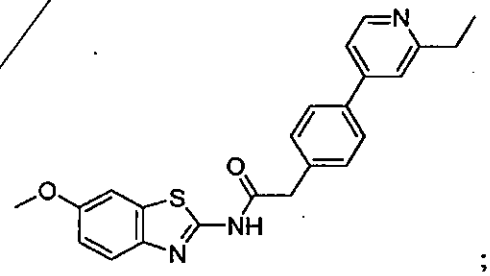
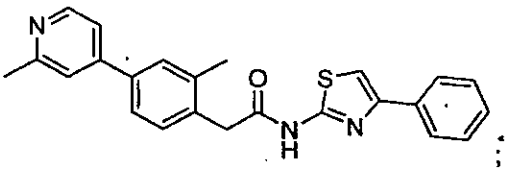
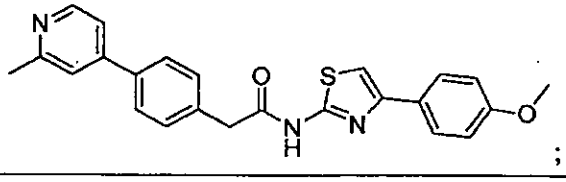
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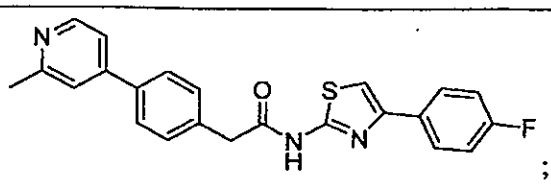
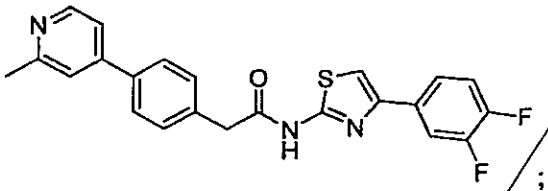
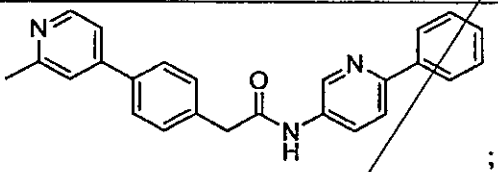
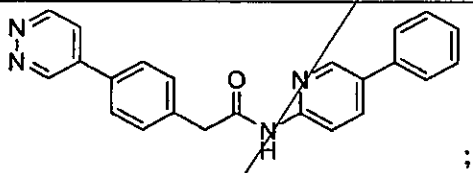
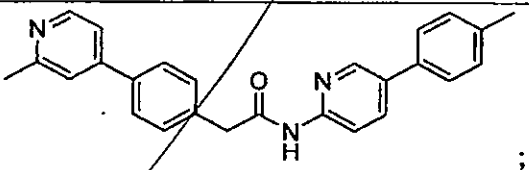
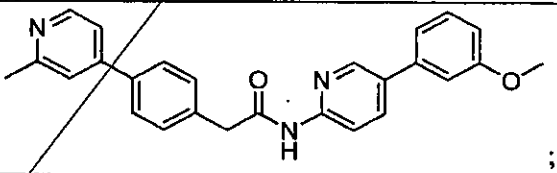
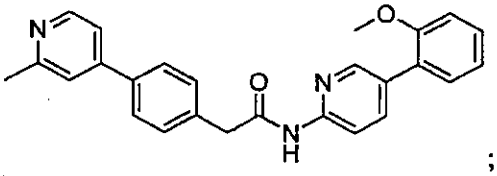
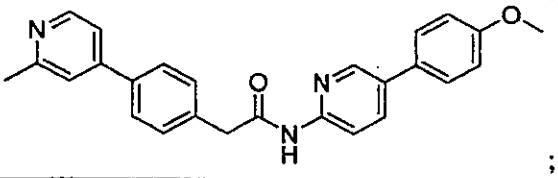
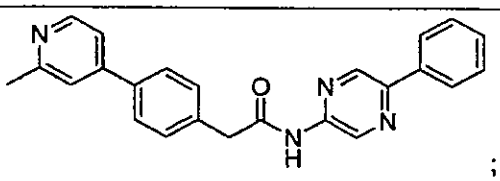
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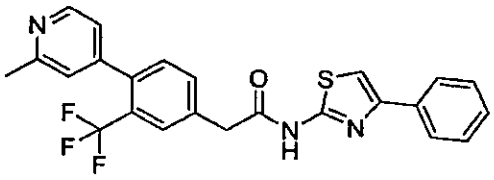
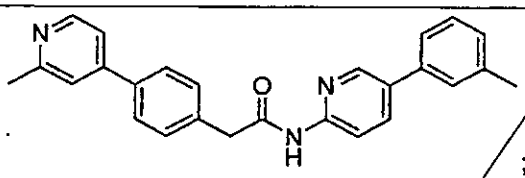
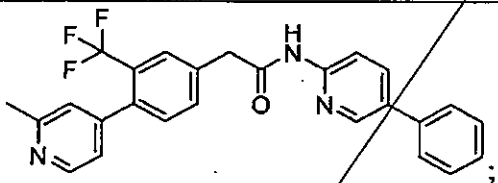
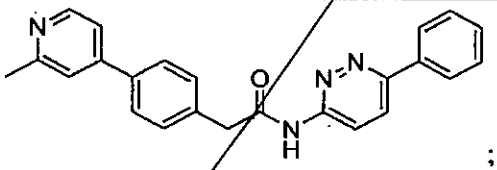
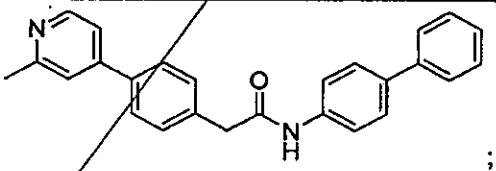
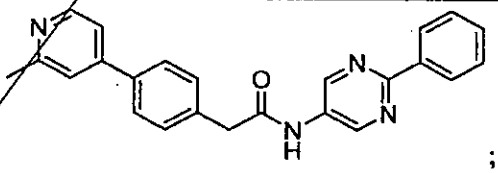
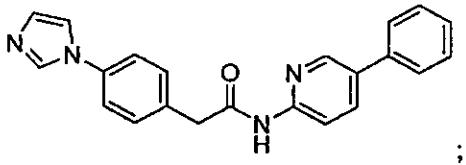
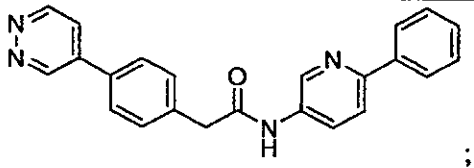
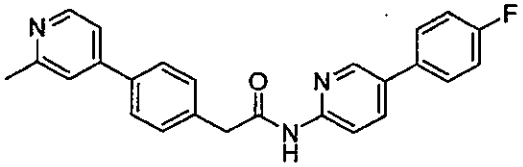
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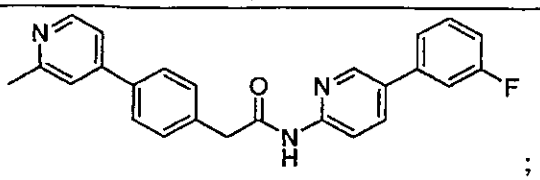
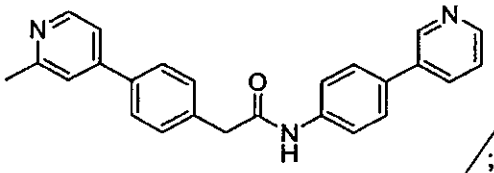
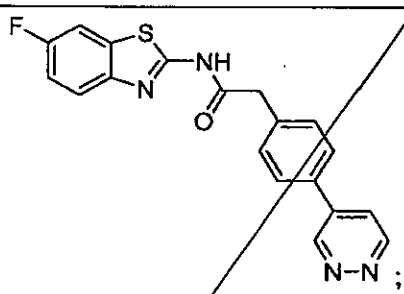
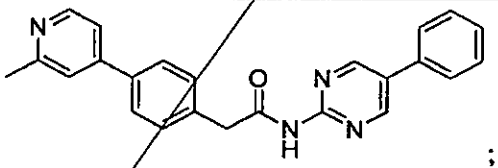
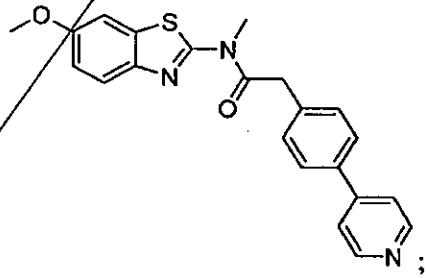
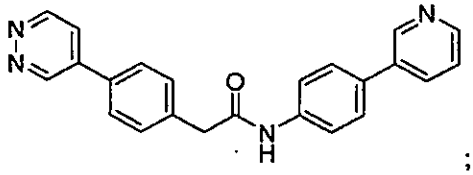
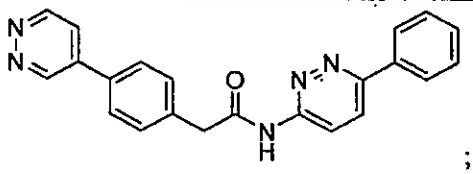
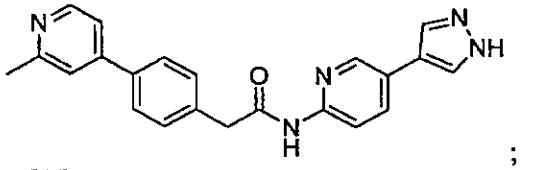
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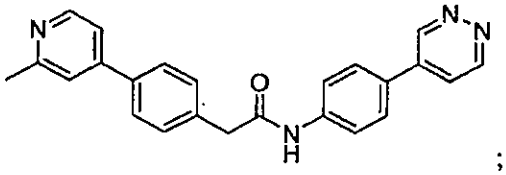
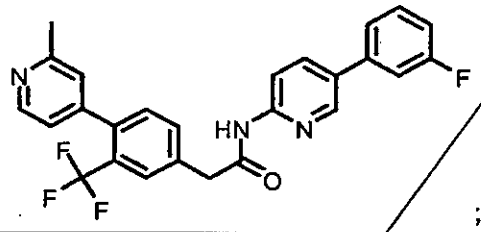
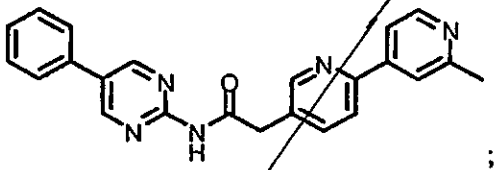
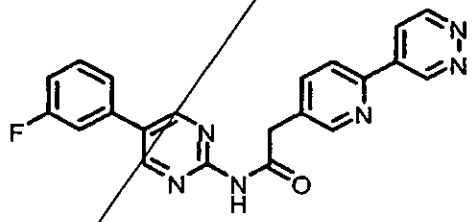
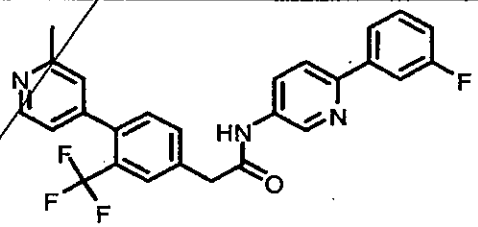
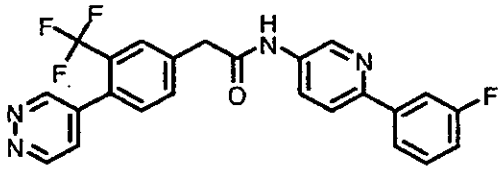
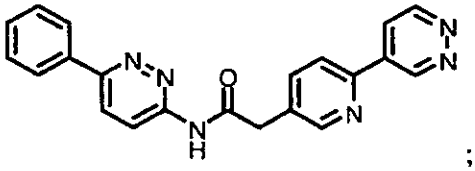
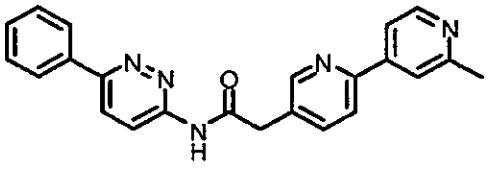
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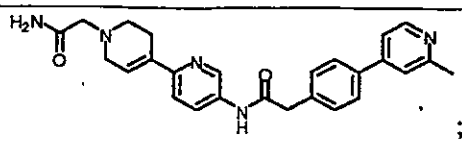
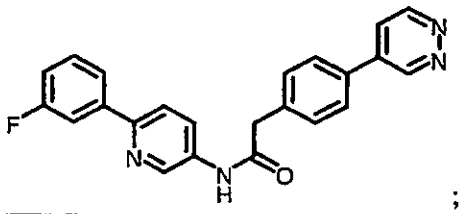
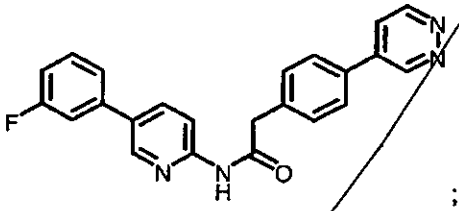
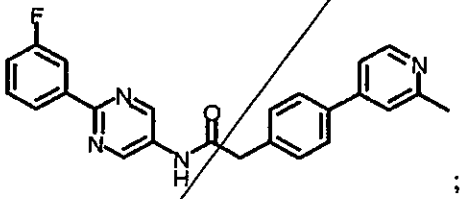
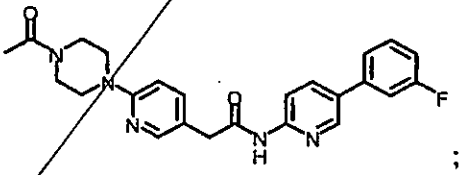
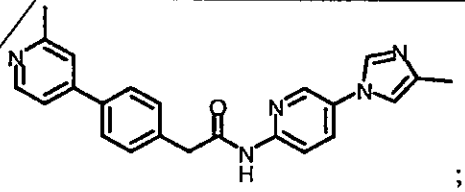
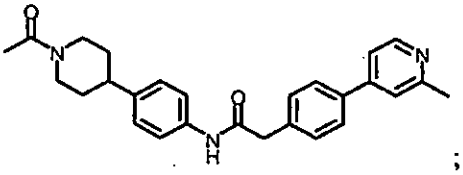
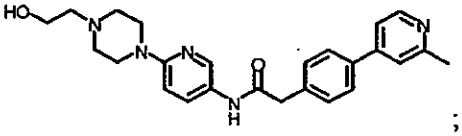
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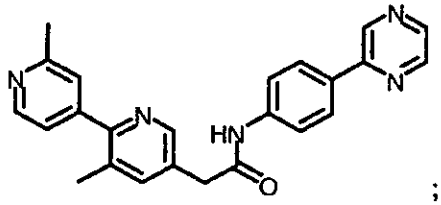
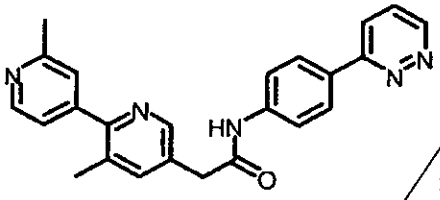
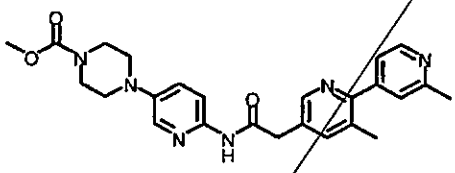
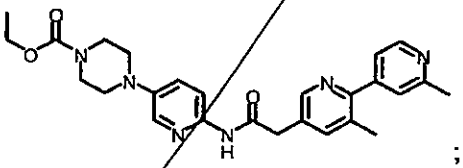
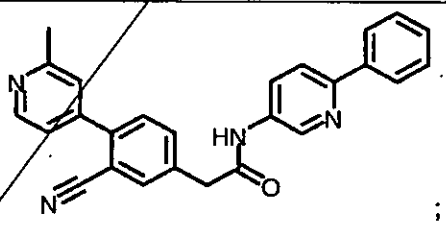
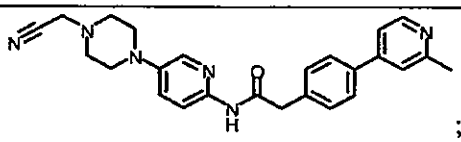
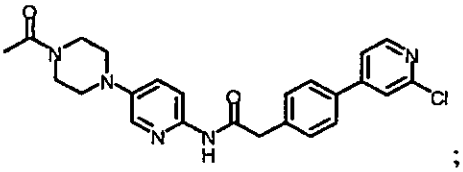
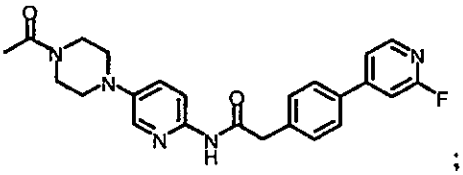
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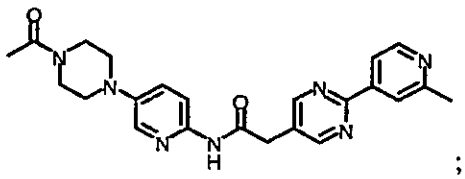
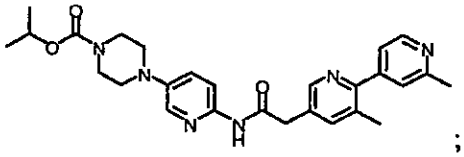
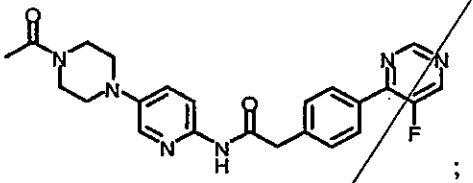
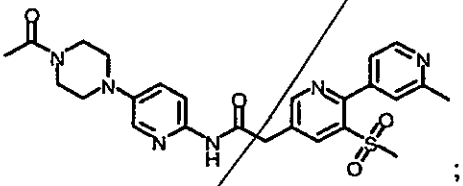
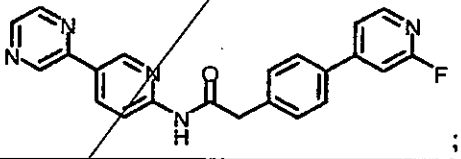
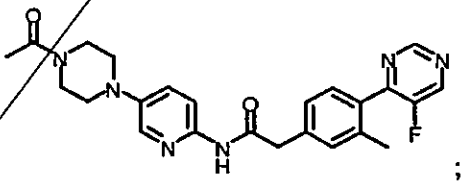
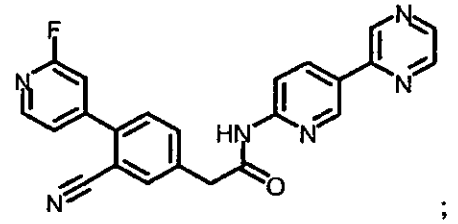
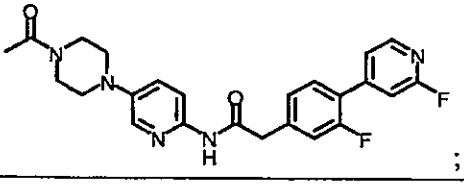
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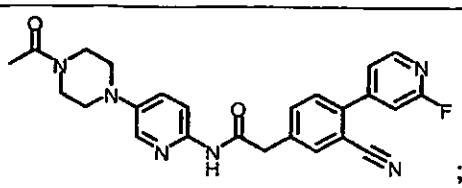
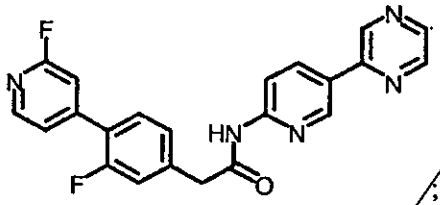
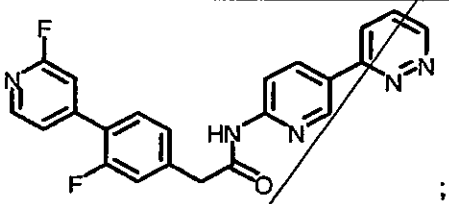
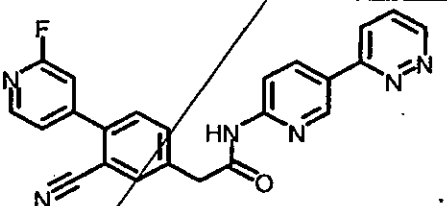
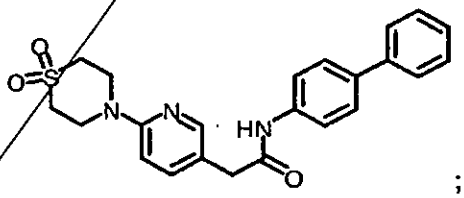
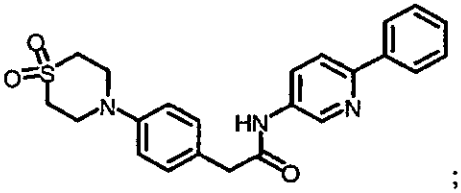
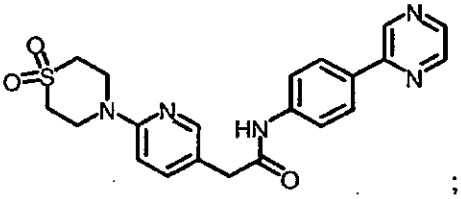
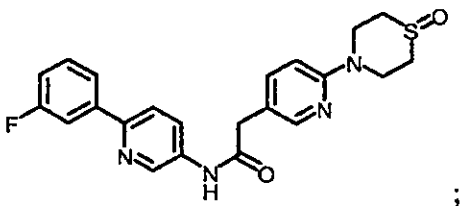
AMENDED SHEET (ARTICLE 19)

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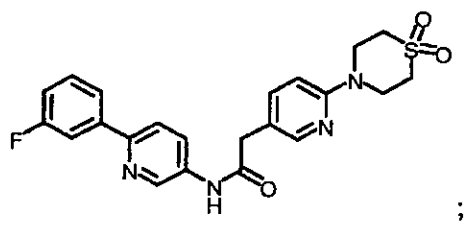
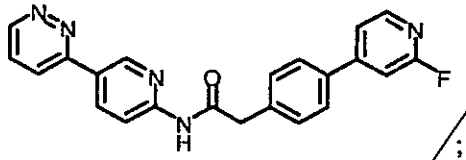
AMENDED SHEET (ARTICLE 19)

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AMENDED SHEET (ARTICLE 19)

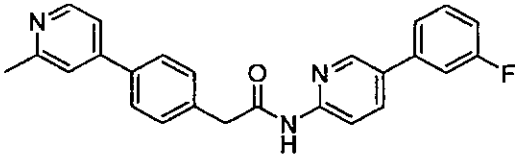
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AMENDED SHEET (ARTICLE 19)

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or a physiologically acceptable salt thereof.

21. The compound of claim 12, wherein said compound is



, or a physiologically acceptable salt thereof.

22. A compound selected from: N-(6-methoxybenzo[d]thiazol-2-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridazin-4-yl)phenyl)acetamide; 2-(3-(2-methoxypyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyridazin-3-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyrazin-2-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-(pyrazin-2-yl)pyridin-3-yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-6-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-2,4'-bipyridin-4-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2-cyano-2'-methyl-3,4'-bipyridin-5-yl)acetamide; 2-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)-5-(pyrazin-2-yl)pyridine 1-oxide; and 2',3-

dimethyl-5-(2-oxo-2-(5-(pyrazin-2-yl)pyridin-2-ylamino)ethyl)-2,4'-bipyridine 1'-oxide; or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-22 and a physiologically acceptable carrier.

24. A method for inhibiting Wnt signaling in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 1-22, or a pharmaceutical composition thereof.

25. A method for inhibiting a Porcupine gene in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 1-22, or a pharmaceutical composition thereof.

26. A method for treating a Wnt-mediated disorder in a mammal suffering therefrom, comprising administering to the mammal a therapeutically effective amount of a compound of any one of claims 1-22, or a pharmaceutical composition thereof, and optionally in combination with a second therapeutic agent.

27. The method of claim 26, wherein said Wnt-mediated disorder is keloids, fibrosis, proteinuria, kidney graft rejection, osteoarthritis, Parkinson's disease, cystoid macular edema, retinopathy, macular degeneration or a cell proliferative disorder associated with aberrant Wnt signaling activity.

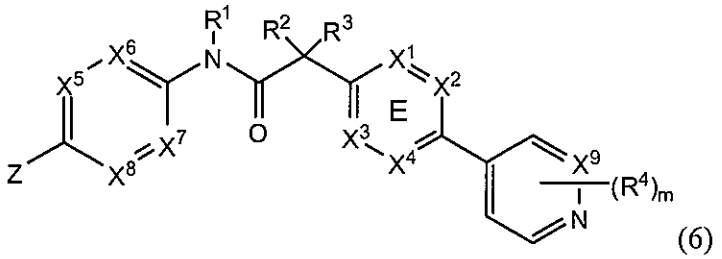
28. The method of claim 27, wherein said disorder is a cell proliferative disorder selected from the group colorectal cancer, breast cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, non-small cell lung cancer, gastric cancer, pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilm's tumor, basal cell carcinoma, melanoma, head and neck cancer, cervical cancer and prostate cancer.

29. The use of a compound of any one of claims 1-22, or a pharmaceutical composition thereof, for inhibiting Wnt signaling.

30. The use of a compound of any one of claims 1-22, or a pharmaceutical composition thereof, for the manufacture of a medicament for treating a Wnt-mediated disorder.

Claims

1. A compound having Formula (6):



(6)

or a physiologically acceptable salt thereof, wherein:

wherein X^1, X^2, X^3 and X^4 is selected from N and CR^7;

one of X^5, X^6, X^7 and X^8 is N and the others are CH;

X^9 is selected from N and CH;

Z is selected from phenyl, pyrazinyl, pyridinyl, pyridazinyl and piperazinyl; wherein each phenyl, pyrazinyl, pyridinyl, pyridazinyl or piperazinyl of Z is optionally substituted with an R^6 group;

R^1, R^2 and R^3 are hydrogen;

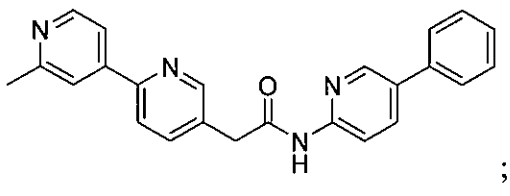
m is 1;

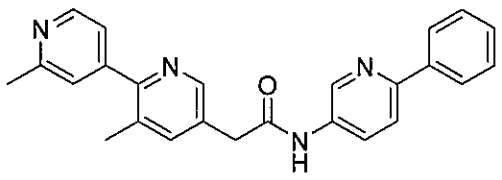
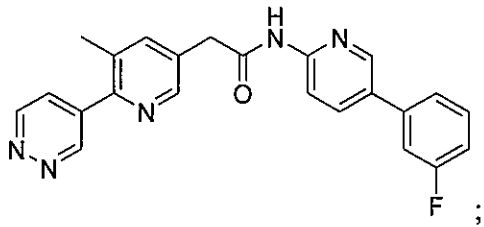
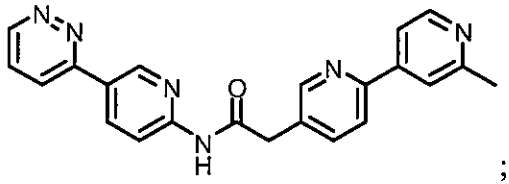
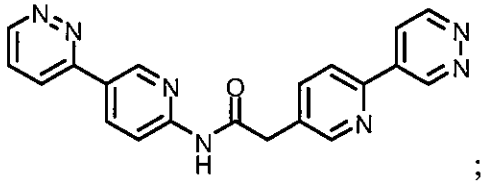
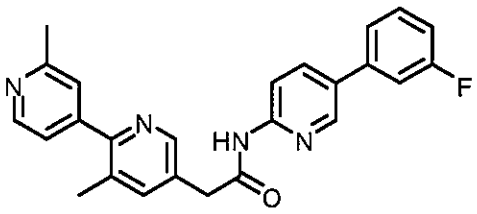
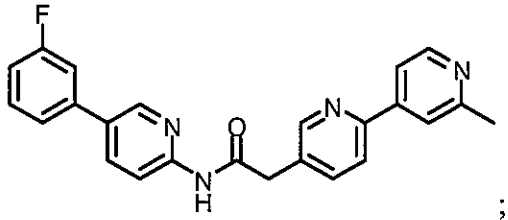
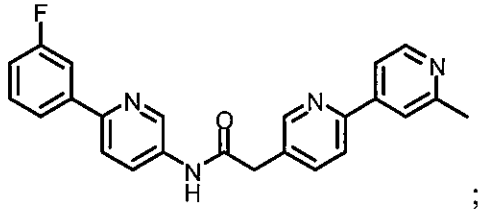
R^4 is selected from hydrogen, halo, difluoromethyl, trifluoromethyl and methyl;

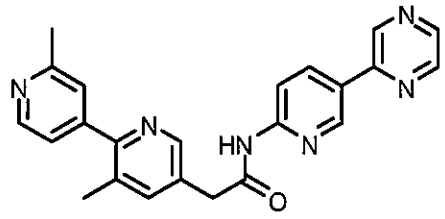
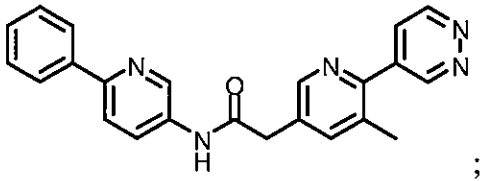
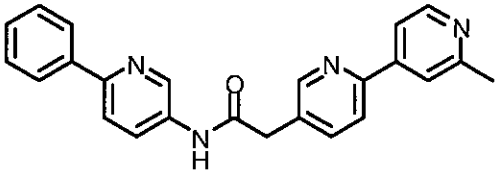
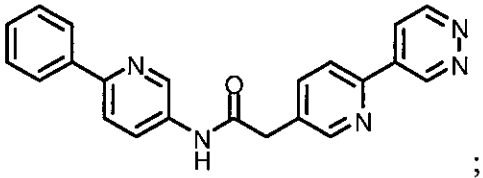
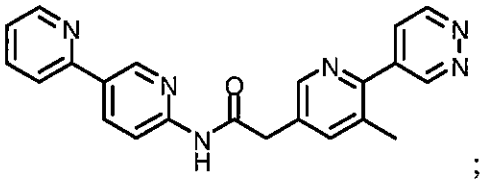
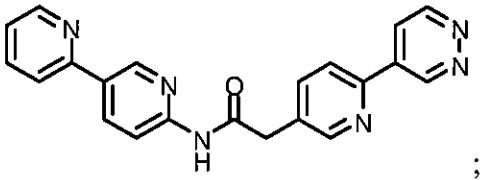
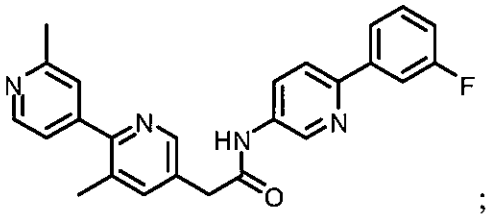
R^6 is selected from hydrogen, halo and $-C(O)R^{10}$; wherein R^{10} is methyl; and

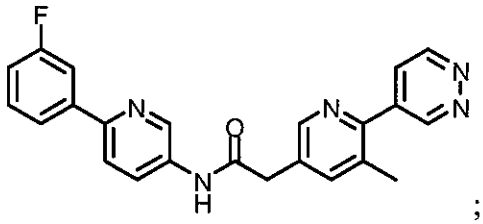
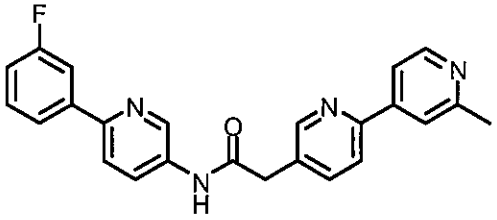
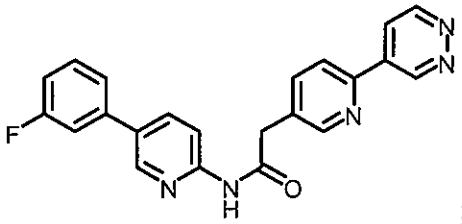
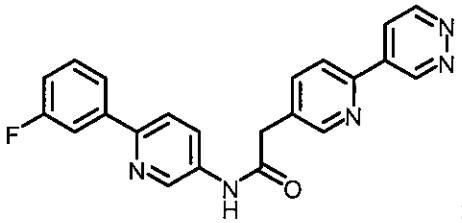
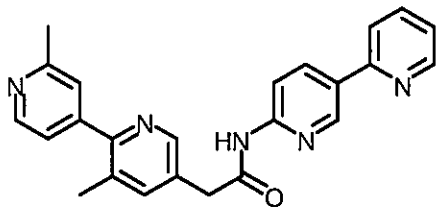
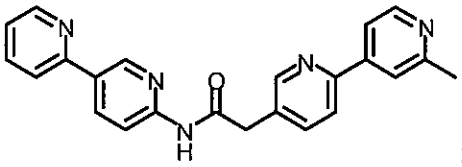
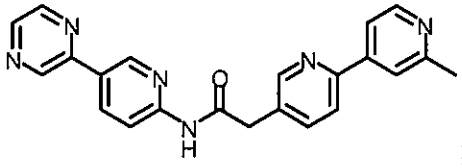
R^7 is selected from hydrogen, halo, cyano, methyl and trifluoromethyl.

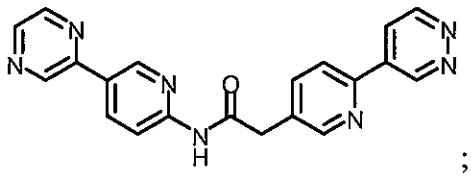
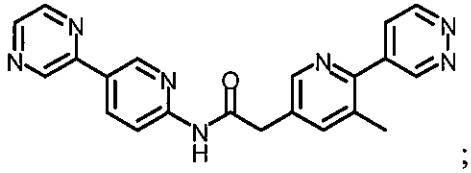
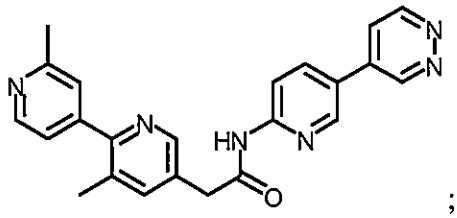
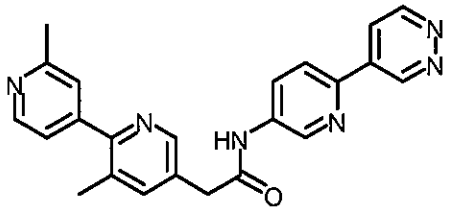
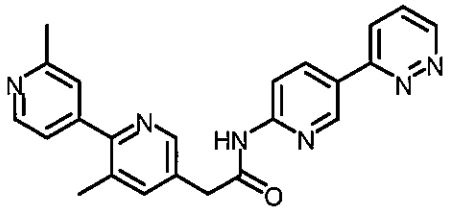
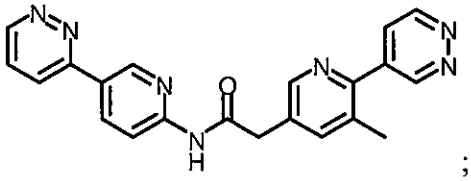
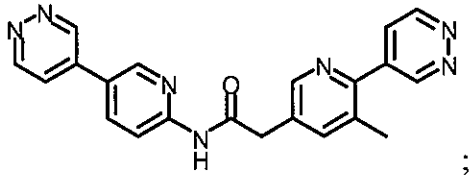
2. A compound or a physiologically acceptable salt thereof, wherein said compound is:

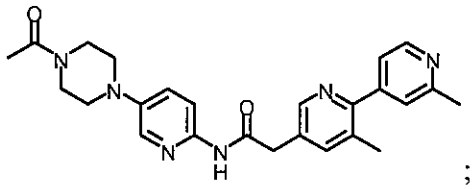
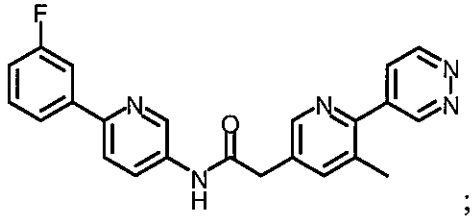
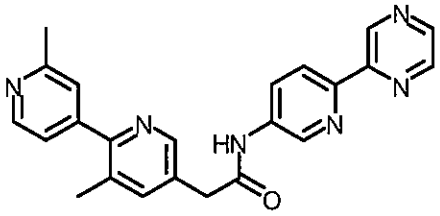
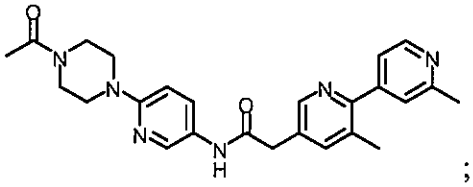
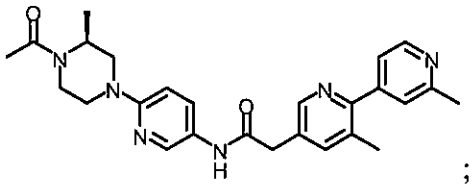
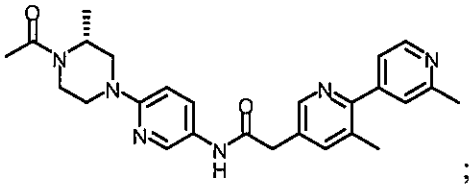
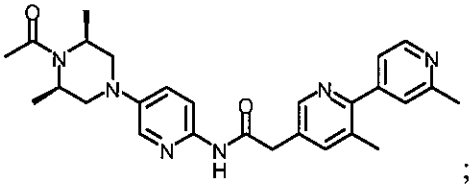
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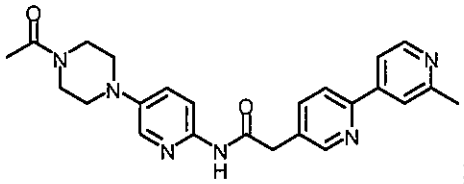
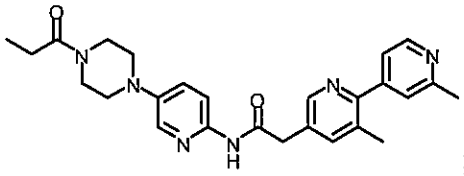
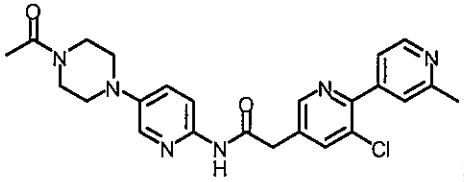
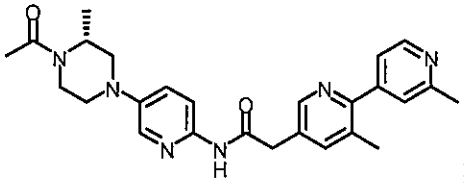
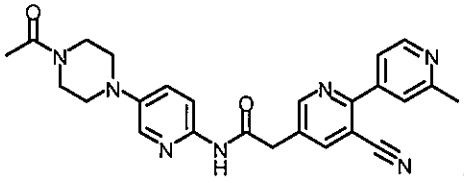
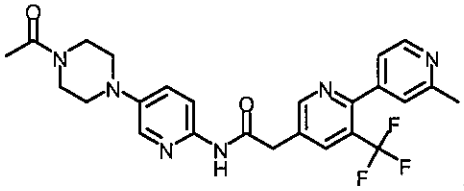
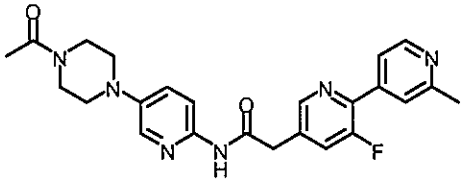
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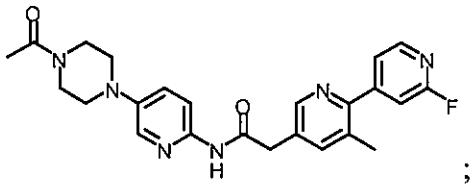
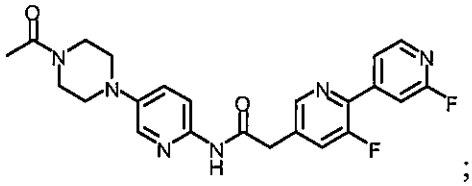
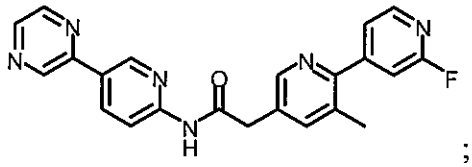
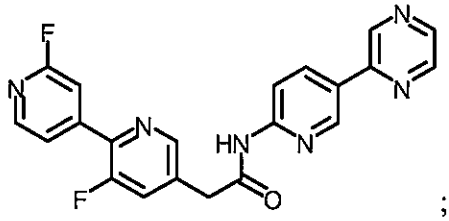
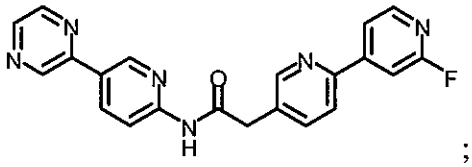
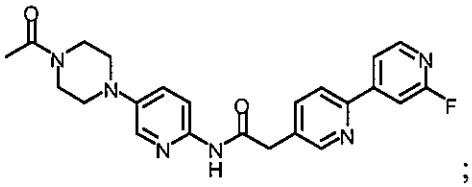
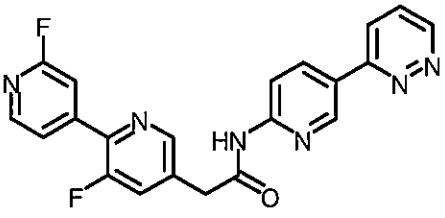
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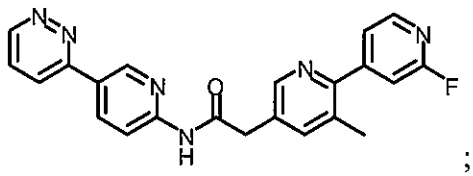
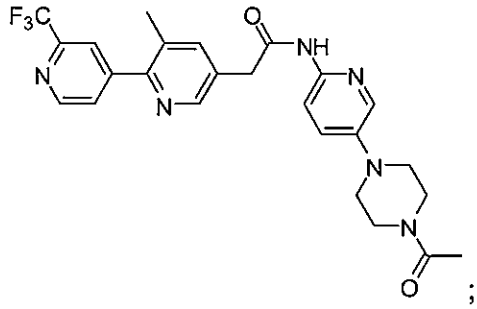
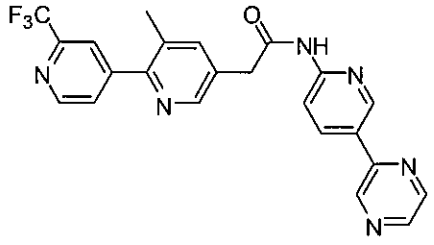
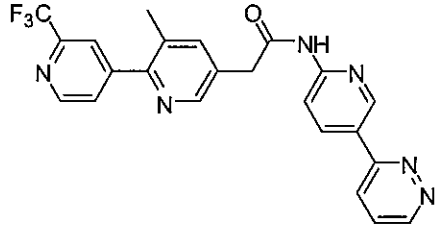
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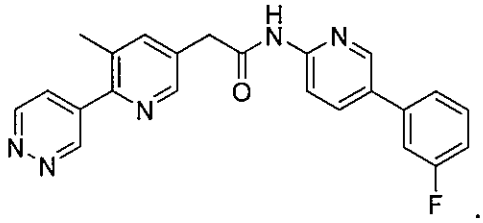
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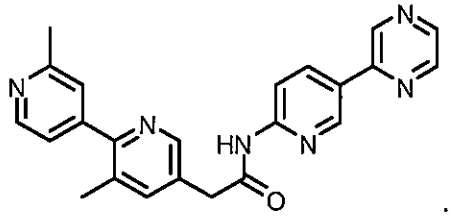
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224	 .

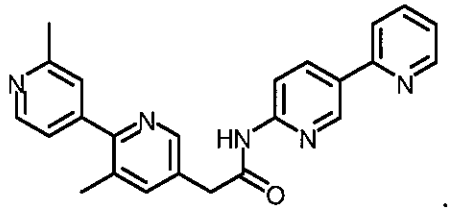
3. A compound or a physiologically acceptable salt thereof, wherein said compound is:

 .

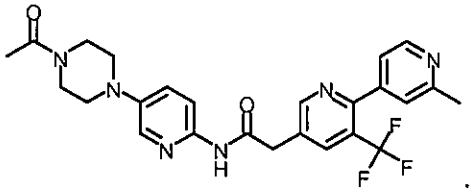
4. A compound or a physiologically acceptable salt thereof, wherein said compound is:



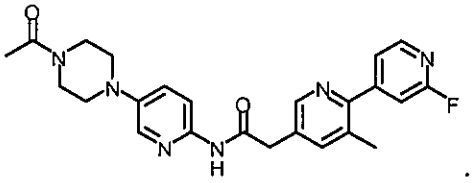
5. A compound or a physiologically acceptable salt therof, wherein said compound is:



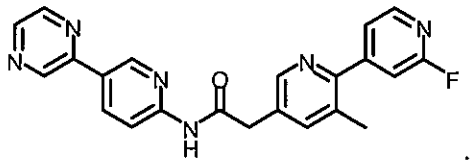
6. A compound or a physiologically acceptable salt thereof, wherein said compound is:



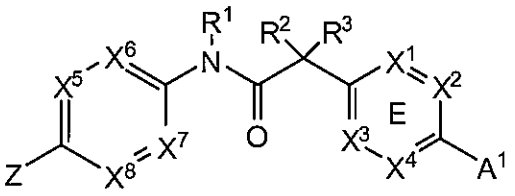
7. A compound or a physiologically acceptable salt thereof, wherein said compound is:



8. A compound or a physiologically acceptable salt thereof, wherein said compound is:

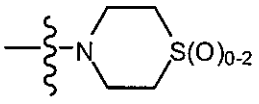


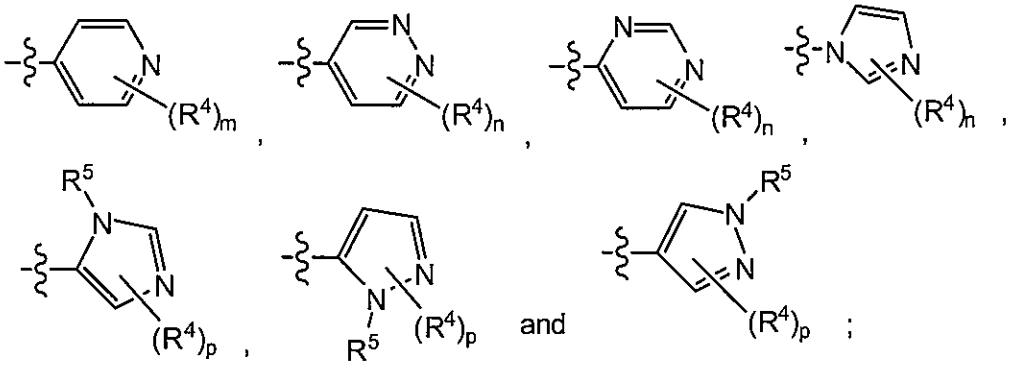
9. A compound having Formula (5):



(5)

or a physiologically acceptable salt thereof, wherein:

wherein A^1 is piperazinyl substituted with $-C(O)CH_3$,  or selected from:



ring E is phenyl or one of X^1, X^2, X^3 and X^4 is N and the others are CR^7;

one of X^5, X^6, X^7 and X^8 is N and the others are CR^{11};

Z is a 6-membered heterocycle or a 6-membered heteroaryl, each containing 1-2 nitrogen heteroatoms and each of which is optionally substituted with 1-2 R^6 groups;

R^1, R^2 and R^3 are H;

R^4 and R^6 are independently hydrogen, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, $-C(O)NR^8R^9$, -L-$C(O)R^{10}$, -L-$C(O)OR^{10}$, C_{1-6} alkyl optionally substituted with halo, C_{2-6} alkenyl or C_{2-6} alkynyl;

R^5 is H or C_{1-6} alkyl;

L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

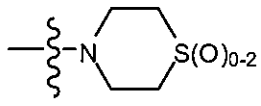
W is C_{3-7}cycloalkyl;

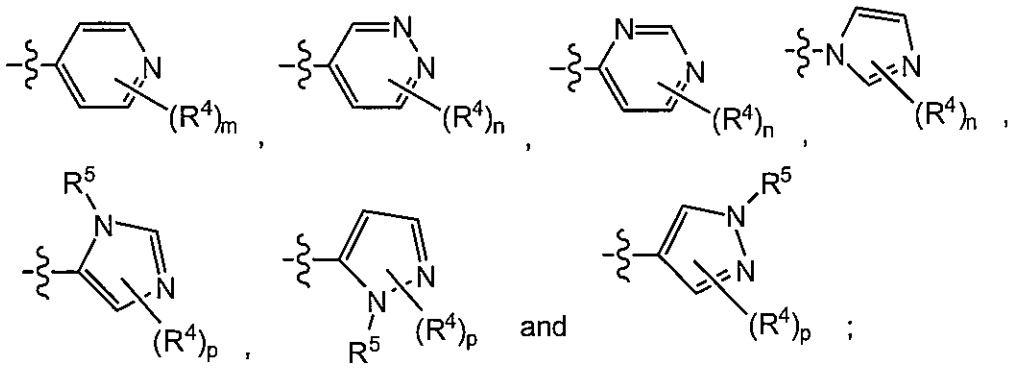
R^7 and R^{11} are independently H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl;

R^8 and R^9 are independently H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; or R^8 and R^9 together with the atoms to which they are attached may form a ring;

R^{10} is C_{1-6} alkyl or -L-W; and

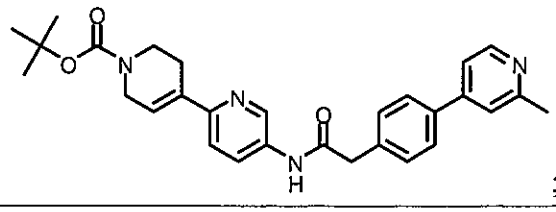
m, n and p are independently 0-2.

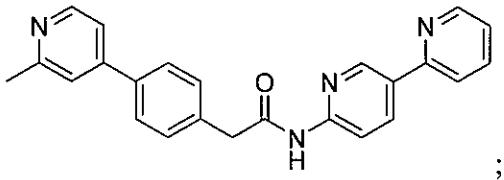
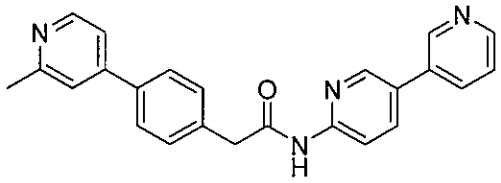
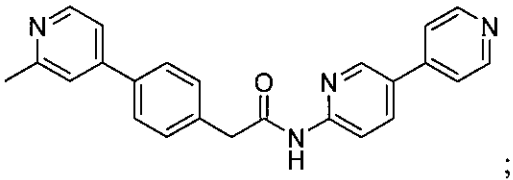
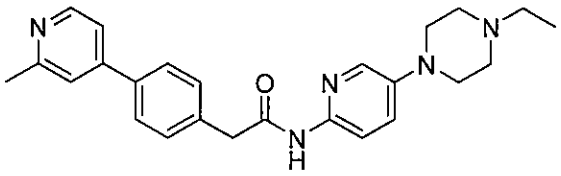
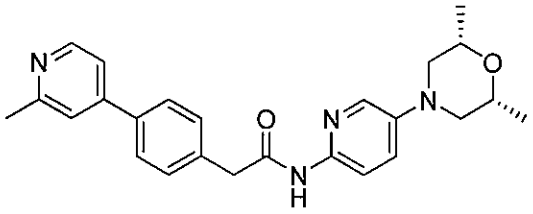
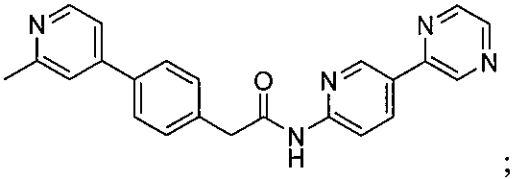
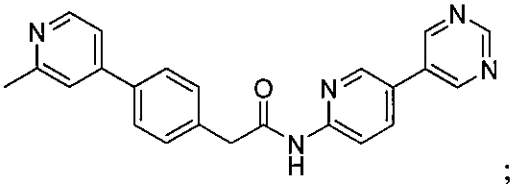
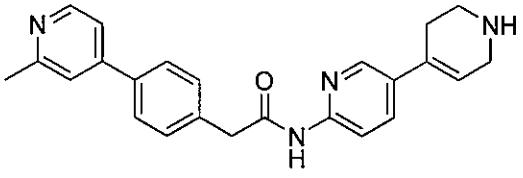
10. The compound or salt thereof of claim 9, wherein A^1 is piperazinyl substituted with $-C(O)CH_3$,  or selected from:

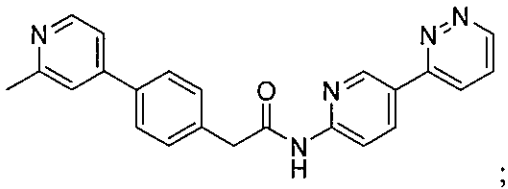
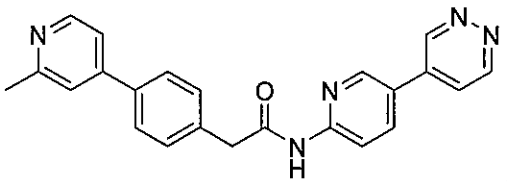
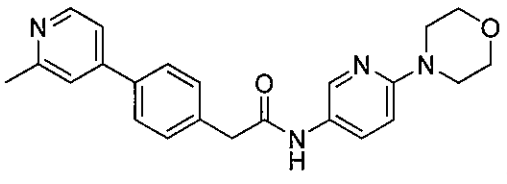
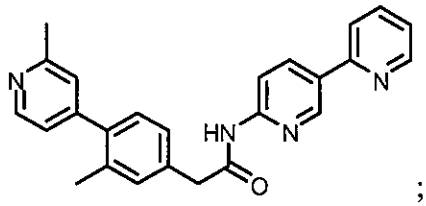
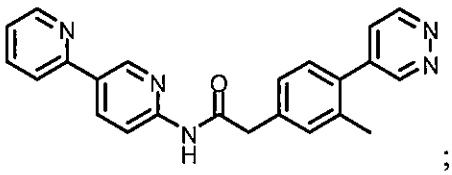
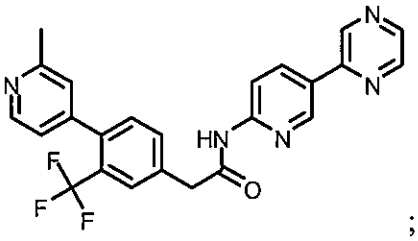
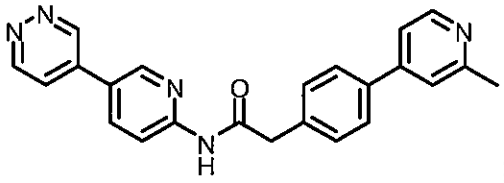
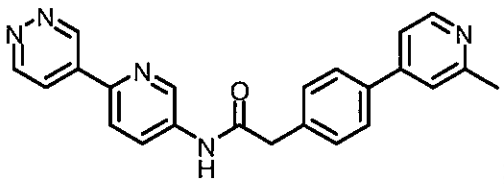


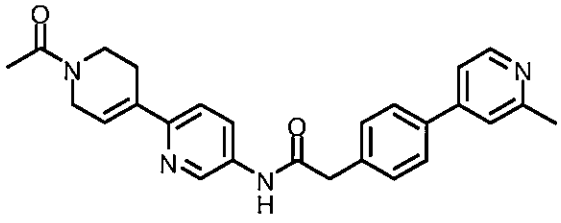
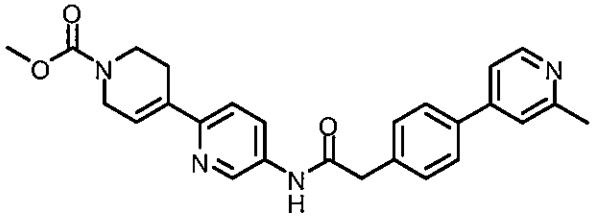
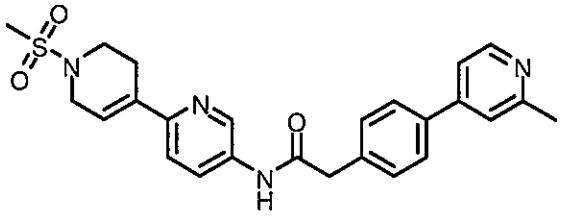
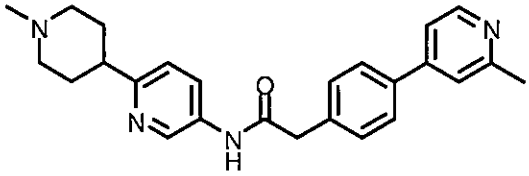
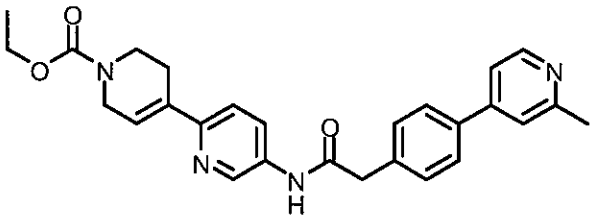
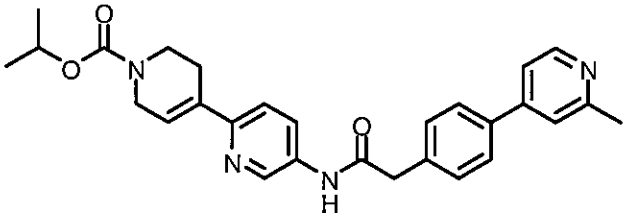
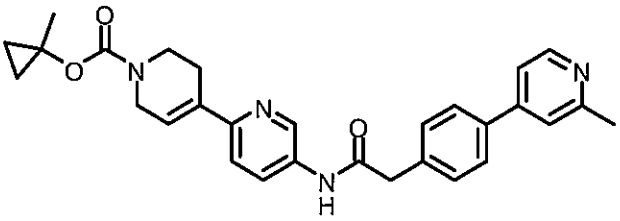
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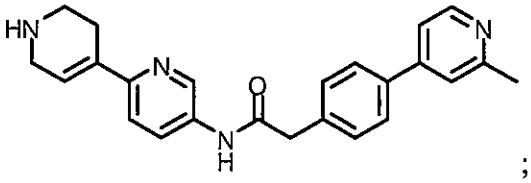
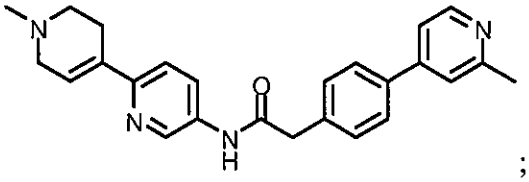
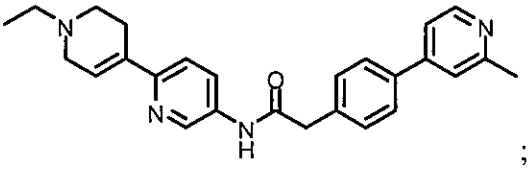
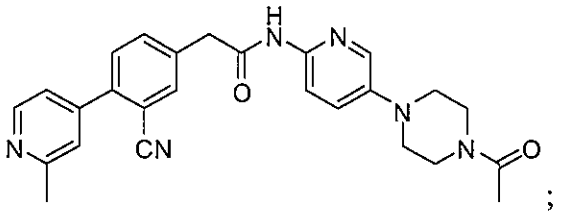
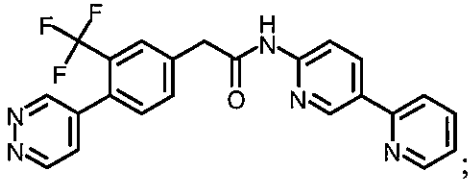
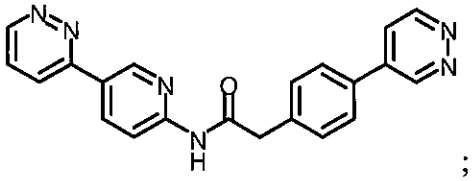
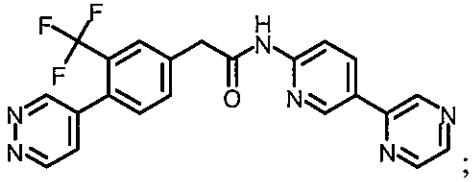
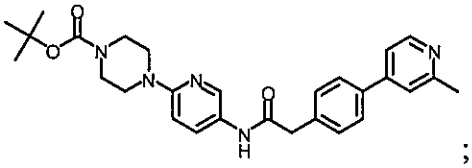
11. A compound or a physiologically acceptable salt thereof, wherein said compound is:

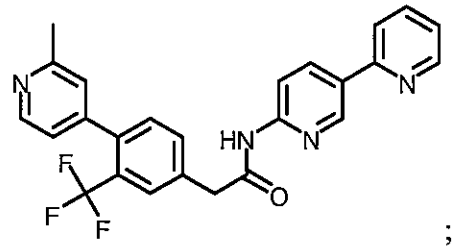
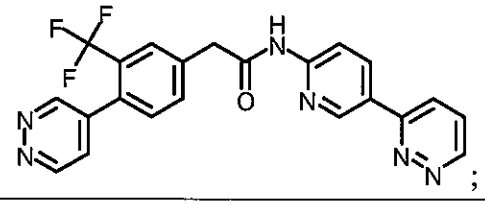
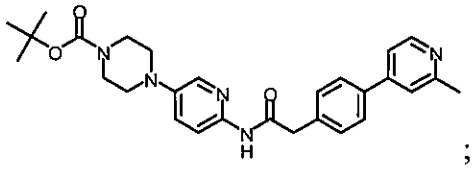
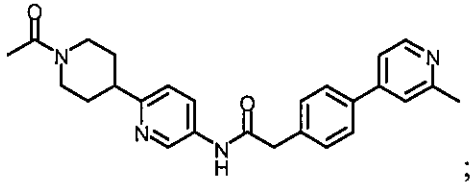
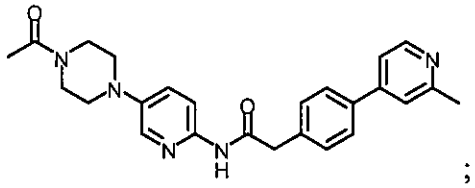
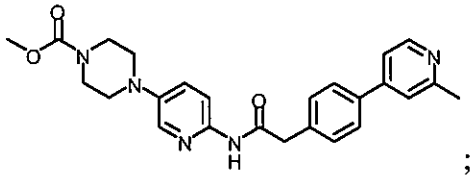
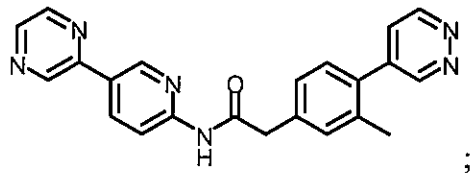
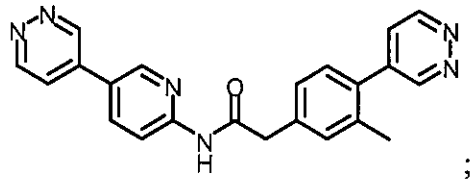
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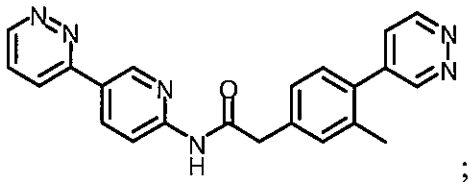
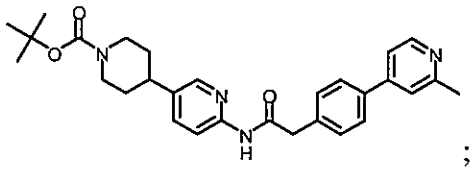
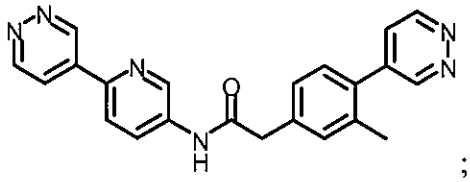
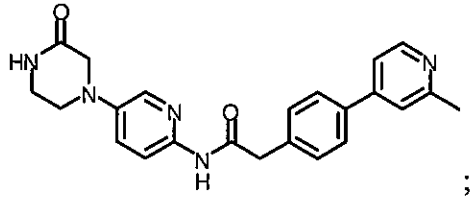
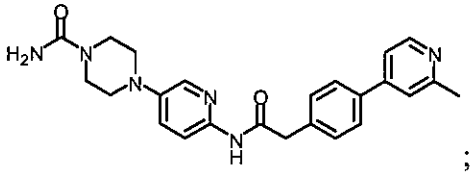
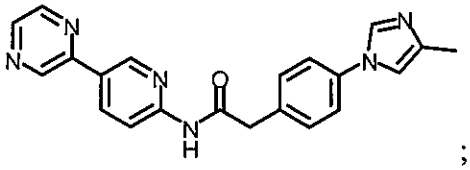
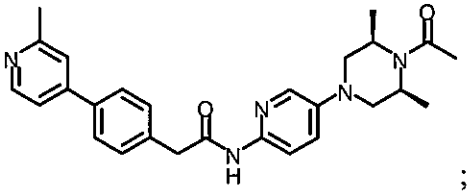
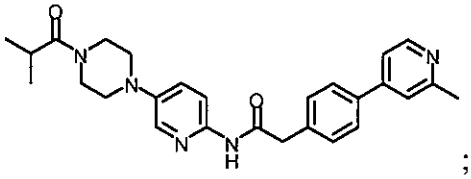
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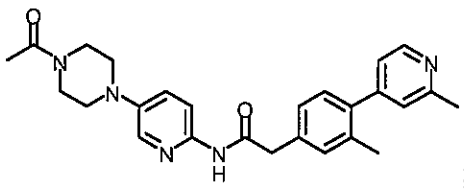
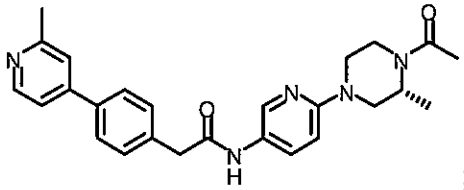
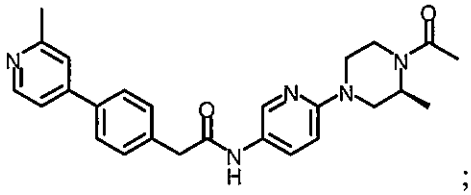
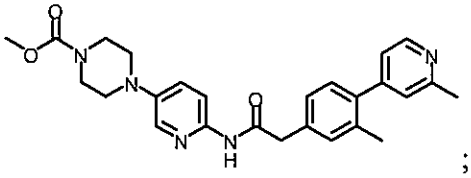
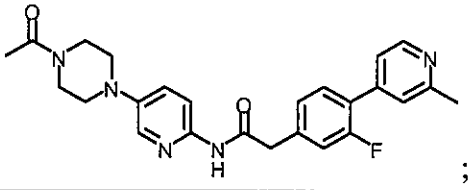
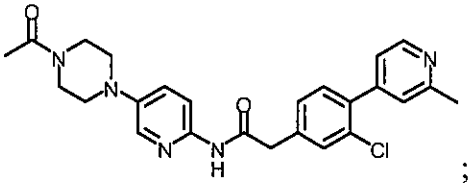
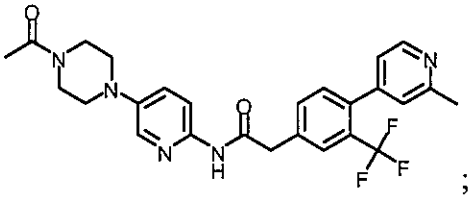
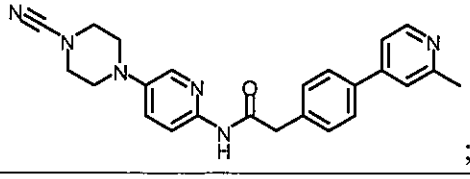
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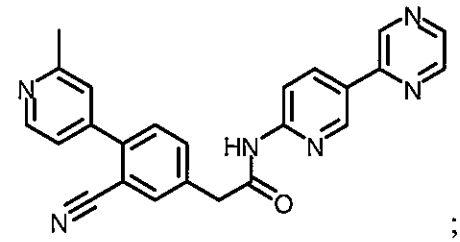
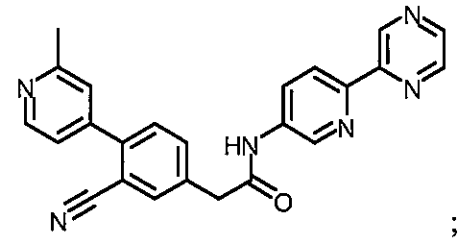
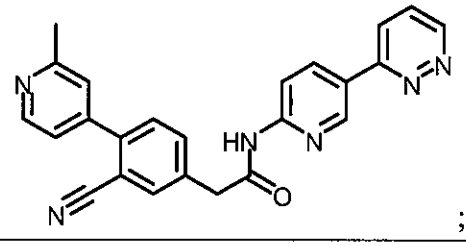
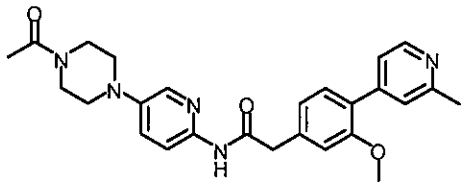
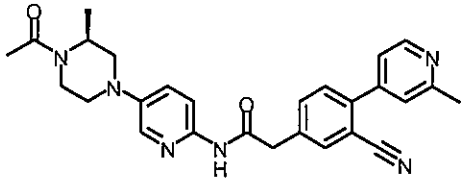
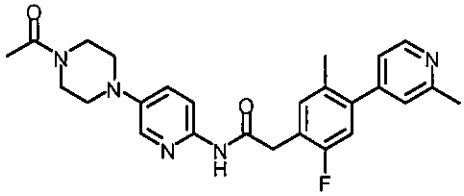
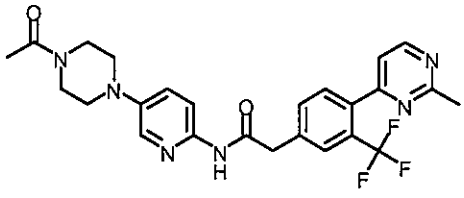
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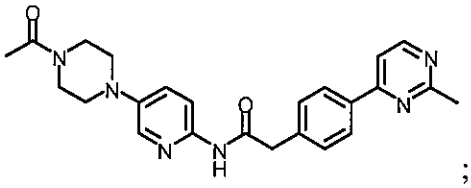
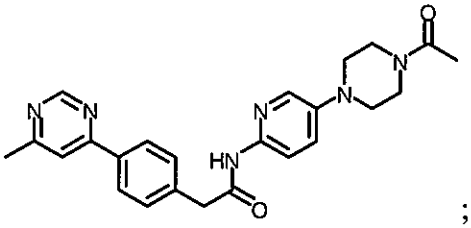
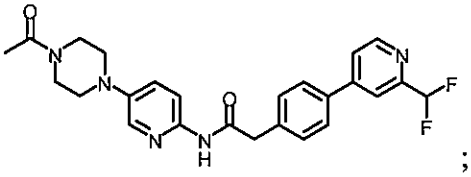
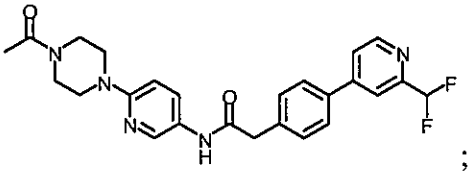
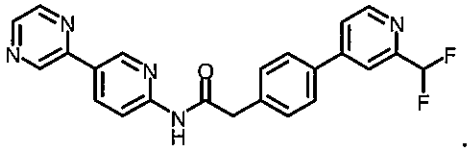
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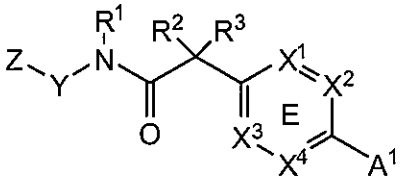
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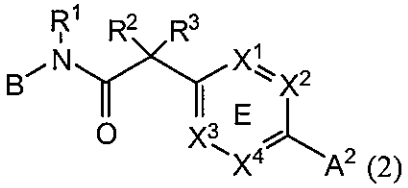
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12. A compound having Formula (1) or (2):

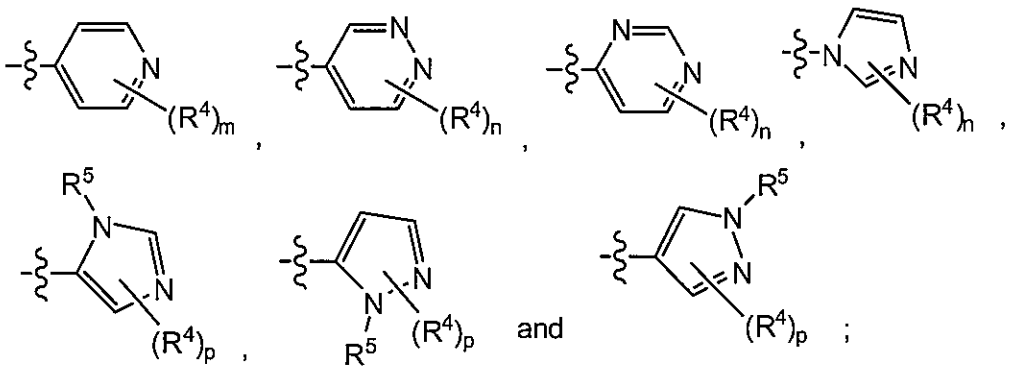
 (1)

 (2)

or a physiologically acceptable salt thereof, wherein:

ring E is an optionally substituted aryl or heteroaryl;

A^1 and A^2 are independently a C_{1-5}heterocycle, quinolinyl, or a heteroaryl selected from the group



wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-LC(O)R^{10}$;

B is benzothiazolyl, quinolinyl or isoquinolinyl, each of which is optionally substituted with 1-3 R^6 groups;

X^1, X^2, X^3 and X^4 are independently CR^7 or N;

Y is phenyl, thiazolyl, pyridinyl, pyridazinyl, pyrimidinyl or pyrazinyl;

Z is aryl, C_{1-5} heterocycle, or a 5-6 membered heteroaryl containing 1-2 heteroatoms selected from N, O and S;

each of Y and Z is optionally substituted with 1-3 R^6 groups;

R^1 and R^5 are independently H or C_{1-6} alkyl;

R^2 and R^3 are independently H, C_{1-6} alkyl or halo;

R^4 is hydrogen, halo, cyano, $-C(O)CH_3$, C_{1-6}alkoxy, or a C_{1-6} alkyl optionally substituted with halo, alkoxy or amino;

R^6 is hydrogen, halo, C_{1-6}alkoxy, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which can be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; CN, -L-W, NR^8R^9, $-L-C(O)R^{10}$, $-L-C(O)OR^{10}$, $-L-C(O)NR^8R^9$, OR^{10}; $-L-S(O)_2R^{10}$ or $-L-S(O)_2NR^8R^9$;

R^7 is H, halo, C_{1-6} alkoxy, C_{1-6} alkyl optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; NR^8R^9, $-L-C(O)R^{10}$, $-L-C(O)NR^8R^9$, OR^{10}; $-L-S(O)_2R^{10}$ or $-L-S(O)_2NR^8R^9$;

R^8 and R^9 are independently H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano; or R^8 and R^9 together with the atoms to which they are attached may form a ring;

R^{10} is H, -L-W, or C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, each of which may be optionally substituted with halo, amino, hydroxyl, alkoxy or cyano;

L is a bond or $(CR_2)_{1-4}$ wherein R is H or C_{1-6} alkyl;

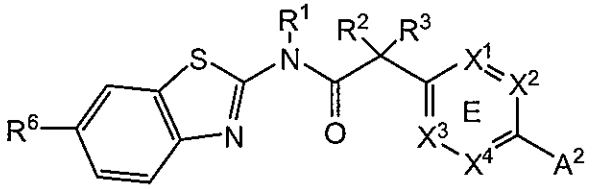
W is C_{3-7}cycloalkyl, C_{1-5}heterocycle, aryl or heteroaryl;

m is 0-4;

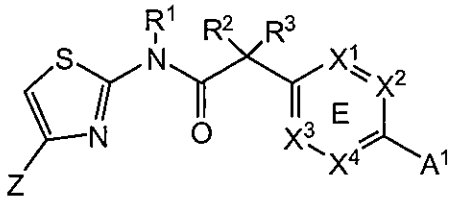
n is 0-3; and

p is 0-2.

13. The compound or physiologically acceptable salt thereof of claim 12, wherein said compound is of Formula (3) or Formula (4):



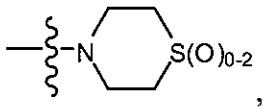
(3)

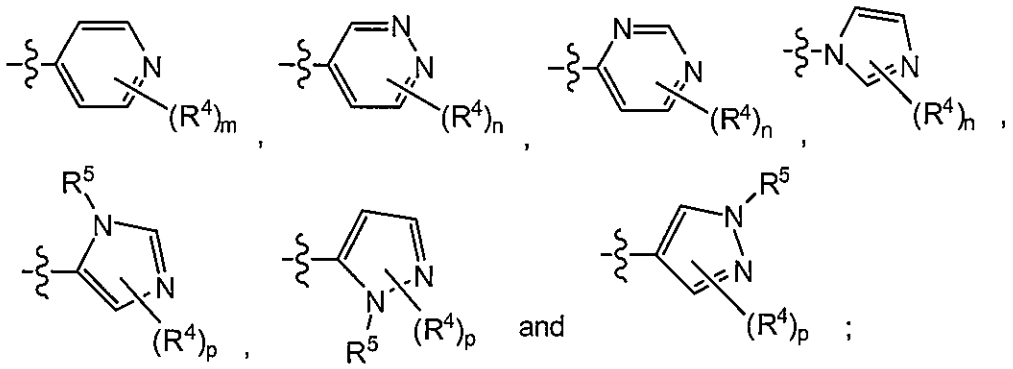


(4)

and wherein R^1, R^2, R^3, X^1, X^2, X^3, X^4, A^1, A^2, Z and R^6 are as defined in claim 12.

14. The compound or salt thereof of claim 12 or 13, wherein Z is phenyl, pyridinyl, pyridazine, pyrimidine, pyrazine, piperazinyl, piperidinyl, morpholinyl, pyrazole or 1,2,3,6-tetrahydropyridine, each of which is optionally substituted with 1-2 R^6 groups and R^6 is as defined in claim 12.

15. The compound or salt thereof of claim 12, 13 or 14, wherein A^1 and A^2 are independently morpholinyl, piperazinyl, quinolinyl, , or a heteroaryl selected from the group:



wherein any heterocycle of A^1 and A^2 can be optionally substituted with $-C(O)CH_3$; R^4 and n are as defined in claim 1.

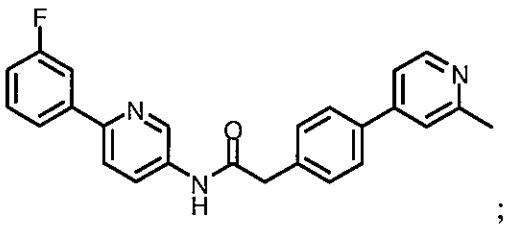
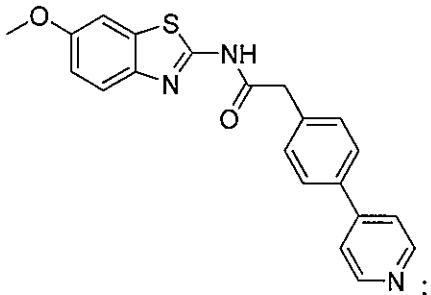
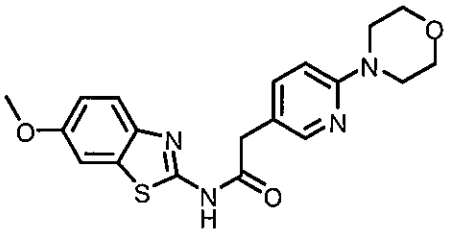
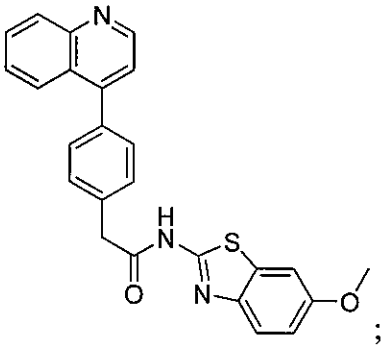
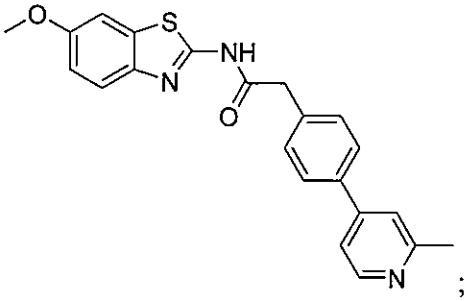
16. The compound or salt thereof of any one of claims 12 to 15, wherein ring E is phenyl, pyridyl or pyrimidinyl, each of which optionally substituted with R^7.

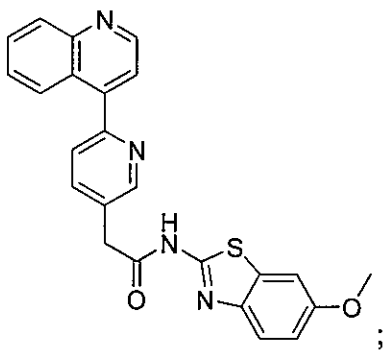
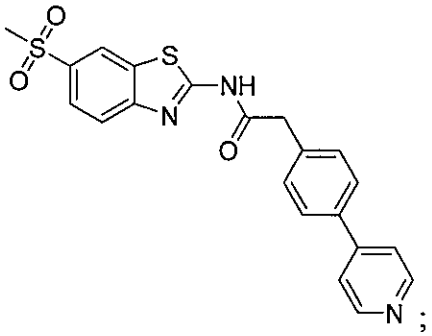
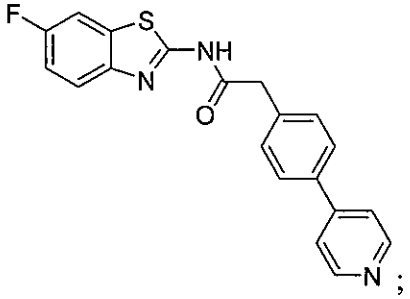
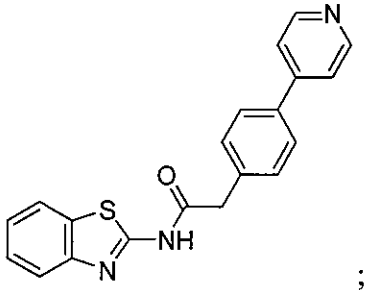
17. The compound or salt thereof of any one of claims 12 to 16, wherein R^7 is H, halo, cyano, C_{1-6}alkoxy, $-S(O)_2R^{10}$, or an optionally halogenated C_{1-6} alkyl.

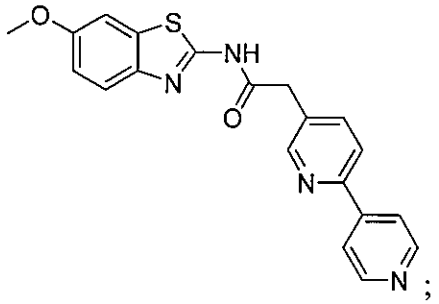
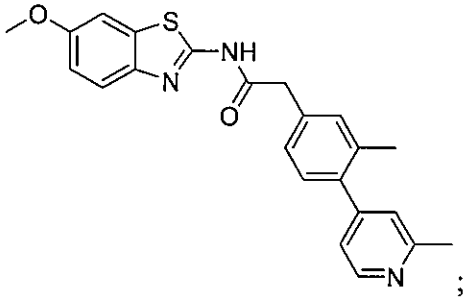
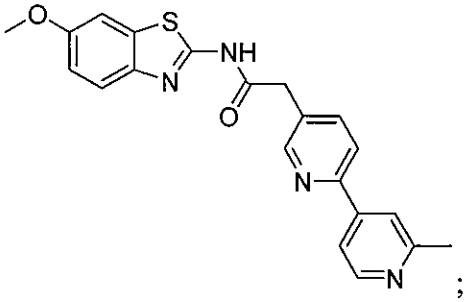
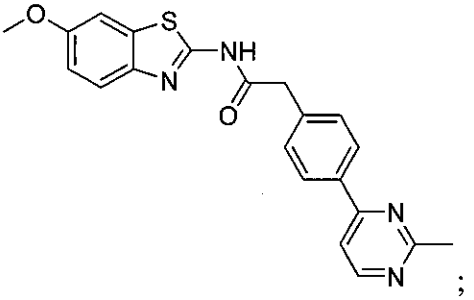
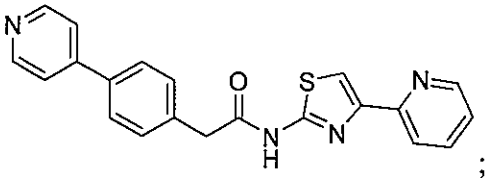
18. The compound or salt thereof of any one of claims 12 to 17, wherein R^1, R^2 and R^3 are H.

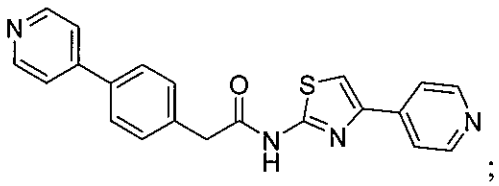
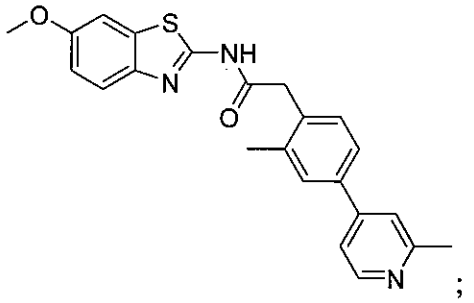
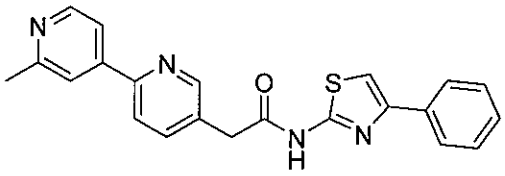
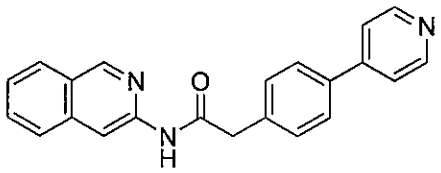
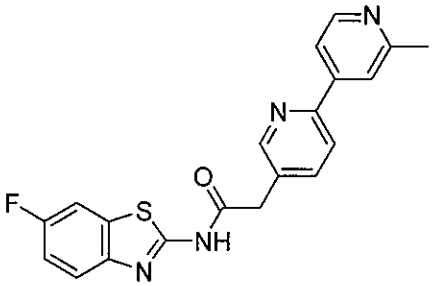
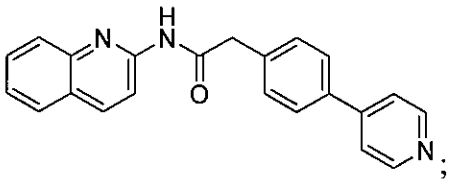
19. The compound or salt thereof of any one of claims 12 to 18, wherein R^4 and R^6 are independently selected from hydrogen, halo, methyl, trifluoromethyl and $-C(O)CH_3$.

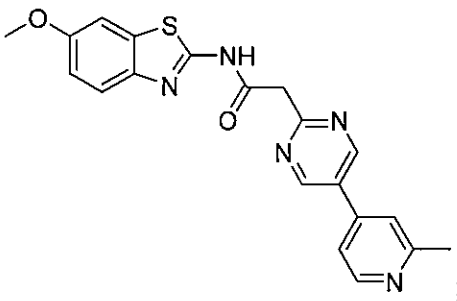
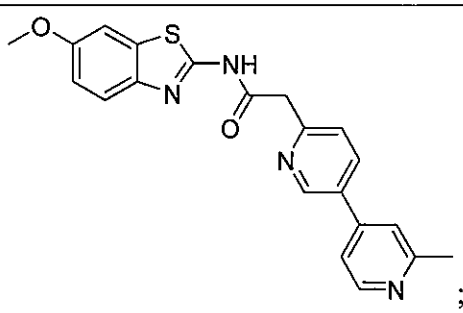
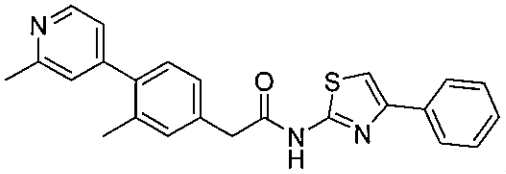
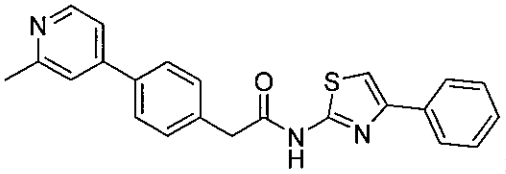
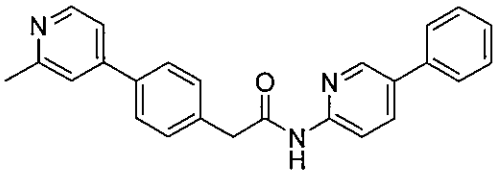
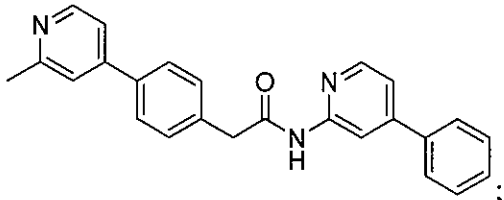
20. A compound or a physiologically acceptable salt thereof, wherein said compound is:

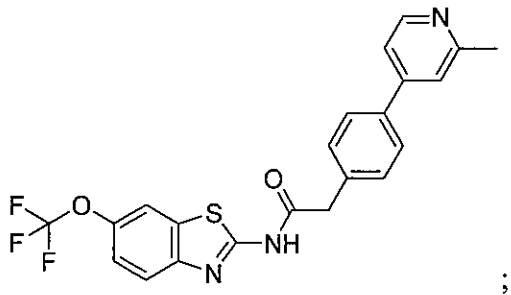
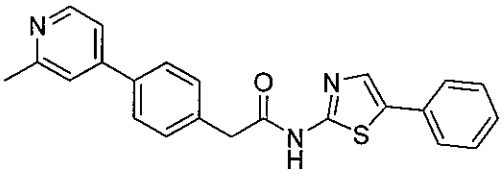
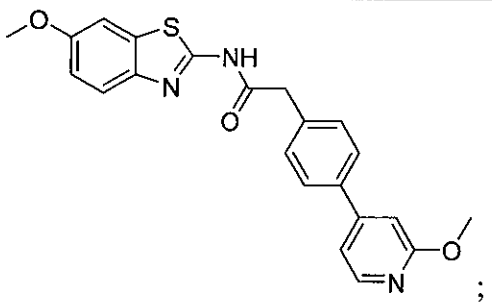
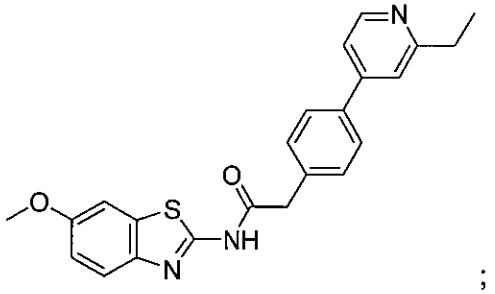
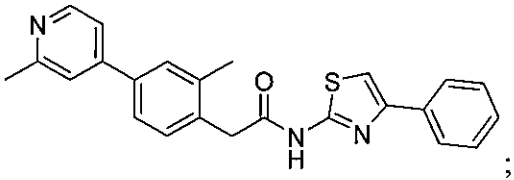
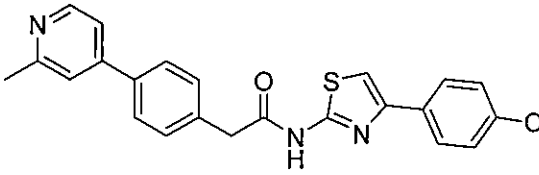
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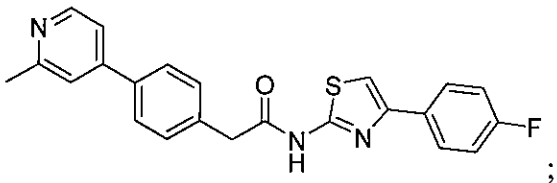
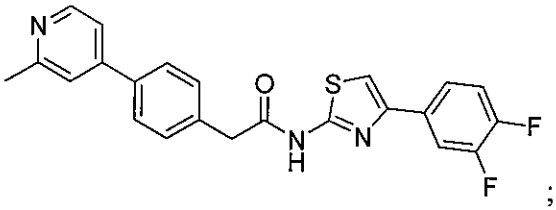
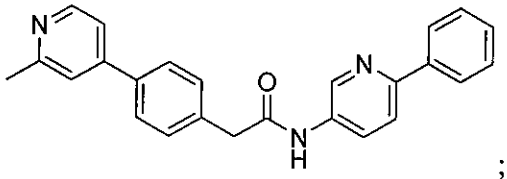
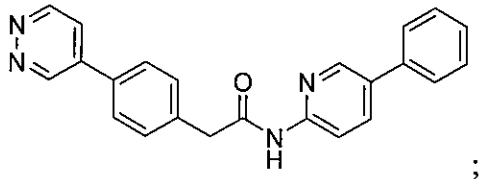
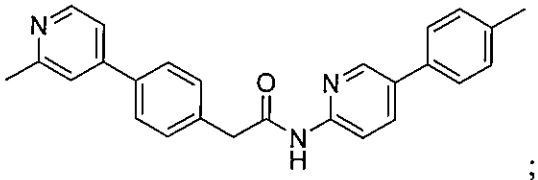
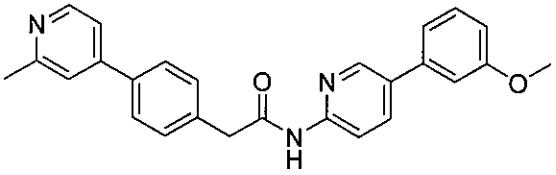
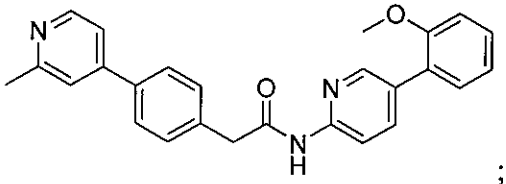
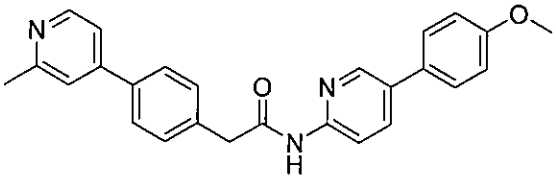
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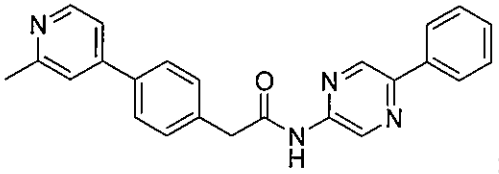
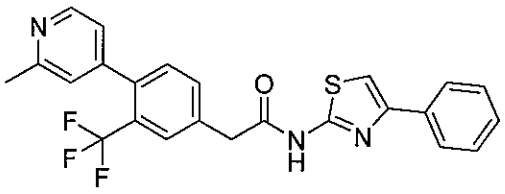
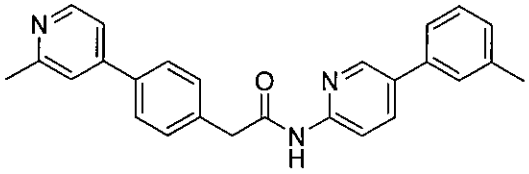
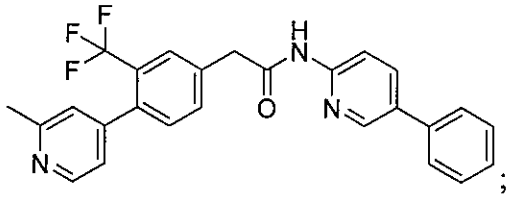
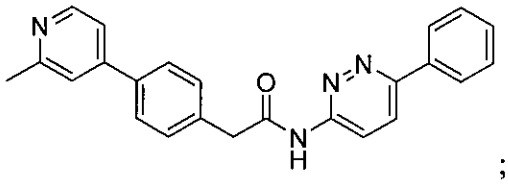
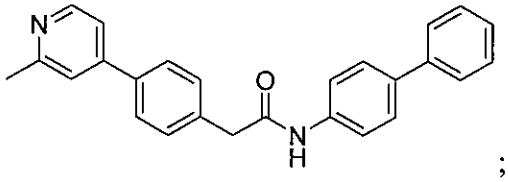
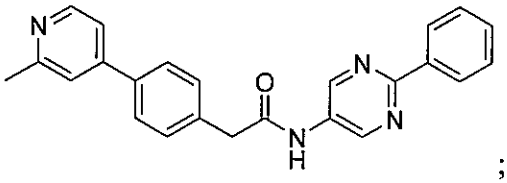
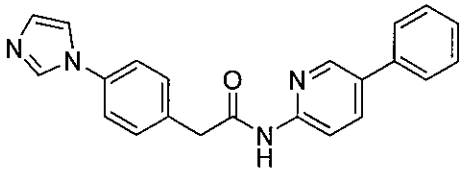
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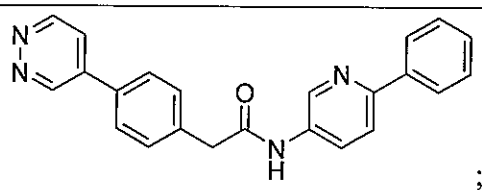
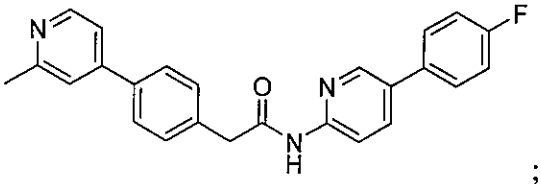
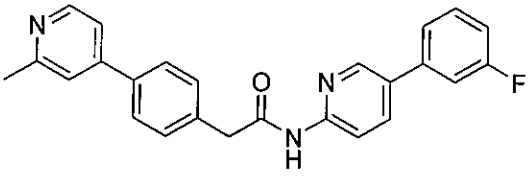
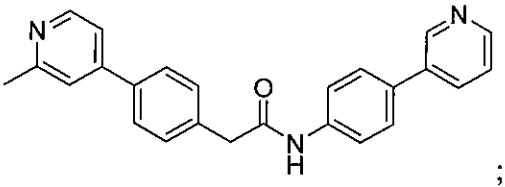
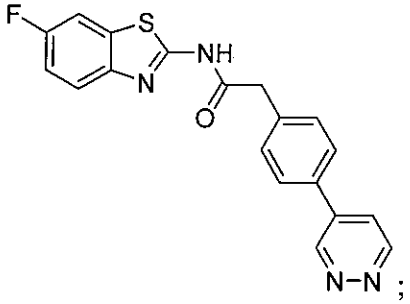
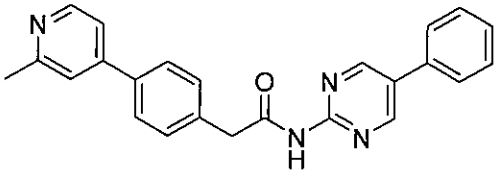
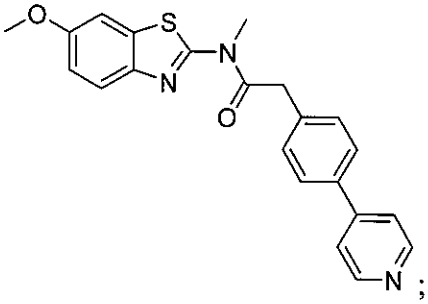
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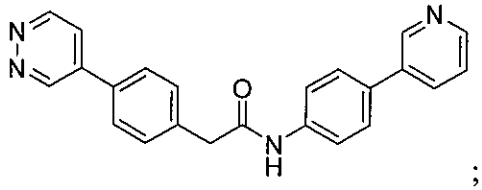
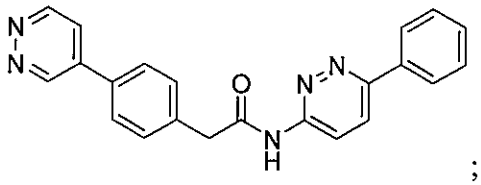
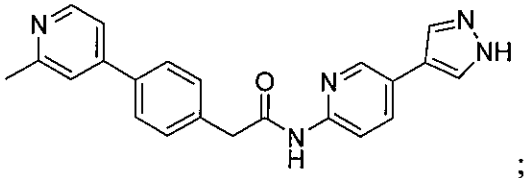
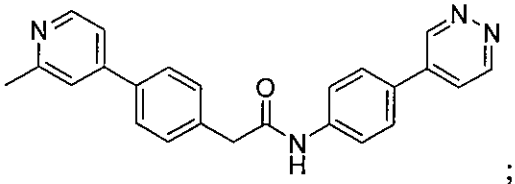
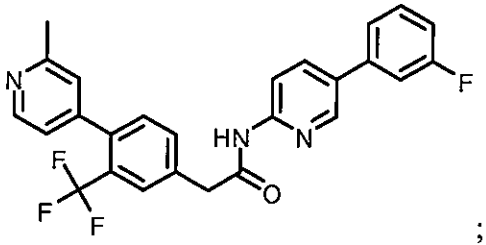
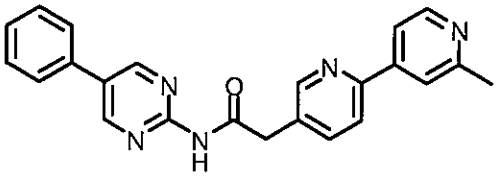
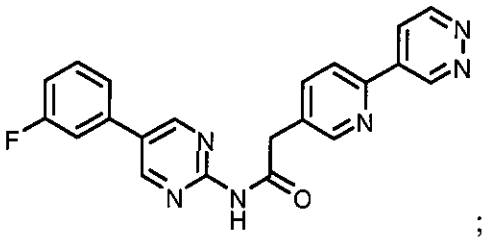
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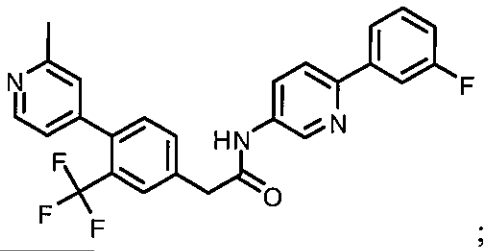
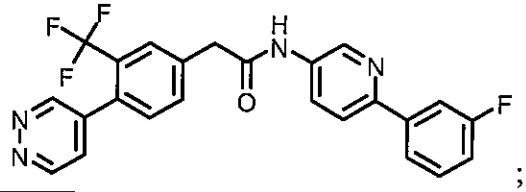
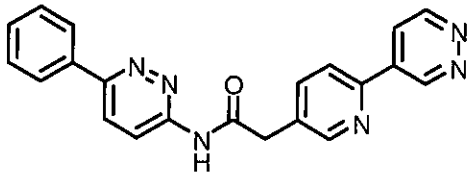
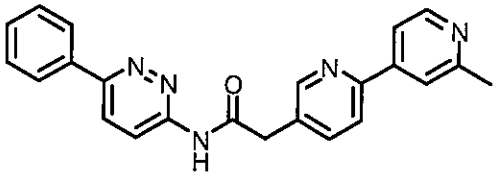
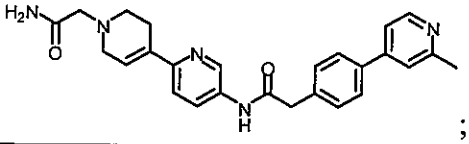
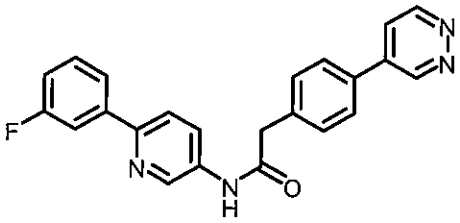
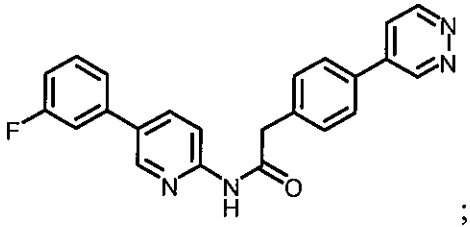
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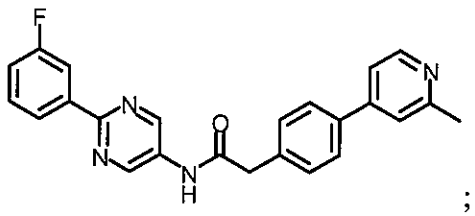
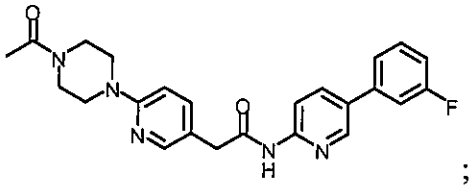
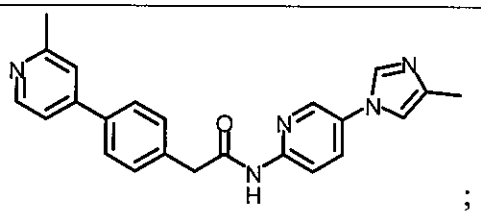
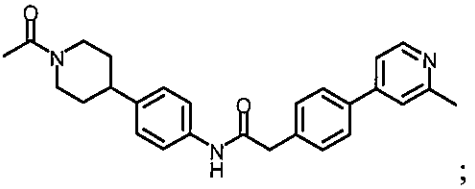
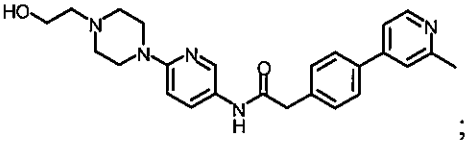
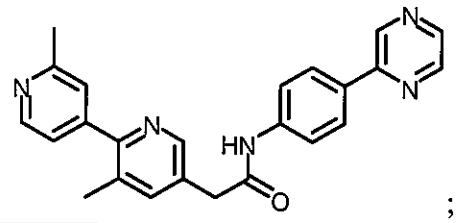
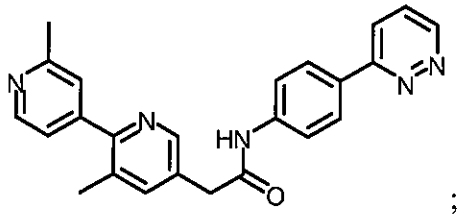
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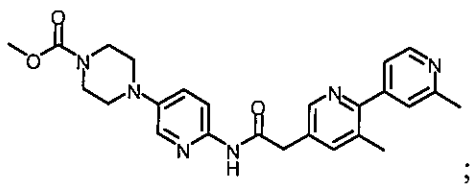
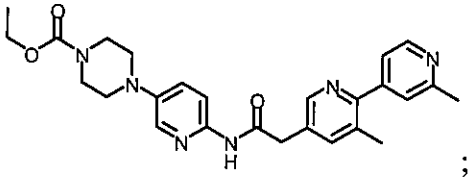
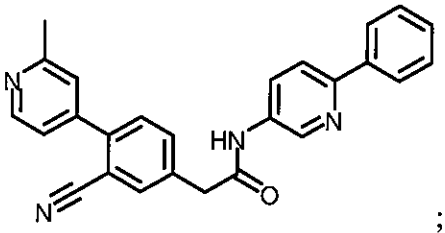
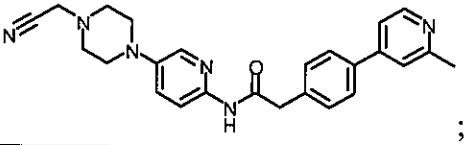
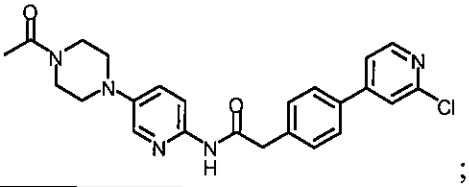
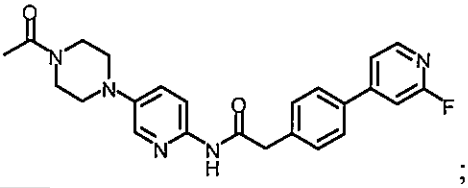
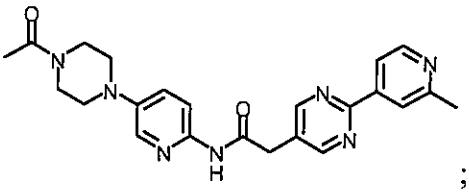
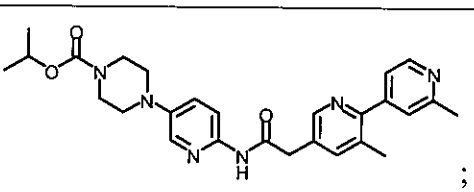
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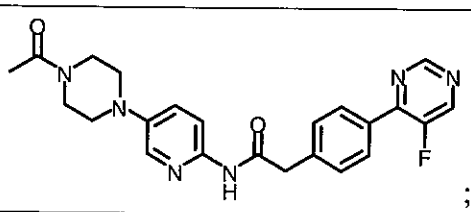
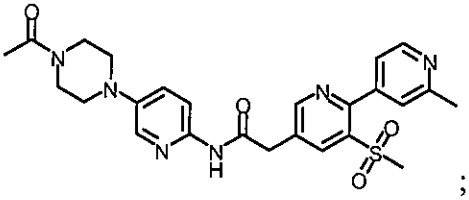
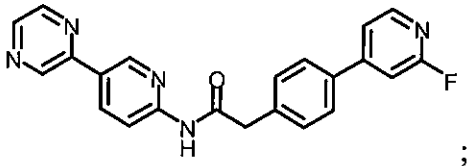
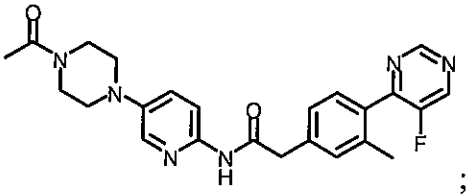
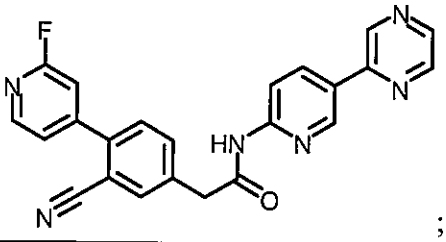
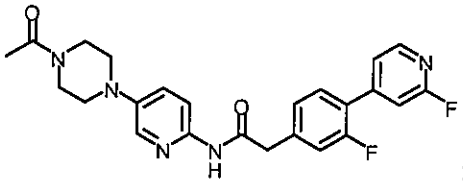
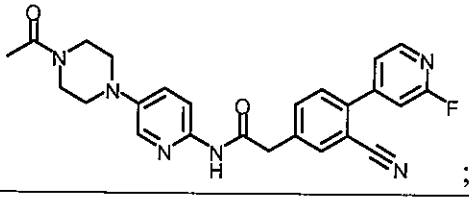
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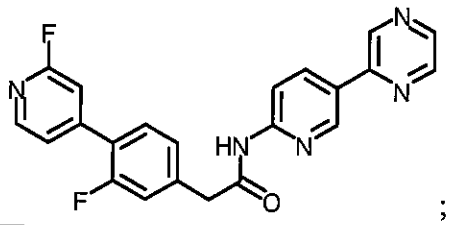
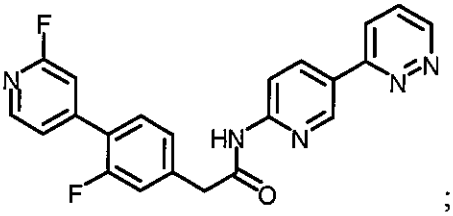
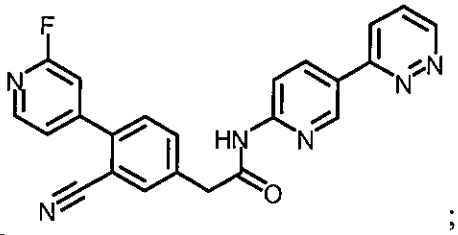
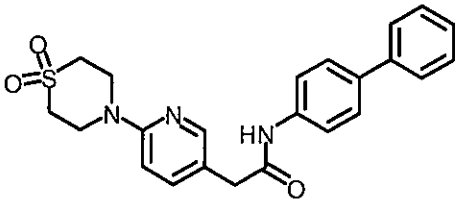
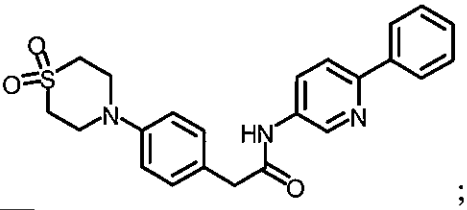
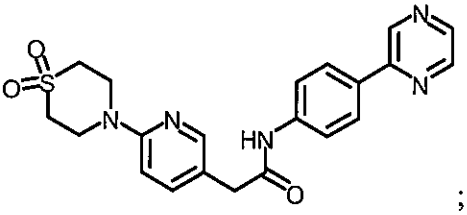
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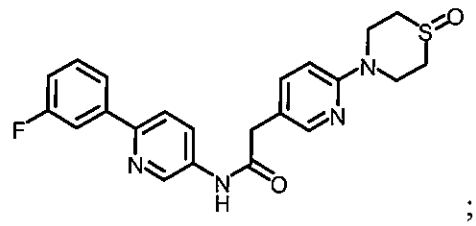
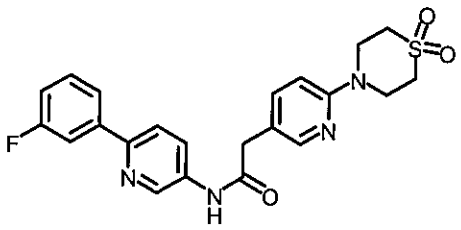
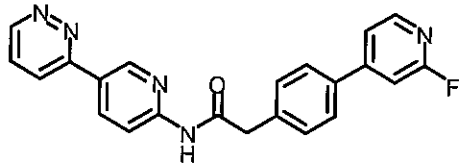
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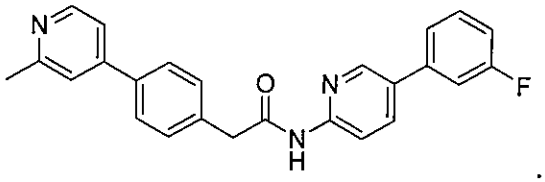
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21. A compound or a physiologically acceptable salt thereof, wherein said compound is:

 .

22. A compound or a physiologically acceptable salt thereof, wherein the compound is: N-(6-methoxybenzo[d]thiazol-2-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(6-phenylpyridin-3-yl)-2-(3-(pyridazin-4-yl)phenyl)acetamide; 2-(3-(2-methoxypyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyridazin-3-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyrazin-2-yl)phenyl)acetamide; 2-(3-(2-methylpyridin-4-yl)phenyl)-N-(6-(pyrazin-2-yl)pyridin-3-

yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-6-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(6-phenylpyridin-3-yl)acetamide; 2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)-N-(6-phenylpyridin-3-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(4-cyano-3-(2-methylpyridin-4-yl)phenyl)acetamide; 2-(2'-methyl-2,4'-bipyridin-4-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2'-methyl-2,4'-bipyridin-4-yl)acetamide; N-(5-(4-acetylpiperazin-1-yl)pyridin-2-yl)-2-(2-cyano-2'-methyl-3,4'-bipyridin-5-yl)acetamide; 2-(2-(2',3-dimethyl-2,4'-bipyridin-5-yl)acetamido)-5-(pyrazin-2-yl)pyridine 1-oxide; or, 2',3-dimethyl-5-(2-oxo-2-(5-(pyrazin-2-yl)pyridin-2-ylamino)ethyl)-2,4'-bipyridine 1'-oxide.

23. A physiologically acceptable salt of a compound as defined in any one of claims 1 to 22, which is a fumaric acid salt.

24. A pharmaceutical composition comprising a compound or salt thereof as defined in any one of claims 1 to 23 and a physiologically acceptable carrier.

25. Use of a compound or salt thereof as defined in any one of claims 1 to 23 or the pharmaceutical composition of claim 24, for inhibiting Wnt signaling in a cell.

26. Use of a compound or salt thereof as defined in any one of claims 1 to 23 or the pharmaceutical composition of claim 24, for inhibiting a Porcupine gene in a cell.

27. Use of a compound or salt thereof as defined in any one of claims 1 to 23 or the pharmaceutical composition of claim 24, optionally in combination with a second therapeutic agent, for treating a Wnt-mediated disorder in a mammal.

28. Use of a compound or salt thereof as defined in any one of claims 1 to 23 or the pharmaceutical composition of claim 24, optionally in combination with a second therapeutic agent in preparation of a medicament for treating a Wnt-mediated disorder in a mammal.

29. The use of claim 27 or 28, wherein said Wnt-mediated disorder is keloids, fibrosis, proteinuria, kidney graft rejection, osteoarthritis, Parkinson's disease, cystoid macular edema, retinopathy, macular degeneration or a cell proliferative disorder associated with aberrant Wnt signaling activity.

30. The use of claim 27 or 28, wherein said Wnt-mediated disorder is a cell proliferative disorder that is: colorectal cancer, breast cancer, head or neck squamous cell carcinoma, esophageal cancer, non-small cell lung cancer, gastric cancer, pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilm's tumor, basal cell carcinoma, melanoma, head or neck cancer, cervical cancer or prostate cancer.

31. The use of claim 30, wherein the proliferative disorder is esophageal squamous cell carcinoma.

32. The use of claim 30, wherein the proliferative disorder is colorectal carcinoma.