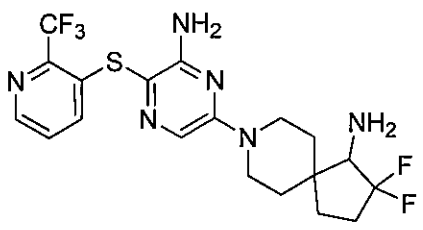
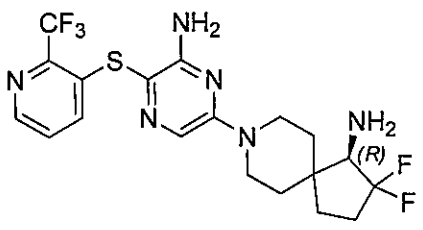
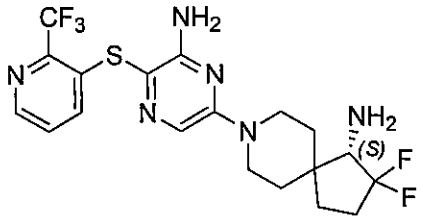
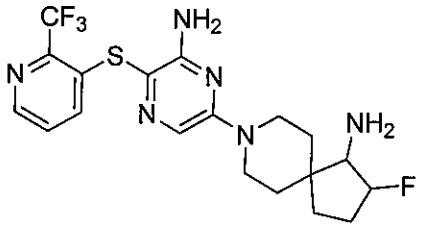
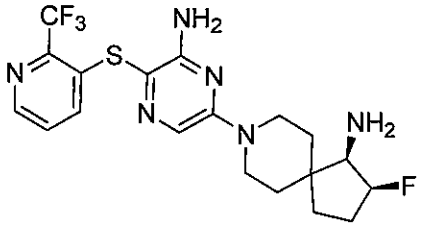
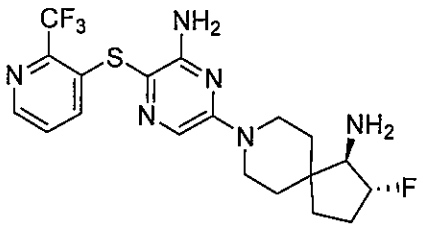
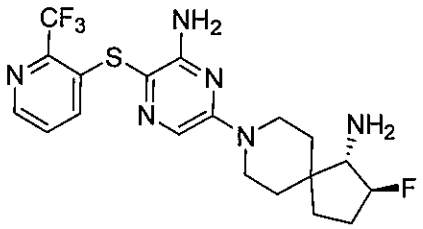
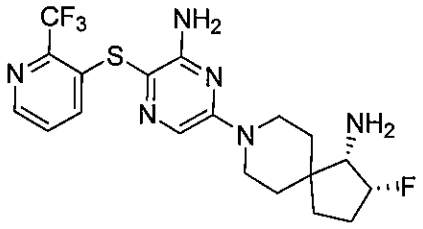
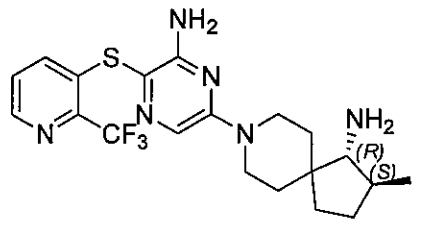
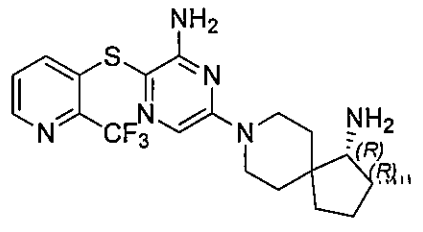
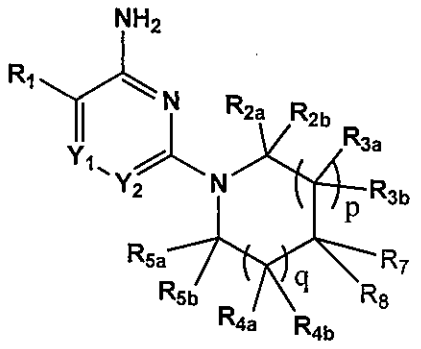
	
	
	
	
	

CLAIMS

1. A compound of formula I:



I

in which:

p is selected from 0 and 1;

q is selected from 0 and 1;

Y_1 is selected from CH and N;

Y_2 is selected from CR_6 and N;

R_1 is $-XR_{1a}$; wherein R_{1a} is selected from $C_{6\text{-}10}$aryl, and a 5-9 member heteroaryl group containing from 1 to 4 heteroatoms or groups independently selected from N, and C(O); wherein said aryl or heteroaryl of R_{1a} is substituted with 1 to 5 R_9 groups independently selected from halo, amino, $C_{1\text{-}4}$alkoxy, dimethyl-amino, halo-substituted-$C_{1\text{-}4}$alkyl, and $-C(O)NH_2$; and X is selected from a bond, and $S(O)_m$; wherein m is selected from 0, 1 and 2;

R_{2a} and R_{2b} are hydrogen;

R_{3a} and R_{3b} are hydrogen;

R_{4a} and R_{4b} are hydrogen;

R_{5a} and R_{5b} are hydrogen;

R_6 is selected from hydrogen, amino-carbonyl, and $-C(O)NR_{6a}R_{6b}$; wherein R_{6a} and R_{6b} are independently selected from hydrogen and $C_{1\text{-}4}$alkyl;

R_7 and R_8 together with the carbon atom to which they are both attached form a 3 to 7 member saturated or partially unsaturated ring that can optionally contain 1 to 3 heteroatoms or

groups independently selected from N, C(O), O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with

a) an amino group;

b) an amino group and a hydroxyl group;

c) an amino group and a methoxy group;

d) an amino group and two halo groups;

e) an amino group and a halo group;

f) an amino group and a methyl group;

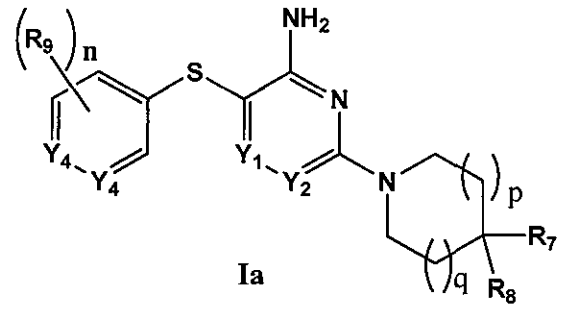
g) an amino group and an isobutyryloxy group;

or

h) an amino-methyl group and a hydroxyl group,

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 of Formula Ia:



Ia

in which:

n is selected from 1, 2, 3 and 4;

p is selected from 0 and 1;

q is selected from 0 and 1;

Y_1 is selected from CH and N;

Y_2 is selected from CR_6 and N;

each Y_4 is independently selected from N, C(O) and CR_9; wherein only one Y_4 is C(O);

R_6 is selected from hydrogen and amino-carbonyl;

R_7 and R_8 together with the carbon atom to which they are both attached form a 3 to 7 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, C(O), O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with

a) an amino group;

b) an amino group and a hydroxyl group;

c) an amino group and a methoxy group;

d) an amino group and two halo groups;

e) an amino group and a halo group;

f) an amino group and a methyl group;

g) an amino group and an isobutyryloxy group;

or

h) an amino-methyl group and a hydroxyl group;

R_9 is selected from halo, amino, dimethyl-amino, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy, and $-C(O)NH_2$;

or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 5 member saturated or partially unsaturated ring that can optionally contain 1 to 2 heteroatoms or groups independently selected from N, O, C(O) and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with

a) an amino group;

b) an amino group and a hydroxyl group;

c) an amino group and a methoxy group;

d) an amino group and two halo groups;

e) an amino group and a halo group;

f) an amino group and a methyl group;

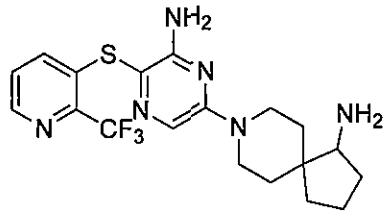
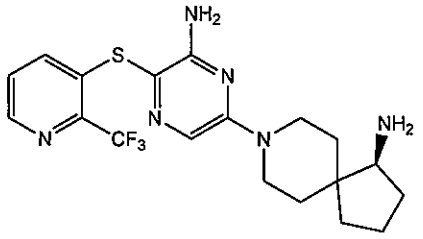
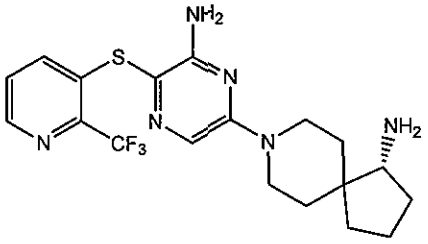
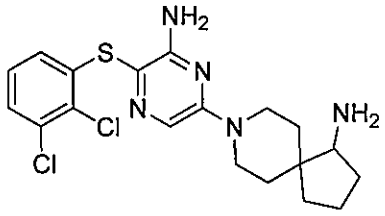
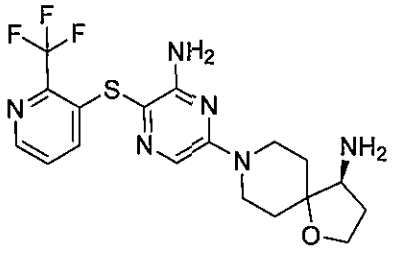
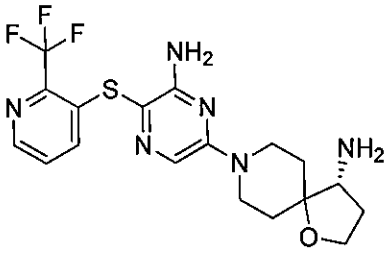
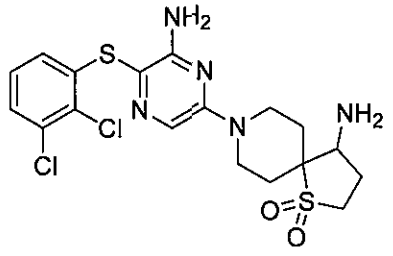
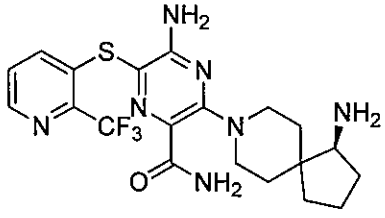
g) an amino group and an isobutyryloxy group;

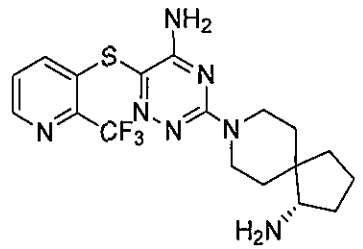
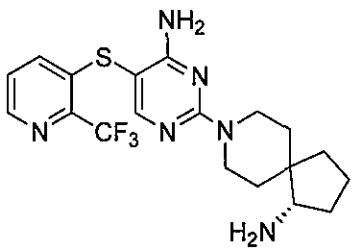
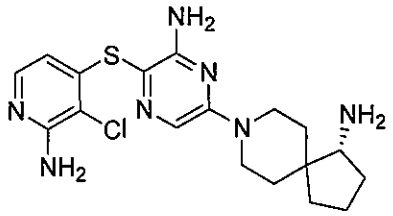
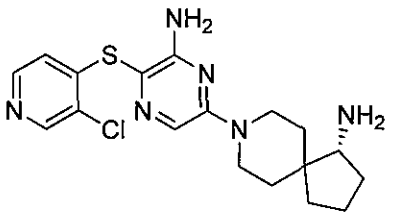
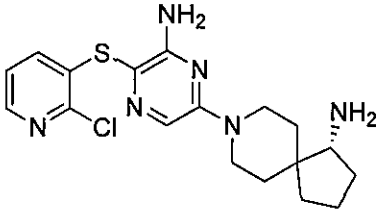
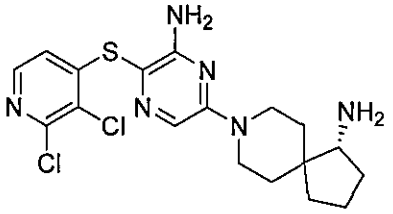
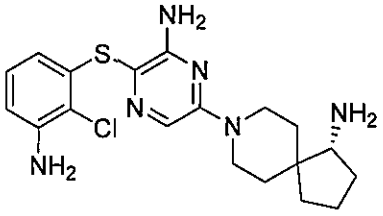
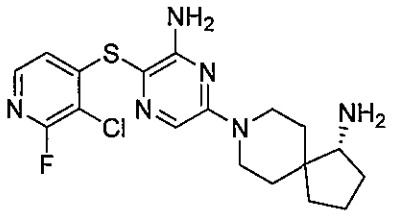
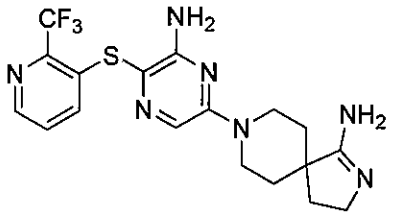
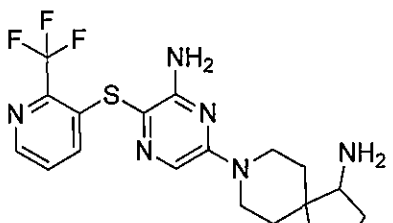
or

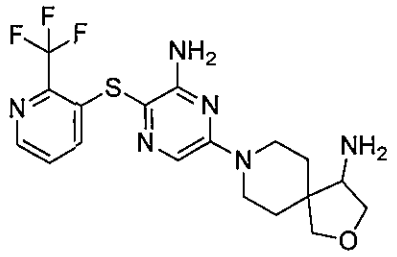
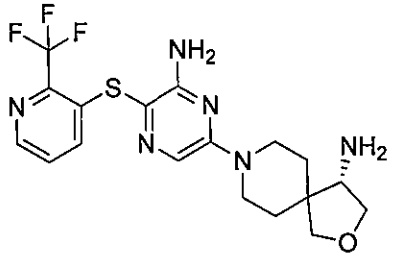
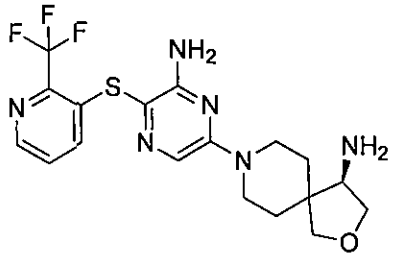
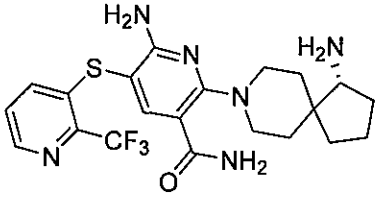
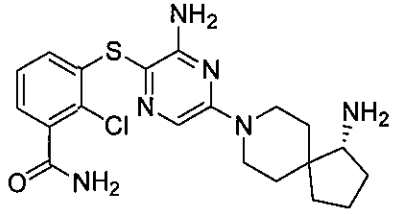
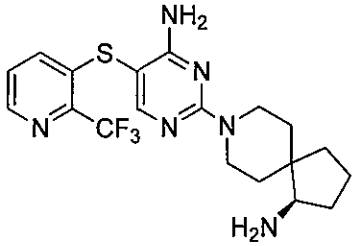
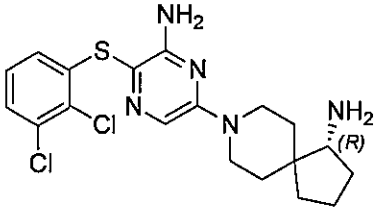
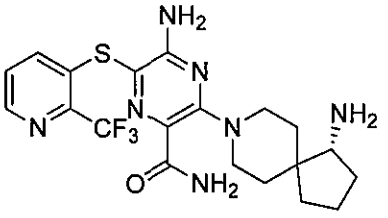
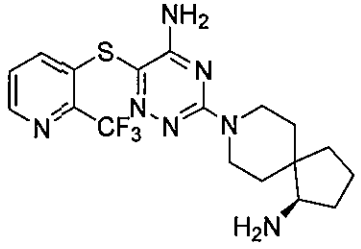
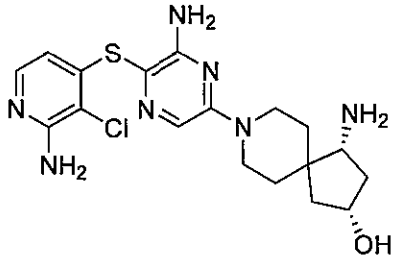
h) an amino-methyl group and a hydroxyl group;

or a pharmaceutically acceptable salt thereof.

4. The compound of claim 3, or the pharmaceutically acceptable salt thereof selected from:

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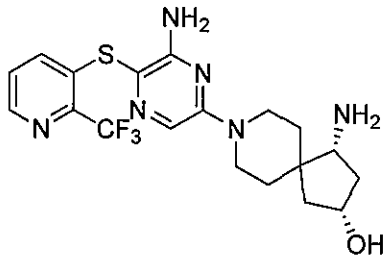
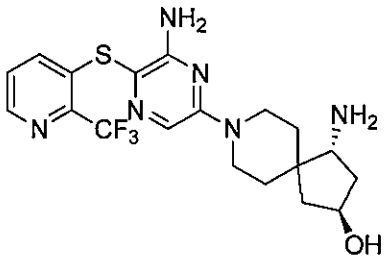
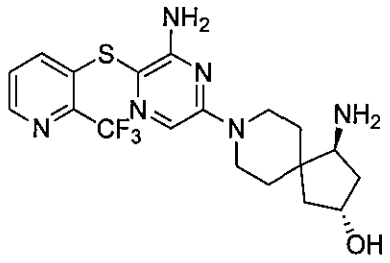
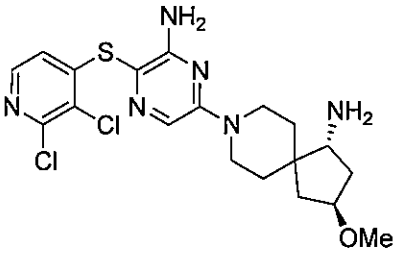
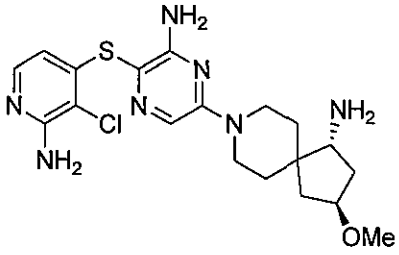
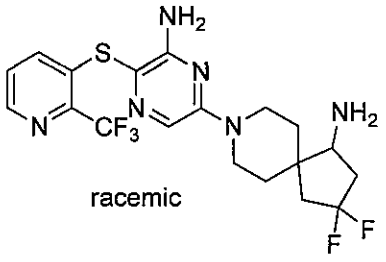
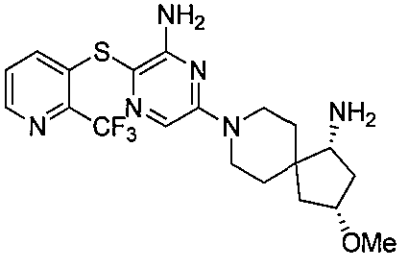
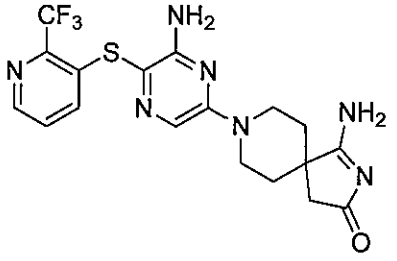
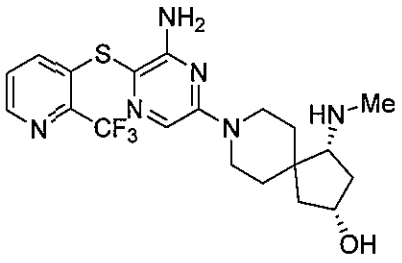
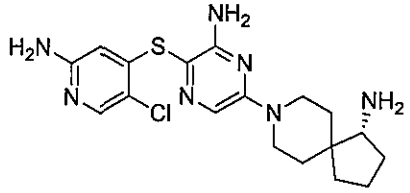
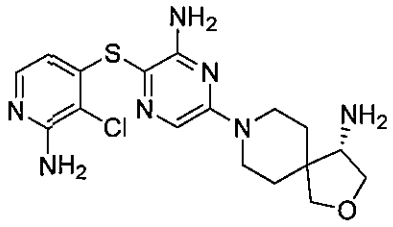
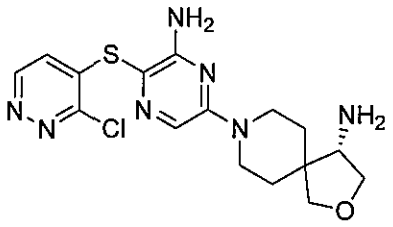
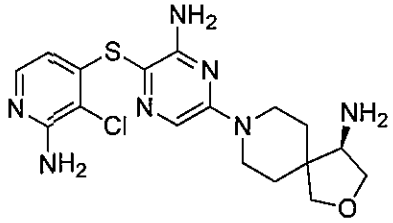
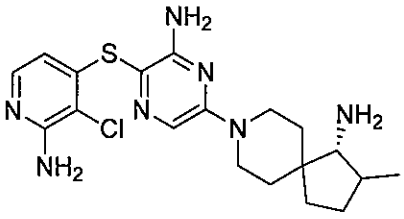
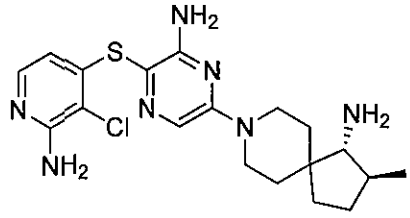
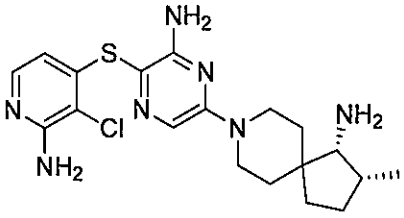
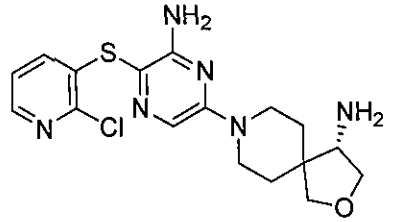
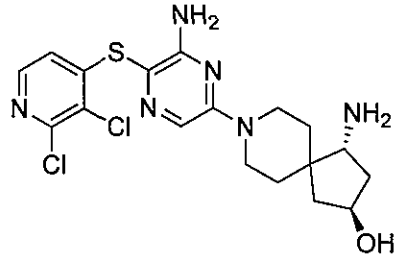
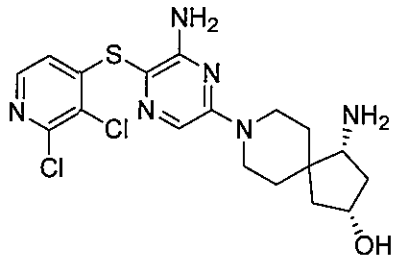
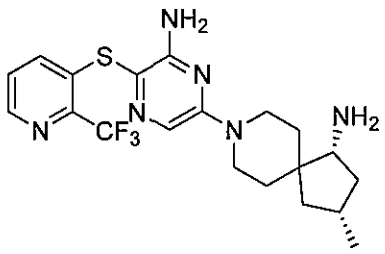
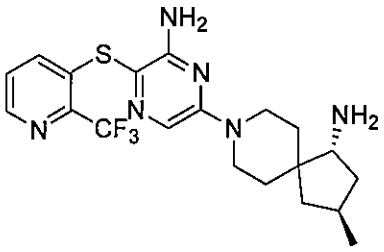
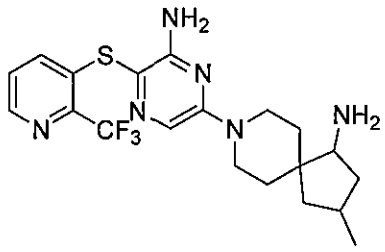
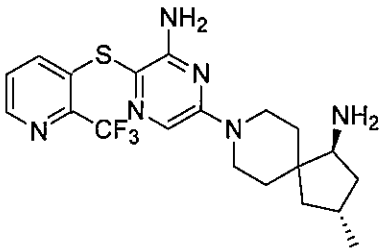
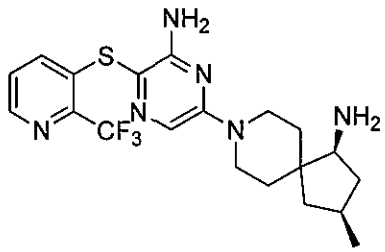
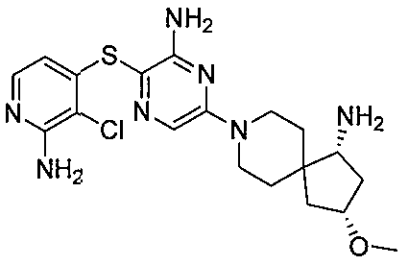
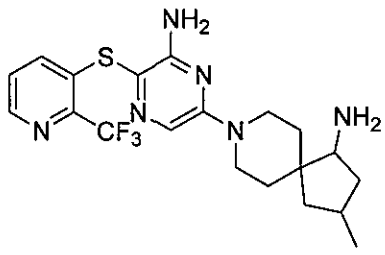
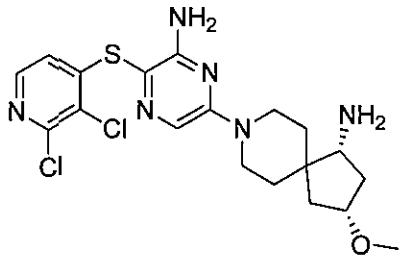
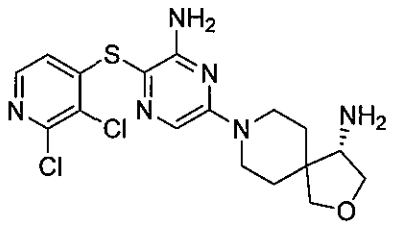
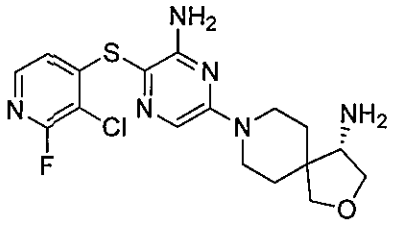
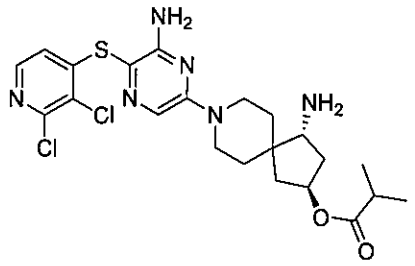
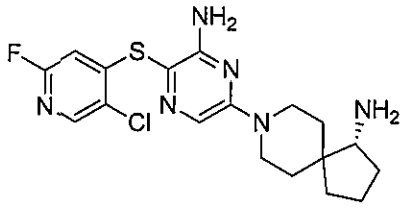
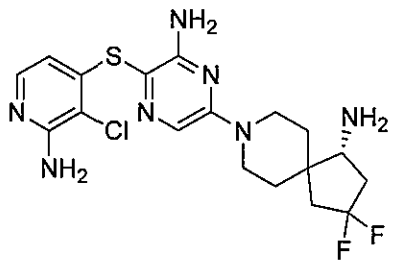
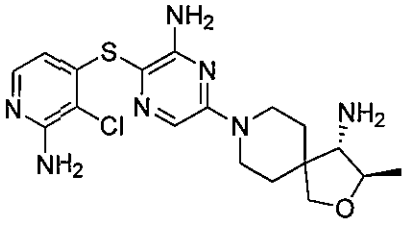
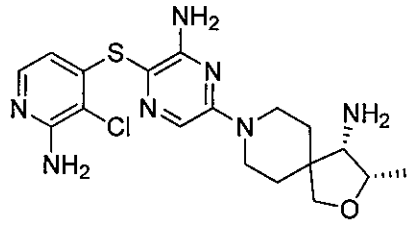
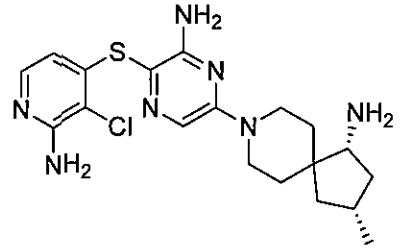
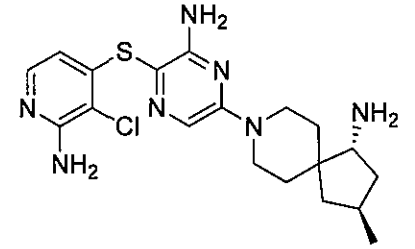
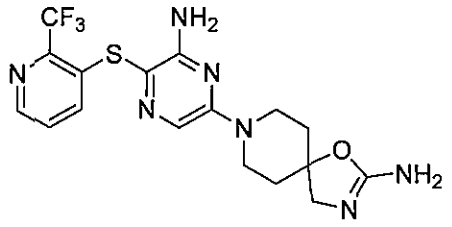
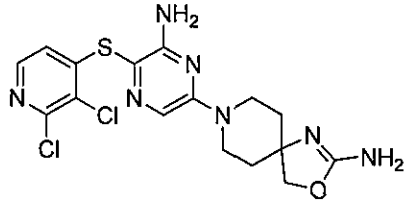
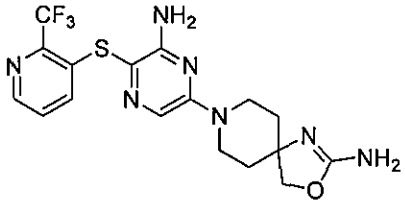
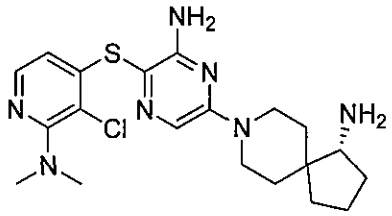
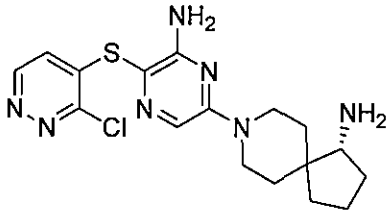
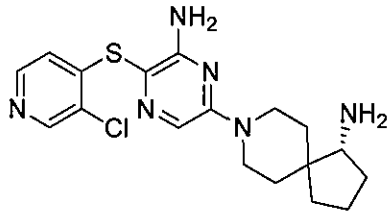
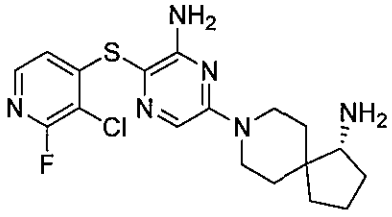
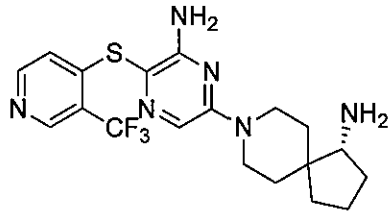
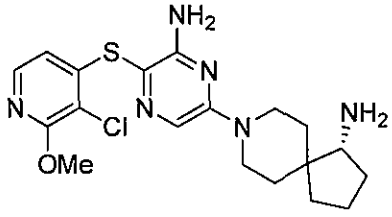
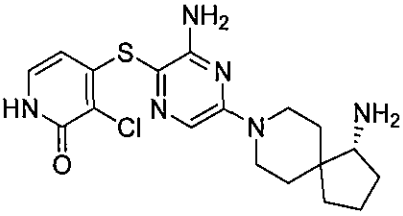
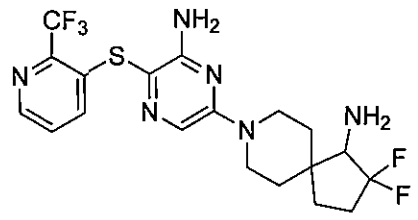
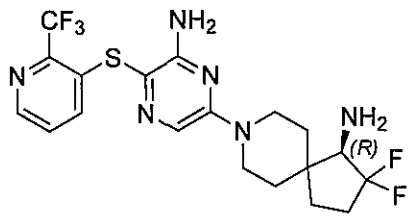
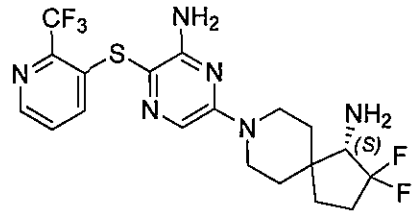
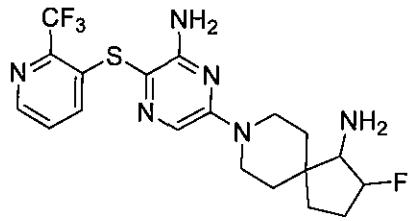
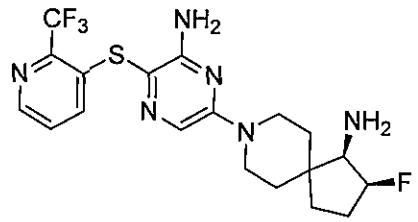
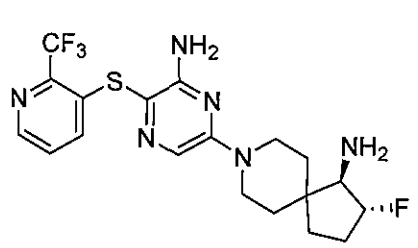
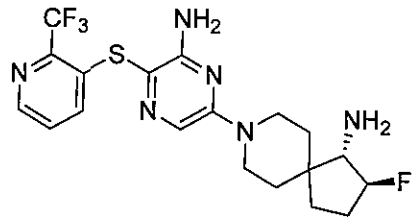
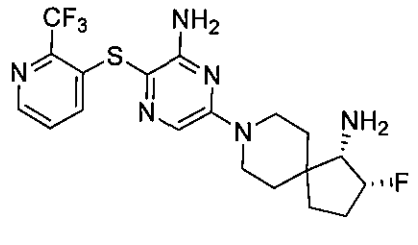
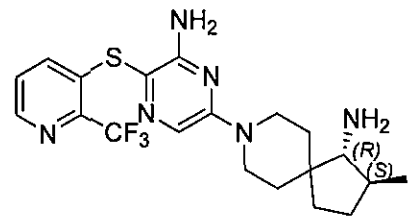
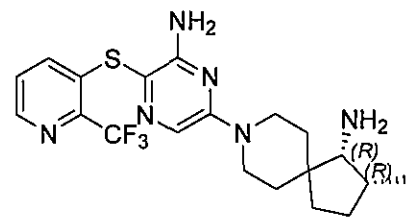
	
	
	 racemic
	

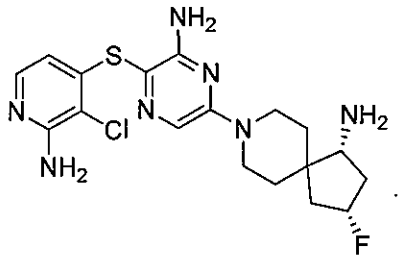
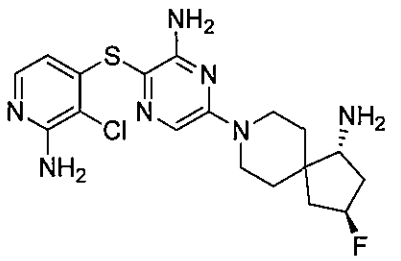
	
	
	
	
	

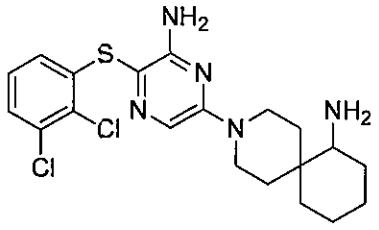
	
	
	
	
	

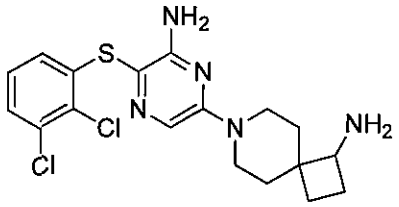
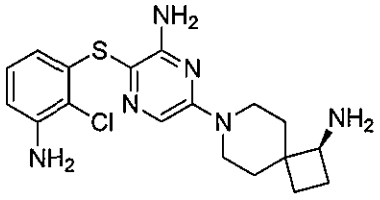
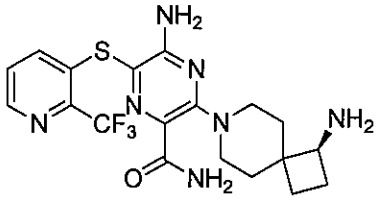
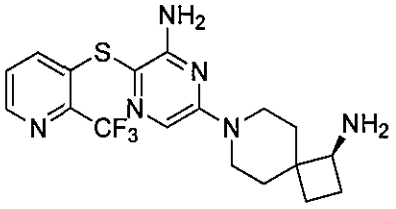
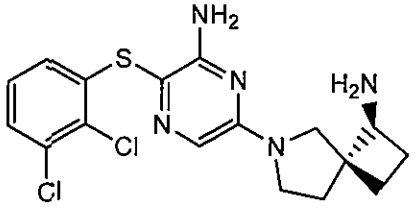
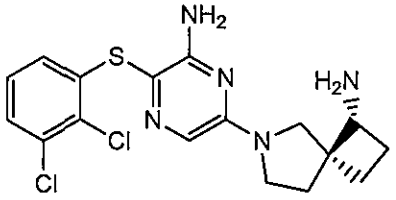
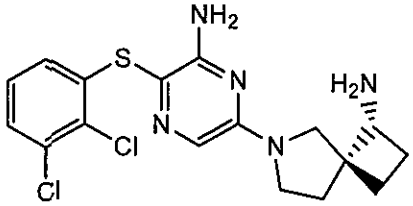
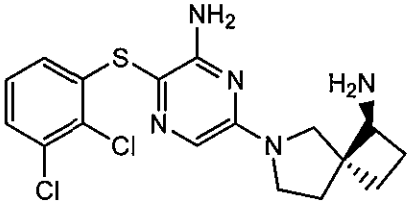
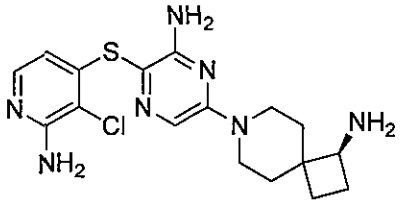
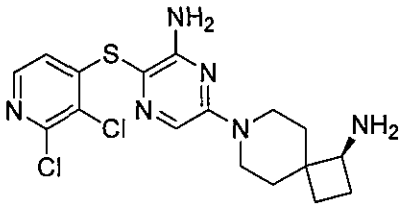
5. The compound of claim 2 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 6 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with amino; or a pharmaceutically acceptable salt thereof.

6. The compound of claim 5, or the pharmaceutically acceptable salt thereof, is:

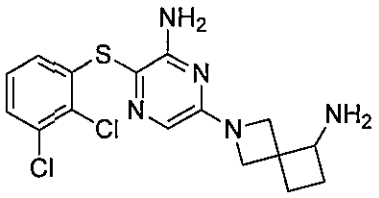
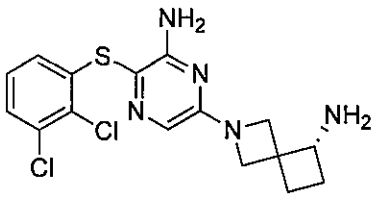
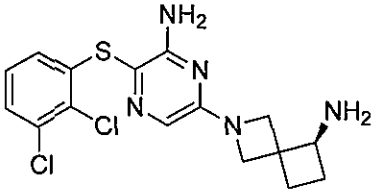
7. The compound of claim 2 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 4 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with group selected from amino, amino-methyl and methyl-amino; or a pharmaceutically acceptable salt thereof.

8. The compound of claim 7, or the pharmaceutically acceptable salt thereof, selected from:

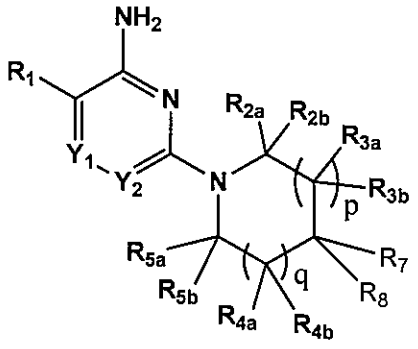
	
	
	
	
	

9. The compound of claim 2 in which p and q are both 0, or the pharmaceutically acceptable salt thereof.

10. The compound of claim 9, or the pharmaceutically acceptable salt thereof, selected from:

11. The compound of claim 1, of formula II:



II

in which:

p is selected from 0 and 1;

q is selected from 0 and 1;

Y_1 is selected from CH and N;

Y_2 is selected from CR_6 and N;

R_1 is selected from C_{6-10}aryl, and a 5-9 member heteroaryl group containing from 1 to 4 N heteroatoms; wherein said aryl or heteroaryl of R_{1a} is substituted with 1 to 5 R_9 groups independently selected from halo, amino, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and -$C(O)NH_2$;

R_{2a} and R_{2b} are hydrogen;

R_{3a} and R_{3b} are hydrogen;

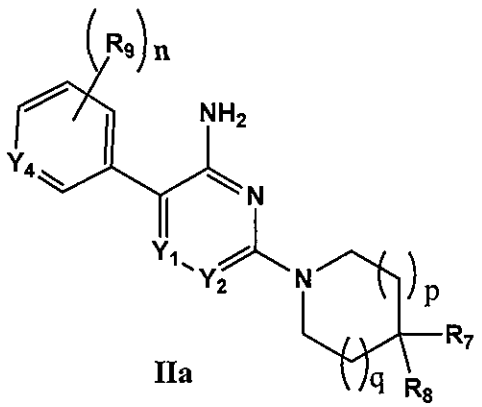
R_{4a} and R_{4b} are hydrogen;

R_{5a} and R_{5b} are hydrogen;

R_6 is selected from hydrogen and amino-carbonyl;

R_7 and R_8 together with the carbon atom to which they are both attached form a 3 to 7 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with a group selected from amino, amino-methyl and methyl-amino; or a pharmaceutically acceptable salt thereof.

12. The compound of claim 11 of Formula IIa:



IIa

in which:

n is selected from 1, 2, 3 and 4;

p is selected from 0 and 1;

q is selected from 0 and 1;

Y_1 is selected from CH and N;

Y_2 is selected from CR_6 and N;

Y_4 is selected from N and CR_9;

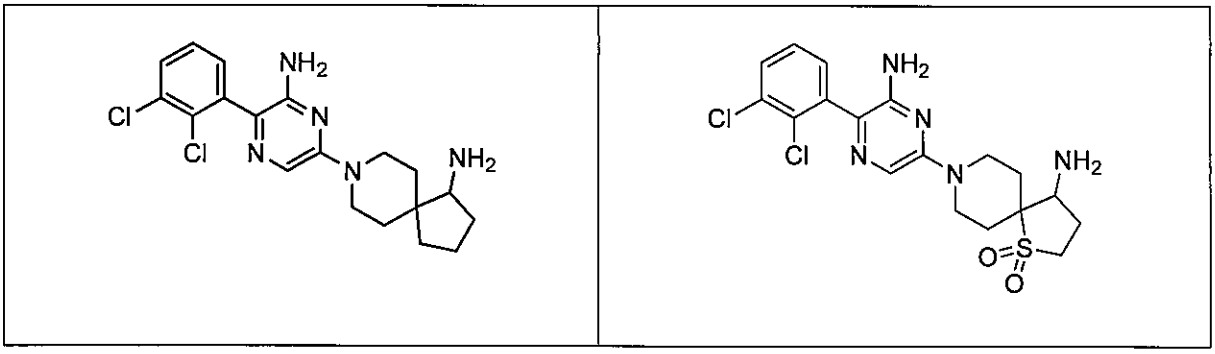
R_6 is selected from hydrogen and amino-carbonyl;

R_7 and R_8 together with the carbon atom to which they are both attached form a 3 to 7 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with a group selected from amino, amino-methyl and methyl-amino;

R_9 is selected from halo, amino, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy, and -$C(O)NH_2$; or a pharmaceutically acceptable salt thereof.

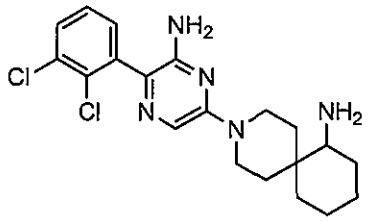
13. The compound of claim 12 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 5 member saturated or partially unsaturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with amino; or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13, or the pharmaceutically acceptable salt thereof, selected from:



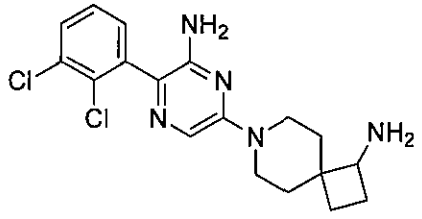
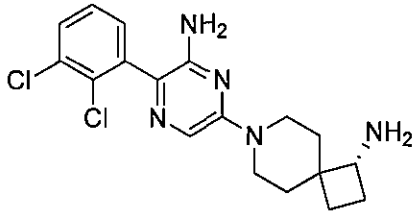
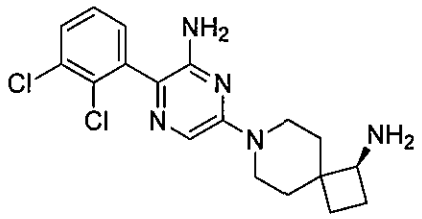
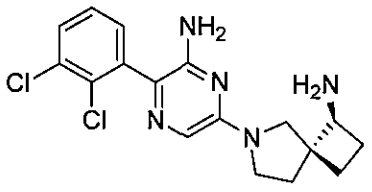
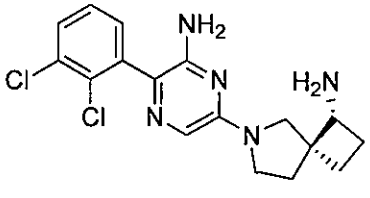
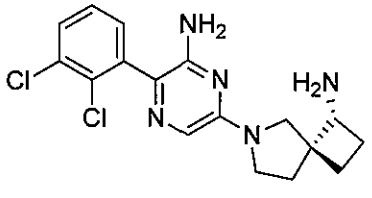
15. The compound of claim 12 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 6 member saturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with amino; or a pharmaceutically acceptable salt thereof.

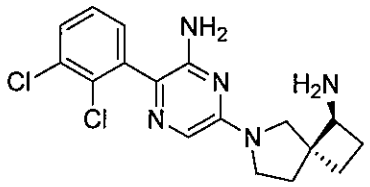
16. The compound of claim 15, or the pharmaceutically acceptable salt thereof, is:

17. The compound of claim 12 in which R_7 and R_8 together with the carbon atom to which they are both attached form a 4 member saturated ring that can optionally contain a heteroatom selected from N, O and $S(O)_m$; wherein m is selected from 0, 1 and 2; wherein said saturated ring formed by R_7 and R_8 is substituted with amino; or a pharmaceutically acceptable salt thereof.

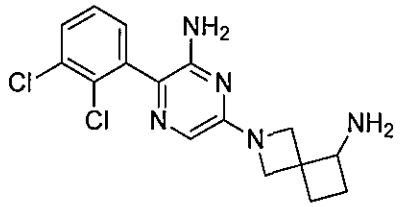
18. The compound of claim 17, or the pharmaceutically acceptable salt thereof, selected from:

19. The compound of claim 12 in which p and q are both 0; or the pharmaceutically acceptable salt thereof.

20. The compound of claim 19, or the pharmaceutically acceptable salt thereof, is:

21. A pharmaceutical composition, comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

22. The use of an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prophylactic or therapeutic treatment of a disease or disorder selected from Noonan Syndrome, Leopard Syndrome, juvenile myelomonocytic leukemias, neuroblastoma, melanoma, acute myeloid leukemia, breast cancer, esophageal cancer, lung cancer, colon cancer, head cancer, neuroblastoma, squamous-cell carcinoma of the head and neck, gastric carcinoma, anaplastic large-cell lymphoma and glioblastoma.