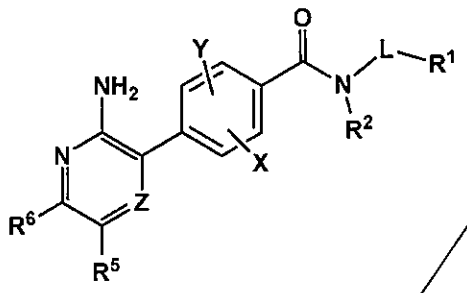
CLAIMS

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is an optionally substituted group selected from C_{3-8} cycloalkyl, 5-8 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S as ring members, phenyl, -SO_2-phenyl, -C(O)-phenyl, -$C(R^8)_2$-phenyl, and 5-6 membered heteroaryl ring, wherein said heterocyclyl and heteroaryl contain 1-2 heteroatoms selected from N, O and S as ring members,

and wherein the optional substituents for R^1 are 1-3 groups independently selected from D, halo, hydroxy, amino, -$N(R^8)_2$, CN, C_{1-4} alkyl, C_{1-4} alkoxy, -$S(C_{1-4}$ alkyl), C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, 3-6 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, oxo (except on aromatic rings), CN, $COOR^8$, $CON(R^8)_2$, -NR^8-C(O)R^8, -NR^8-C(O)OR^8 -SO_2R^8, -$NR^8SO_2R^8$, and $SO_2N(R^8)_2$, where each R^8 is independently H or C_{1-4} alkyl;

L is a bond, or L can be a C_{1-4} alkylene, C_{2-4} alkenylene, C_{1-4} alkynylene, C_{3-6} cycloalkyl or a 4-7 membered heterocycloyl containing 1-2 heteroatoms selected from N, O and S as ring members, wherein L is optionally substituted with 1-3 groups independently selected from R^{11}, D, OH, NH_2, -NHR^{11}, -NHC(=O)R^{11}, -NHC(=O)-OR^{11}, -NHC(=O)-NH_2, -NHC(=O)-NHR^{11}, -$N(R^{11})_2$, CN, halo, N_3, $CON(R^7)_2$, and $COOR^7$; where each R^{11} is independently C_{1-4} alkyl, which may be substituted with up to three groups

independently selected from D, halo, OH, NH_2,-NHMe, -NMe_2, -OP(O)$(OH)_2$ and O-C_{1-4} alkyl;

X and Y are independently selected from H, D, halo, CN, amino, hydroxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

R^2 is H, C_{1-4} alkyl, or aryl-C_{1-2}-alkyl-, wherein the aryl and C_{1-4} alkyl are optionally substituted with halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, or C_{1-4} alkylsulfonyl;

or R^2 can cyclize with X to form a 5-7 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S fused to the phenyl ring to which X is attached,

or R^2 can cyclize with L to form a 5-7 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S,

wherein the optional heterocyclic ring formed by R^2 cyclizing with X, or by R^2 cyclizing with L, can be optionally substituted with one or two groups independently selected from CN, halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, oxo, CN, $COOR^7$, $CON(R^7)_2$, and -SO_2R^7;

each R^7 is independently H or C_{1-4} alkyl;

Z is N or CR^4;

R^4 is H, D, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy;

R^5 is selected from –C(O)-R^{5a} and R^{5a}; wherein R^{5a} is an optionally substituted C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, saturated or unsaturated 3-8 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S, phenyl, or 5-6 membered heteroaryl ring containing 1-3 heteroatoms selected from N, O and S, wherein the optional substituents for R^5 are 1-4 groups independently selected from D, halo, hydroxy, amino, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, 3-6 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, oxo (except on aromatic rings), CN, -$COOR^9$, -$C(O)R^9$, $CON(R^9)_2$, -$NR^9C(O)R^9$, -$NR^9CO_2R^9$, -SO_2R^9, -$NR^9SO_2R^9$, and -$SO_2N(R^9)_2$, where each R^9 is independently H or C_{1-4} alkyl optionally substituted with 1-3 groups independently selected from D, halo, OH,

NH_2, NHMe and NMe_2; and two substituents on the same or adjacent carbon atoms of R^5 can optionally be taken together to form a 5-6 membered ring that can be saturated or aromatic and contains 1-2 heteroatoms selected from N, O and S and can optionally be substituted with 1-2 groups independently selected from D, Me, halo, OH, oxo, $O(C_{1-4}$ alkyl), NH_2, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino; and

R^6 is H, D, halo, C_{1-4} alkyl, or C_{1-4} haloalkyl.

2. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein Z is N.

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein Z is CH.

4. The compound according to any of claims 1-3 or a pharmaceutically acceptable salt thereof, wherein R^2 is H or Me.

5. The compound according to any one of claims 1 to 4 or a pharmaceutically acceptable salt thereof, wherein R^6 is H.

6. The compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is selected from C_{3-8} cycloalkyl, 5-8 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, phenyl, and 5-6 membered heteroaryl, and is optionally substituted with 1-3 groups independently selected from D, halo, CN, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, $-SO_2R'$, $-N(R')_2$, $-NR'-C(O)-R'$, and $-SO_2NR'_2$, where each R' is independently H or C_{1-4} alkyl.

7. The compound according to any of claims 1-6, wherein R^5 is selected from –C(O)-R^{5a} and R^{5a}; wherein R^{5a} is selected from phenyl, pyridine, pyridone, pyrazine, pyridazine, pyrazole, triazole, tetrazole, thiazole, oxazole, imidazole, isothiazole, isoxazole, furan, and thiophene, each of which is optionally substituted with one or two groups independently selected from halo, D, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, CN, $COOR^9$, $CON(R^9)_2$, and $-SO_2R^9$, where each R^9 is independently H or C_{1-4} alkyl

8. The compound of claim 3 or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from –C(O)-R^{5a} and R^{5a}; wherein R^{5a} is C_{5-6} heteroaryl containing at least one N as a ring member, which is optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

9. The compound of claim 8 or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from –C(O)-R^{5a} and R^{5a}; wherein R^{5a} is pyrazole or triazole and is optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

10. The compound according to any of claims 1-6, wherein R^5 is selected from –C(O)-R^{5a} and R^{5a}; wherein R^{5a} is selected from cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, tetrahydropyran, dihydropyran, tetrahydrofuran, oxetane, azetidine, pyrrolidine, piperidine, piperazine, morpholine, tetrahydrothiopyran (thiacyclohexane), and tetrahydrothiofuran (thiacyclopentane), each of which is optionally substituted with 1-3 groups independently selected from halo, D, CN, $N(R^9)_2$, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, oxo, CN, $COOR^9$, $CON(R^9)_2$, $-NHC(O)R^9$, $-NHCOOR^9$, $-NHSO_2R^9$, and $-SO_2R^9$, where each R^9 is independently H or C_{1-4} alkyl.

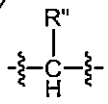
11. The compound of any of claims 1-10, wherein R^1 is phenyl and is optionally substituted with one to three groups independently selected from halo, D, CN, C_{1-4} alkoxy,

C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, SR', $-SO_2R'$, $-N(R')_2$, -NR'-C(O)-R', and $-SO_2NR'_2$, where each R' is independently H, C_{1-4} alkyl or C_{1-4} haloalkyl.

12. The compound of any of claims 1-10, wherein R^1 is thiophene, thiazole, pyridine, pyrimidine, pyrazine or pyridazine, and is optionally substituted with up to three groups independently selected from halo, CN, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-SO_2R'$, $-N(R')_2$, -NR'-C(O)-R', and $-SO_2NR'_2$, where each R' is independently H or C_{1-4} alkyl.

13. The compound according to any of claims 1 to 12 or a pharmaceutically acceptable salt thereof, wherein L is selected from the group consisting of: cyclopropane-1,1-diyl; cyclopropane-1,2-diyl; and –CHR"-, wherein R" is H, D, or C_{1-2} alkyl optionally substituted with up to three groups independently selected from D, hydroxy, halo, amino, C_{1-2} alkylamino, di(C_{1-2} alkyl)amino, and C_{1-2} alkoxy.

14. The compound of claim 13, wherein L is



wherein R" is methyl or ethyl, and is optionally substituted with fluoro, amino, hydroxy, methylamino, ethylamino, dimethylamino, $-OP(O)(OH)_2$, methoxy or ethoxy.

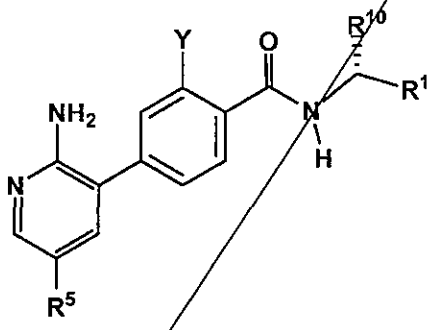
15. The compound according to any of claims 1 to 14 or a pharmaceutically acceptable salt thereof, wherein R^2 and L are linked together to form a heterocyclic group selected from morpholine, piperidine, thiomorpholine, piperazine, and pyrrolidine that is attached to R^1 and is also optionally substituted with one or two groups independently

selected from C_{1-4} alkyl, C_{1-4} alkoxy, oxo, CN, $COOR^7$, $CON(R^7)_2$, and $-SO_2R^7$, where each R^7 is independently H or C_{1-4} alkyl.

16. The compound of any of claims 1-15, wherein Y is H, methyl, or halo.

17. The compound of any of claims 1-16, wherein X is H, or R^2 cyclizes with X to form a 5-7 membered heterocyclic ring fused to the phenyl ring to which X is attached.

18. The compound of claim 1, which is of the Formula IA:



(IA)

wherein R^5 is pyrazole, imidazole, isoxazole, isothiazole, oxazole, triazole, or thiazole, which can be substituted with up to two groups independently selected from D, F, Cl, CN, Me, OMe, Et, iPr, OEt, and CF_3;

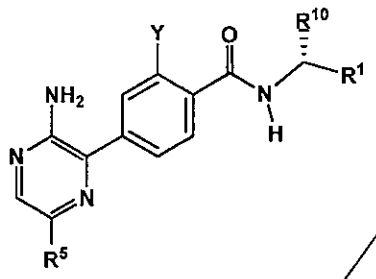
Y is H, F, Cl, or Me;

R^{10} is H or $-CH_2-R^*$, where R* is H, -OH, F, $-NH_2$, -NHMe, $-NMe_2$, $-OP(O)(OH)_2$, or –OMe; and

R^1 is phenyl or thienyl, optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN, $COOR^8$, $CON(R^8)_2$, -SMe, and $-SO_2R^8$, where each R^8 is independently H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt thereof.

19. The compound of claim 1, which is of the Formula IB:



(IB)

wherein R^5 is a 4-7 membered cyclic ether or C_{5-6} cycloalkyl, and R^5 can be substituted with up to four groups independently selected from D, F, Cl, CN, amino, NHMe, NMe_2, -CH_2OH, -NHC(O)Me, -$NHCOOMe$, -$NHSO_2Me$, Me Et, OMe, OH, oxo, Et, iPr, OEt, CN, and CF_3;

Y is H, F, Cl, or Me;

R^{10} is H or $-CH_2-R^*$, where R^* is H, -OH, F, -NH_2, -NHMe, -$OP(O)(OH)_2$, -NMe_2, or –OMe; and

R^1 is phenyl, optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN, $COOR^8$, $CON(R^8)_2$, and -SO_2R^8, where each R^8 is independently H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt thereof.

20. The compound of any one of claims 1-6 or 19, wherein R^5 is cyclohexyl substituted with 1-3 groups groups independently selected from D, F, Cl, CN, amino, NHMe, NMe_2, Me, $NHSO_2Me$, NHCOMe, OMe, OH, Et, CN, -CH_2OH, and CF_3.

21. The compound of any one of claims 1-6 or 19, wherein R^5 is tetrahydropyranyl.

22. The compound of any one of claims 1-20, wherein R^1 is phenyl substituted with 0, 1 or 2 groups independently selected from F, Cl, Br, I, SMe, SO_2Me, and CH_3.

23. The compound of claim 1, which is selected from the group consisting of the compounds of Examples 1-478 and pharmaceutically acceptable salts thereof.

24. A pharmaceutical composition comprising a compound according to any one of claims 1-23 admixed with at least one pharmaceutically acceptable excipient.

25. The pharmaceutical composition of claim 24, further comprising a therapeutic co-agent.

26. The pharmaceutical composition of claim 25, wherein the therapeutic co-agent is selected from anticancer compounds, analgesics, and anti-inflammatory compounds.

27. A method to treat cancer, comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound according to any of claims 1-23 or a pharmaceutical composition of any of claims 24-26.

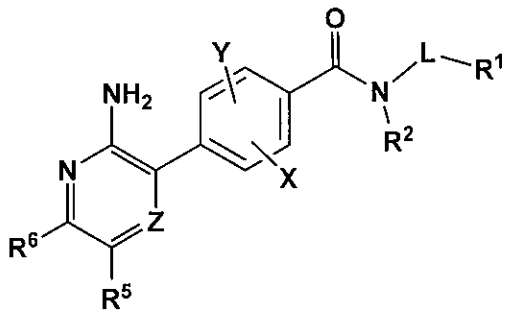
28. The method of claim 27, wherein the cancer is selected from adenoma, bladder cancer, brain cancer, breast cancer, cervical cancer, colorectal cancer, colon cancer, epidermal carcinoma, follicular carcinoma, genitourinary cancers, glioblastoma, head and neck cancers, Hodgkin's disease, non-Hodgkin's lymphoma, hepatoma, kidney cancer, lung cancers such as small cell or non-small cell lung cancer, leukemias such as AML or CML, multiple myeloma, lymphoid disorders, skin cancers including melanoma, neuroblastoma, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, sarcoma, testicular cancer, and thyroid cancer.

29. A compound according to any one of claims 1-23 for use as a medicament.

30. Use of a compound according to any one of claims 1 to 23 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cancer.

Claims:

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is an optionally substituted group selected from C_{3-8} cycloalkyl, 5-8 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S as ring members, phenyl, -SO_2-phenyl, -C(O)-phenyl, -$C(R^8)_2$-phenyl, and 5-6 membered heteroaryl ring, wherein said heterocyclyl and heteroaryl contain 1-2 heteroatoms selected from N, O and S as ring members,

and wherein the optional substituents for R^1 are 1-3 groups independently selected from D, halo, hydroxy, amino, -$N(R^8)_2$, CN, C_{1-4} alkyl, C_{1-4} alkoxy, -$S(C_{1-4}$ alkyl), C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, 3-6 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, oxo (except on aromatic rings), CN, $COOR^8$, $CON(R^8)_2$, -NR^8-C(O)R^8, -NR^8-C(O)OR^8 -SO_2R^8, -$NR^8SO_2R^8$, and $SO_2N(R^8)_2$, where each R^8 is independently H or C_{1-4} alkyl;

L is a bond, or L is selected from C_{1-4} alkylene, C_{2-4} alkenylene, C_{1-4} alkynylene, C_{3-6} cycloalkyl or a 4-7 membered heterocycloyl containing 1-2 heteroatoms selected from N, O and S as ring members, wherein L is optionally substituted with 1-3 groups independently selected from R^{11}, D, OH, NH_2, -NHR^{11}, -NHC(=O)R^{11}, -NHC(=O)-OR^{11}, -NHC(=O)-NH_2, -NHC(=O)-NHR^{11}, -$N(R^{11})_2$, CN, halo, N_3, $CON(R^7)_2$, and $COOR^7$; where each R^{11} is independently C_{1-4} alkyl, which may be substituted with up to three groups independently selected from D, halo, OH, NH_2,-NHMe, -NMe_2, -OP(O)$(OH)_2$ and O-C_{1-4} alkyl;

X and Y are independently selected from H, D, halo, CN, amino, hydroxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy;

R^2 is H, C_{1-4} alkyl, or aryl-C_{1-2}-alkyl-, wherein the aryl and C_{1-4} alkyl are optionally substituted with halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, or C_{1-4} alkylsulfonyl;

or R^2 can cyclize with X to form a 5-7 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S fused to the phenyl ring to which X is attached,

or R^2 can cyclize with L to form a 5-7 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S,

wherein the optional heterocyclic ring formed by R^2 cyclizing with X, or by R^2 cyclizing with L, can be optionally substituted with one or two groups independently selected from CN, halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, oxo, CN, $COOR^7$, $CON(R^7)_2$, and $-SO_2R^7$;

each R^7 is independently H or C_{1-4} alkyl;

Z is N or CR^4;

R^4 is H, D, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy;

R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is an optionally substituted C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, saturated or unsaturated 3-8 membered heterocyclic ring containing 1-2 heteroatoms selected from N, O and S, phenyl, or 5-6 membered heteroaryl ring containing 1-3 heteroatoms selected from N, O and S, wherein the optional substituents for R^5 are 1-4 groups independently selected from D, halo, hydroxy, amino, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, C_{3-6} cycloalkyl, 3-6 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, oxo (except on aromatic rings), CN, $-COOR^9$, $-C(O)R^9$, $CON(R^9)_2$, $-NR^9C(O)R^9$, $-NR^9CO_2R^9$, $-SO_2R^9$, $-NR^9SO_2R^9$, and $-SO_2N(R^9)_2$, where each R^9 is independently H or C_{1-4} alkyl optionally substituted with 1-3 groups independently selected from D, halo, OH, NH_2, NHMe and NMe_2; and two substituents on the same or adjacent carbon atoms of R^5 can optionally be taken together to form a 5-6 membered ring that can be saturated or aromatic and contains 1-2 heteroatoms selected from N, O and S and can optionally be substituted with 1-2 groups independently selected from D, Me, halo, OH, oxo, $O(C_{1-4}$ alkyl), NH_2, C_{1-4} alkylamino, $di(C_{1-4}$ alkyl)amino; and

R^6 is H, D, halo, C_{1-4} alkyl, or C_{1-4} haloalkyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

Z is N or CH;

R^2 is H or Me;

R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is selected from C_{3-8} cycloalkyl, 5-8 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S, phenyl, and 5-6 membered heteroaryl, and is optionally substituted with 1-3 groups independently selected from D, halo, CN, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, $-SO_2R'$, $-N(R')_2$, $-NR'-C(O)-R'$, and $-SO_2NR'_2$, where each R' is independently H or C_{1-4} alkyl; and

R^6 is H.

3. The compound of claim 2, wherein R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is selected from phenyl, pyridine, pyridone, pyrazine, pyridazine, pyrazole, triazole, tetrazole, thiazole, oxazole, imidazole, isothiazole, isoxazole, furan, and thiophene, each of which is optionally substituted with one or two groups independently selected from halo, D, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, CN, $COOR^9$, $CON(R^9)_2$, and $-SO_2R^9$, where each R^9 is independently H or C_{1-4} alkyl.

4. The compound of claim 3 or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is pyrazole or triazole and is optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} alkoxy, and C_{1-4} haloalkoxy.

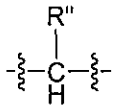
5. The compound of claim 2, wherein R^5 is selected from $-C(O)-R^{5a}$ and R^{5a}; wherein R^{5a} is selected from cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, tetrahydropyran, dihydropyran, tetrahydrofuran, oxetane, azetidine, pyrrolidine, piperidine, piperazine, morpholine, tetrahydrothiopyran (thiacyclohexane), and tetrahydrothiofuran (thiacyclopentane), each of which is optionally substituted with 1-3 groups independently selected from halo, D, CN, $N(R^9)_2$, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, C_{1-4} haloalkoxy, oxo, CN, $COOR^9$, $CON(R^9)_2$, $-NHC(O)R^9$, $-NHCOOR^9$, $-NHSO_2R^9$, and $-SO_2R^9$, where each R^9 is independently H or C_{1-4} alkyl.

6. The compound of claim 2, wherein R^1 is phenyl and is optionally substituted with one to three groups independently selected from halo, D, CN, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, SR', $-SO_2R'$, $-N(R')_2$, -NR'-C(O)-R', and $-SO_2NR'_2$, where each R' is independently H, C_{1-4} alkyl or C_{1-4} haloalkyl.

7. The compound of claim 2, wherein R^1 is thiophene, thiazole, pyridine, pyrimidine, pyrazine or pyridazine, and is optionally substituted with up to three groups independently selected from halo, CN, C_{1-4} alkoxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-SO_2R'$, $-N(R')_2$, -NR'-C(O)-R', and $-SO_2NR'_2$, where each R' is independently H or C_{1-4} alkyl.

8. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein L is selected from the group consisting of: cyclopropane-1,1-diyl; cyclopropane-1,2-diyl; and –CHR"-, wherein R" is H, D, or C_{1-2} alkyl optionally substituted with up to three groups independently selected from D, hydroxy, halo, amino, C_{1-2} alkylamino, di(C_{1-2} alkyl)amino, and C_{1-2} alkoxy.

9. The compound of claim 8, wherein L is



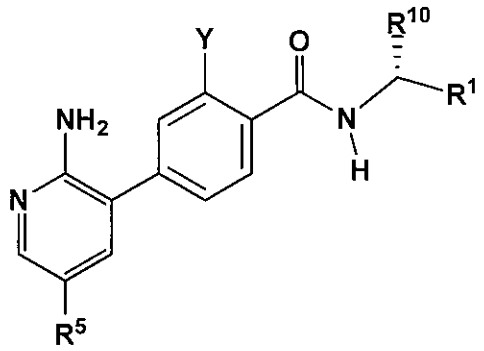
wherein R" is methyl or ethyl, and is optionally substituted with fluoro, amino, hydroxy, methylamino, ethylamino, dimethylamino, $-OP(O)(OH)_2$, methoxy or ethoxy.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 and L are linked together to form a heterocyclic group selected from morpholine, piperidine, thiomorpholine, piperazine, and pyrrolidine that is attached to R^1 and is also optionally substituted with one or two groups independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, oxo, CN, $COOR^7$, $CON(R^7)_2$, and $-SO_2R^7$, where each R^7 is independently H or C_{1-4} alkyl.

11. The compound of claim 1, wherein Y is H, methyl, or halo.

12. The compound of claim 1, wherein X is H, or R^2 cyclizes with X to form a 5-7 membered heterocyclic ring fused to the phenyl ring to which X is attached.

13. The compound of claim 1, which is of the Formula IA:



(IA)

wherein R^5 is pyrazole, imidazole, isoxazole, isothiazole, oxazole, triazole, or thiazole, which can be substituted with up to two groups independently selected from D, F, Cl, CN, Me, OMe, Et, iPr, OEt, and CF_3;

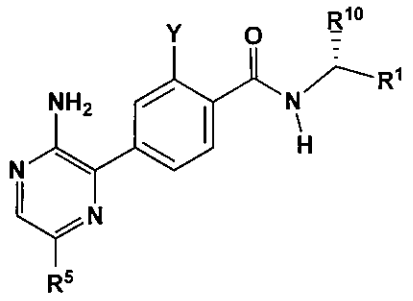
Y is H, F, Cl, or Me;

R^{10} is H or $-CH_2$-R*, where R* is H, -OH, F, $-NH_2$, -NHMe, $-NMe_2$, $-OP(O)(OH)_2$, or –OMe; and

R^1 is phenyl or thienyl, optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN, $COOR^8$, $CON(R^8)_2$, -SMe, and $-SO_2R^8$, where each R^8 is independently H or C_{1-4} alkyl;

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1, which is of the Formula IB:



(IB)

wherein R^5 is a 4-7 membered cyclic ether or C_{5-6} cycloalkyl, and R^5 can be substituted with up to four groups independently selected from D, F, Cl, CN, amino, NHMe, NMe_2, $-CH_2OH$, -NHC(O)Me, -NHCOOMe, $-NHSO_2Me$, Me Et, OMe, OH, oxo, Et, iPr, OEt, CN, and CF_3;

Y is H, F, Cl, or Me;

R^{10} is H or $-CH_2-R^*$, where R* is H, -OH, F, $-NH_2$, -NHMe, $-OP(O)(OH)_2$, $-NMe_2$, or –OMe; and

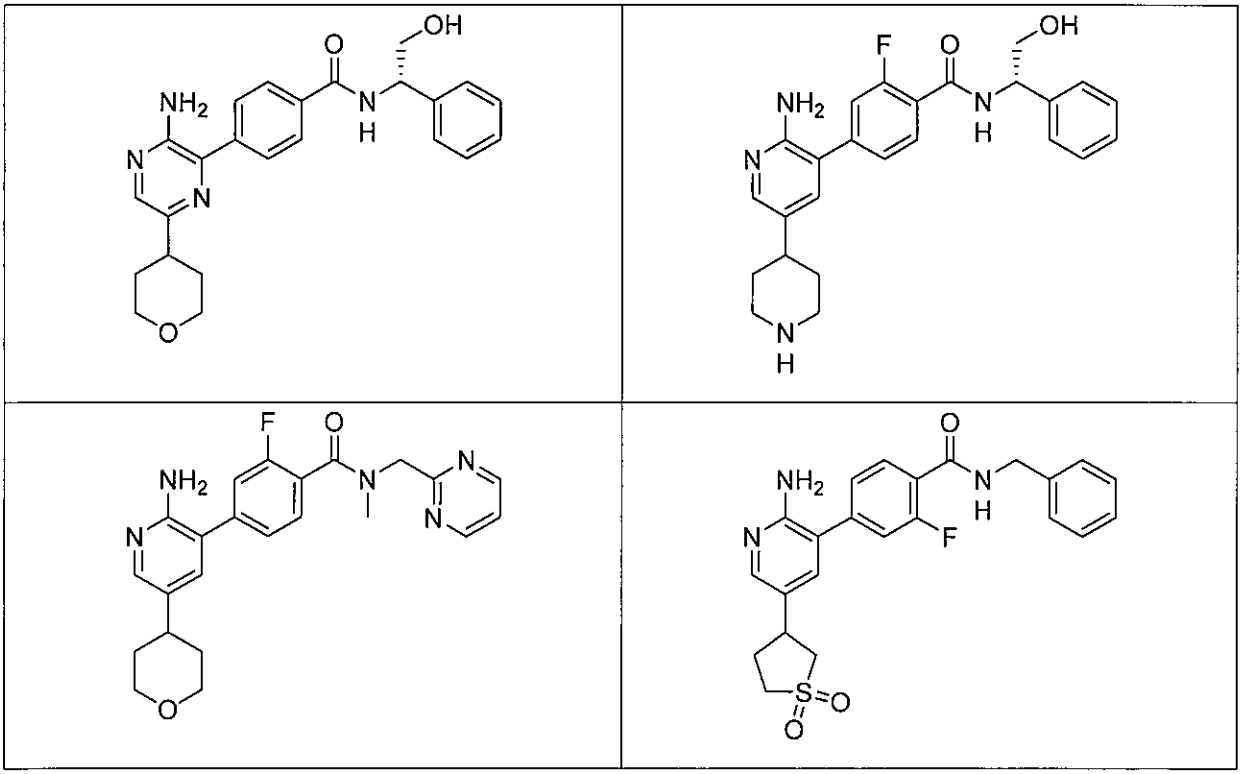
R^1 is phenyl, optionally substituted with 1-2 groups independently selected from halo, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN, $COOR^8$, $CON(R^8)_2$, and $-SO_2R^8$, where each R^8 is independently H or C_{1-4} alkyl;

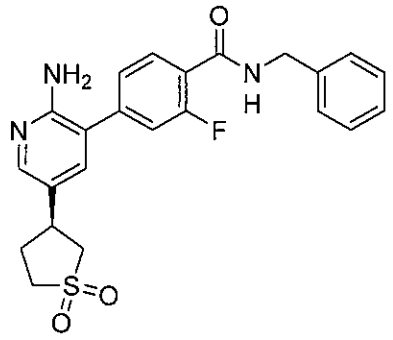
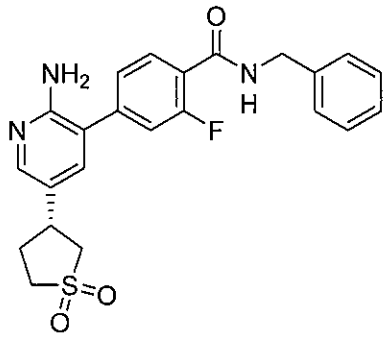
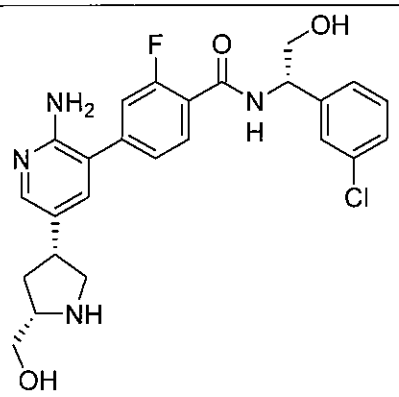
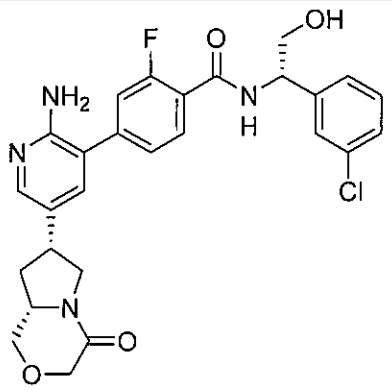
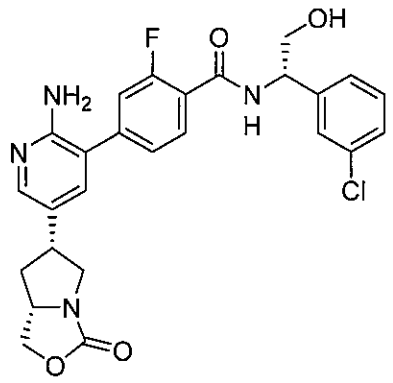
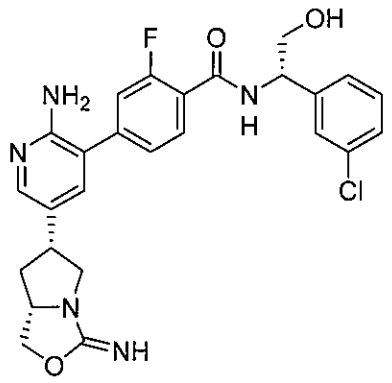
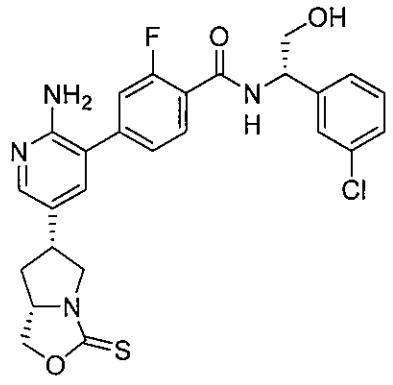
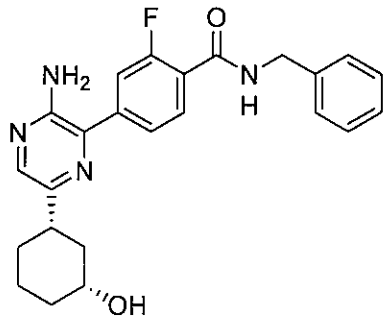
or a pharmaceutically acceptable salt thereof.

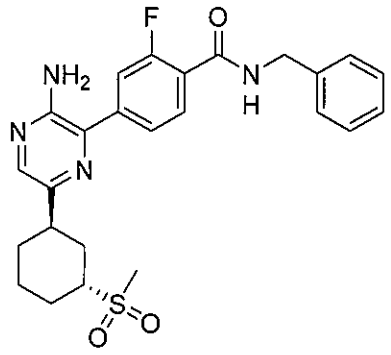
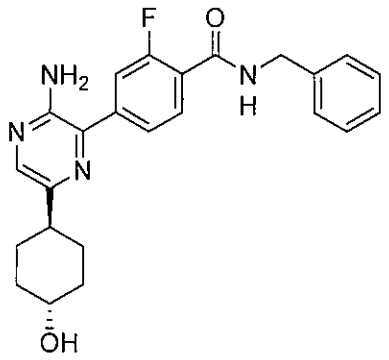
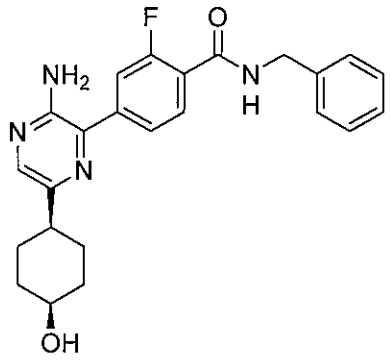
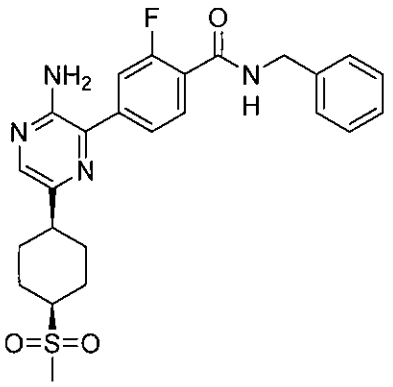
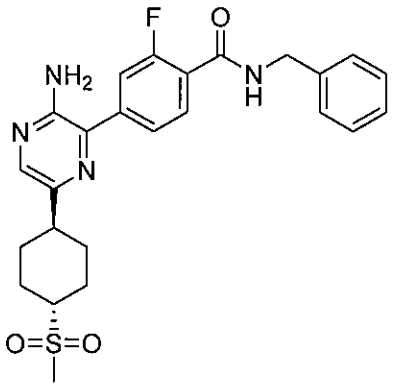
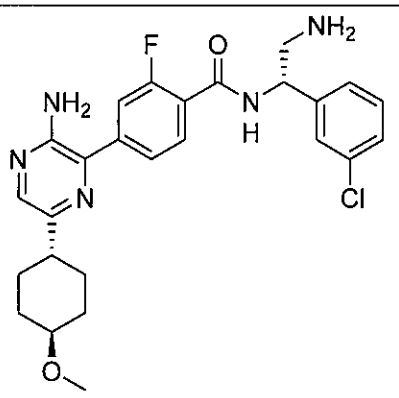
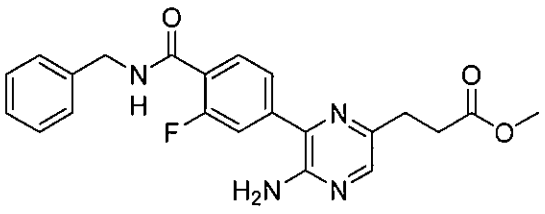
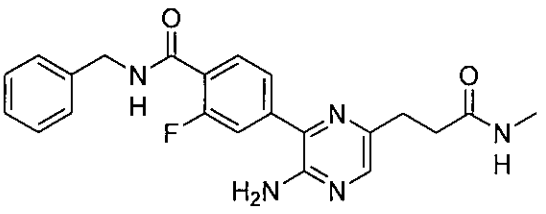
15. The compound of claim 14, wherein R^5 is cyclohexyl substituted with 1-3 groups independently selected from D, F, Cl, CN, amino, NHMe, NMe_2, Me, $NHSO_2Me$, NHCOMe, OMe, OH, Et, CN, $-CH_2OH$, and CF_3.

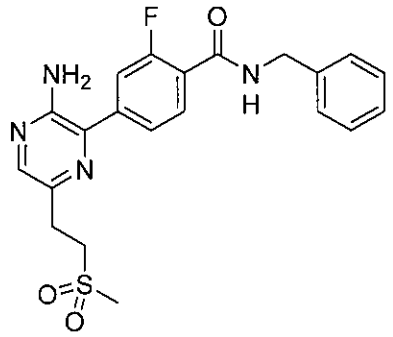
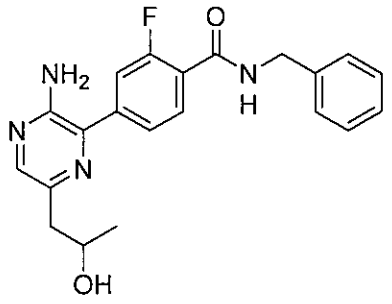
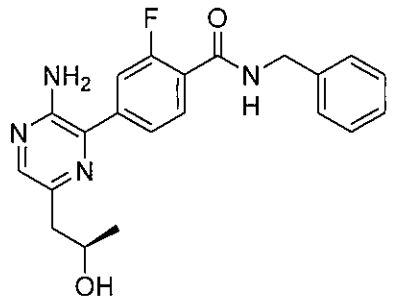
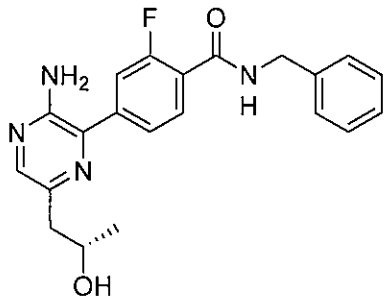
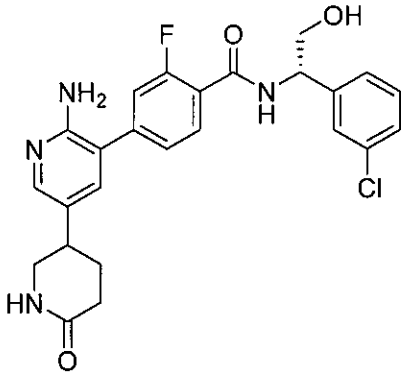
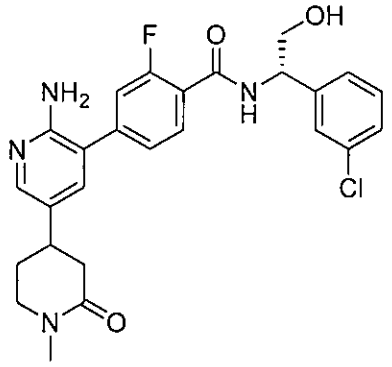
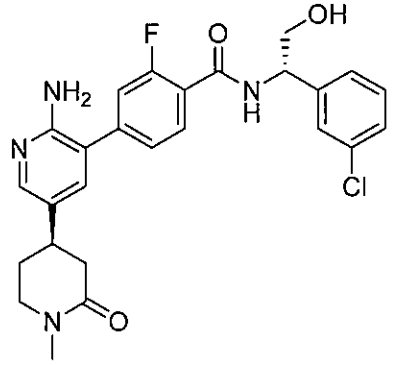
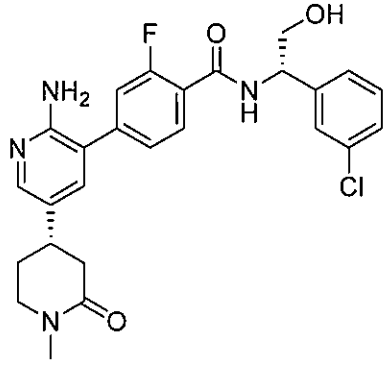
16. The compound of claim 14, wherein R^1 is phenyl substituted with 0, 1 or 2 groups independently selected from F, Cl, Br, I, SMe, SO_2Me, and CH_3.

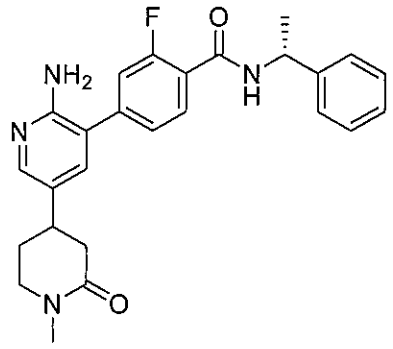
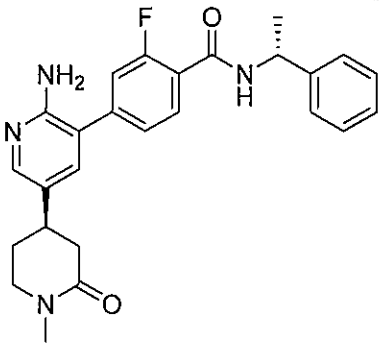
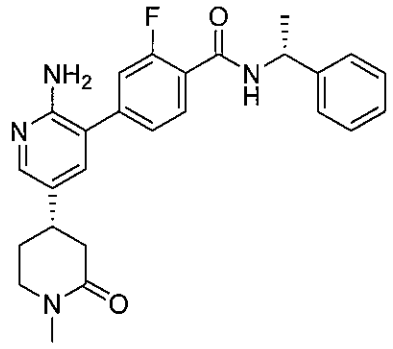
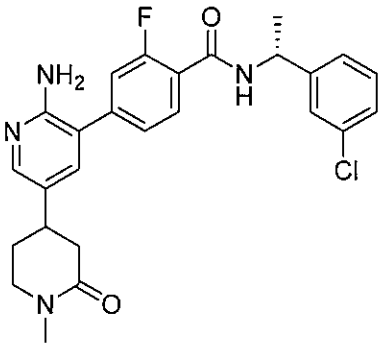
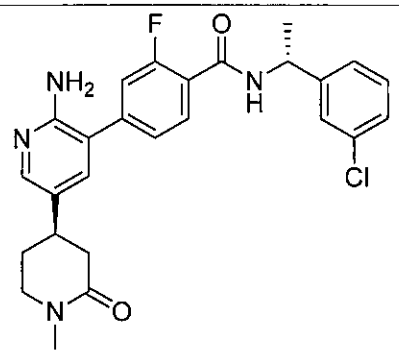
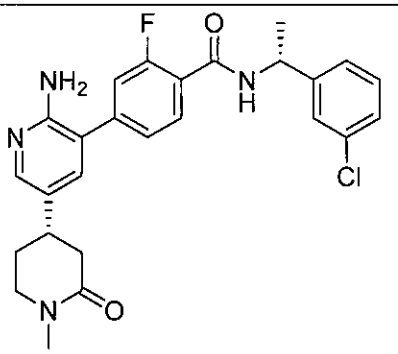
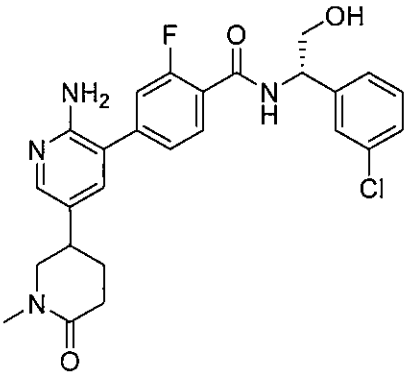
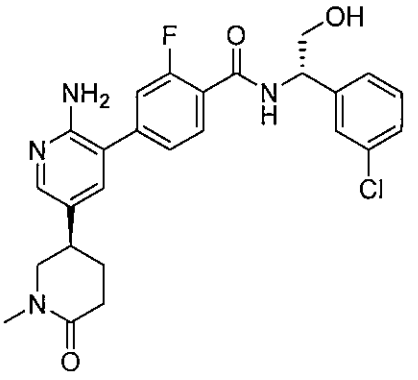
17. A compound, or a pharmaceutically acceptable salt thereof, selected from:

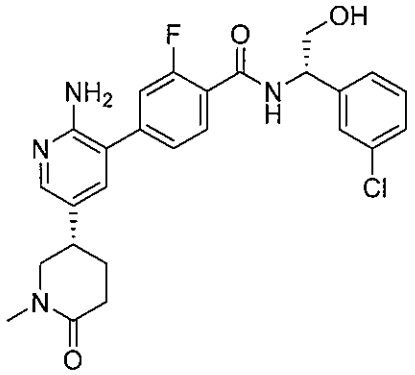
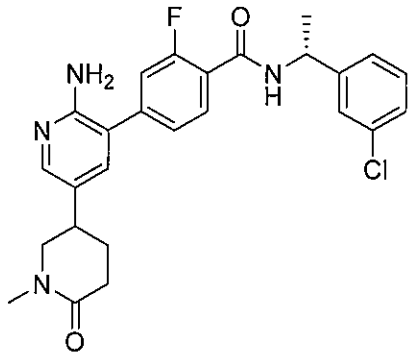
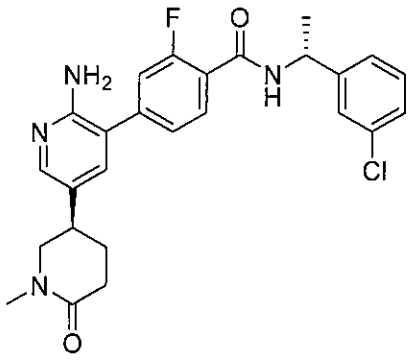
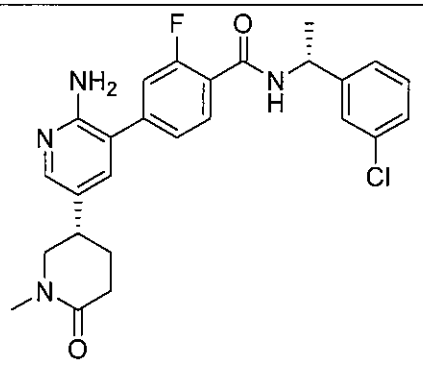
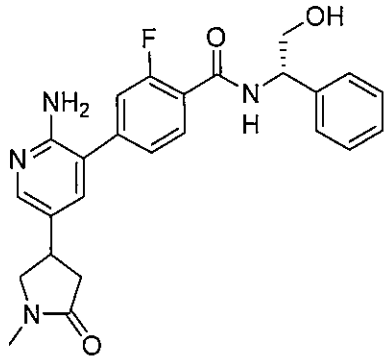
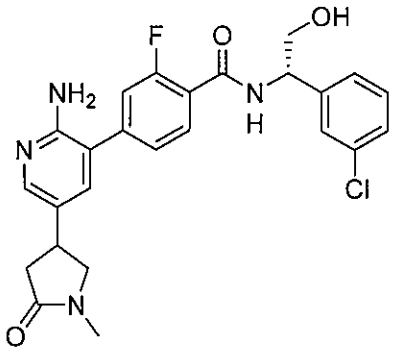
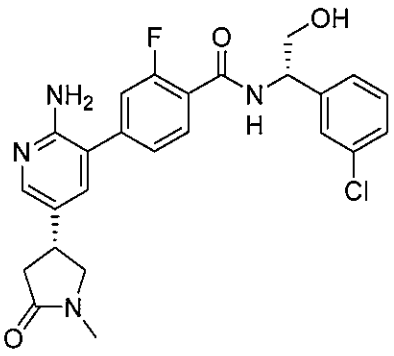
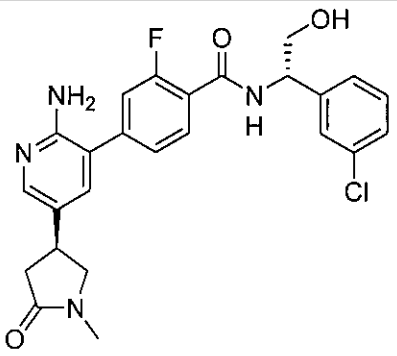


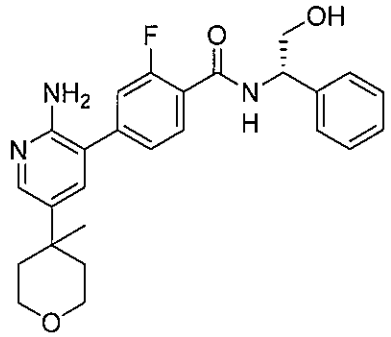
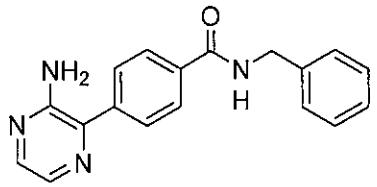
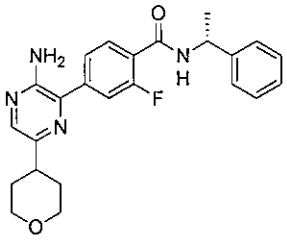
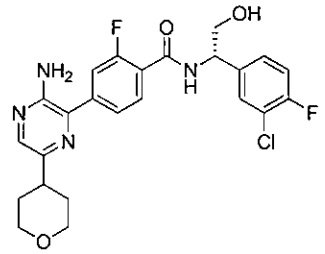
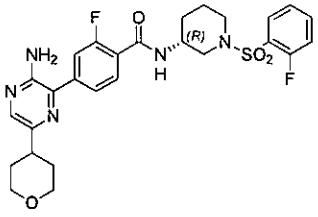
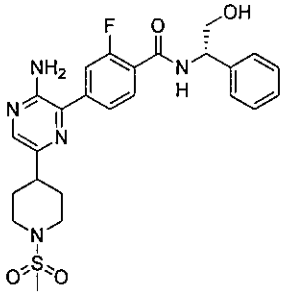
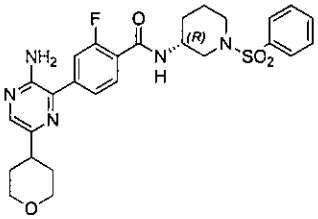
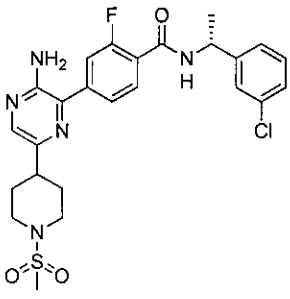
	
	
	
	

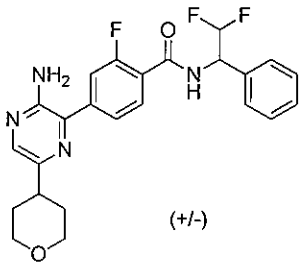
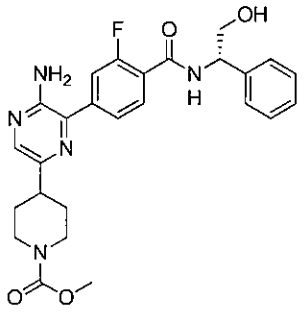
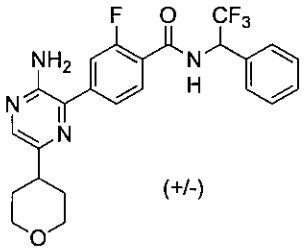
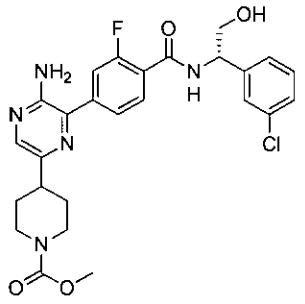
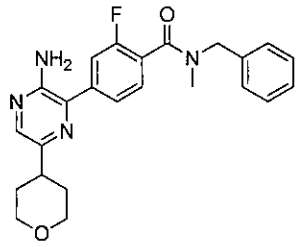
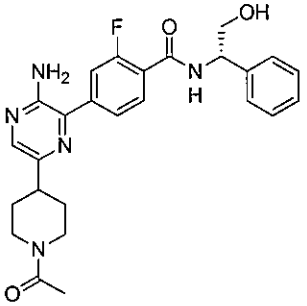
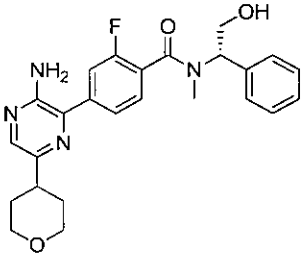
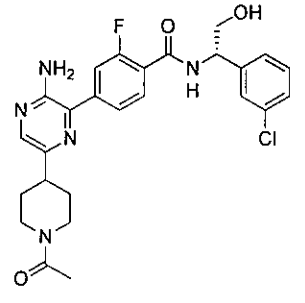
	
	
	
	

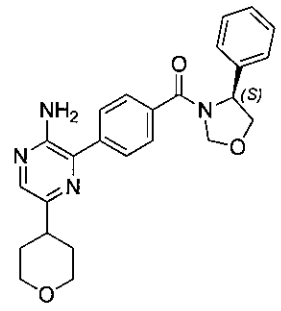
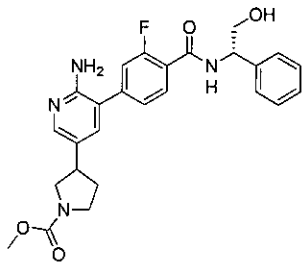
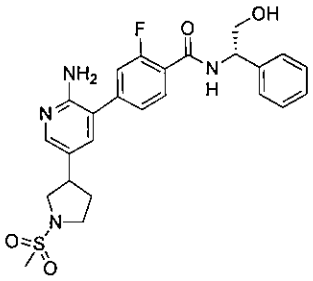
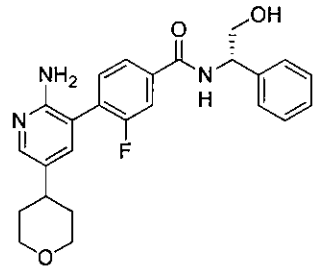
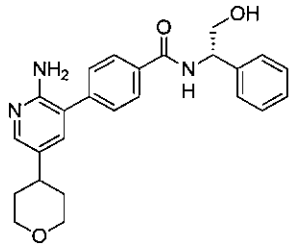
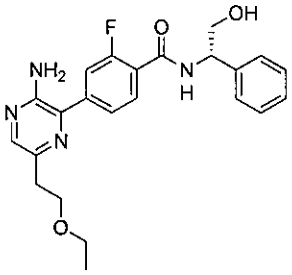
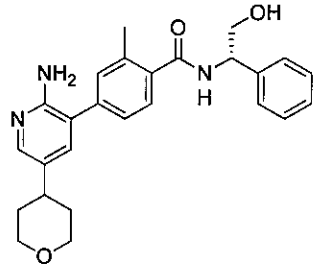
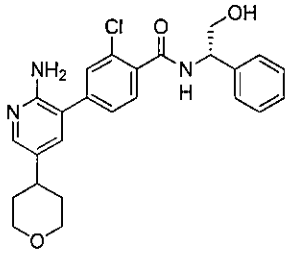
	
	
	
	

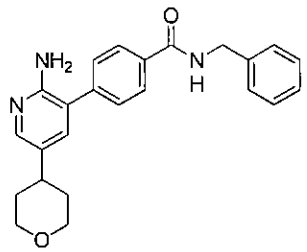
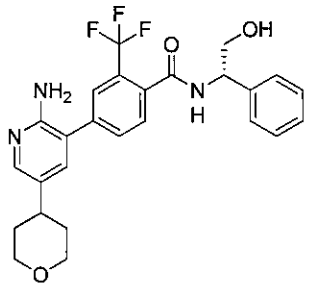
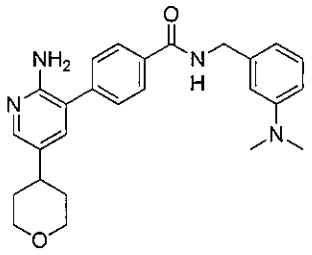
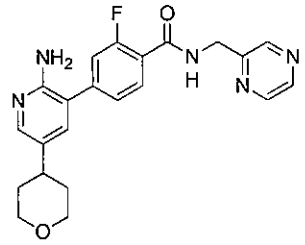
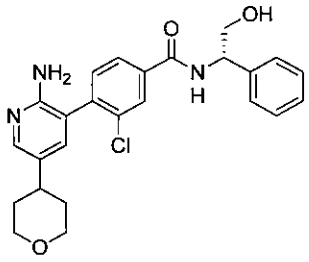
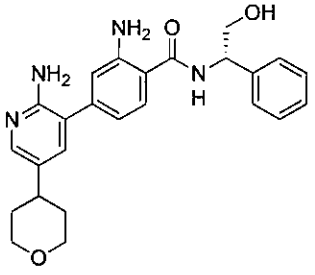
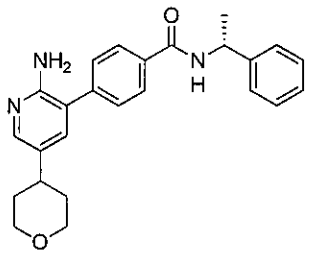
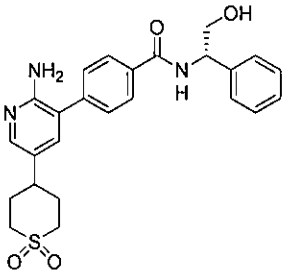
	
	
	
	

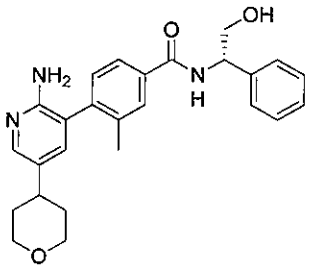
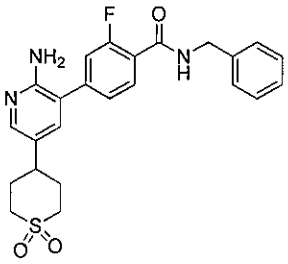
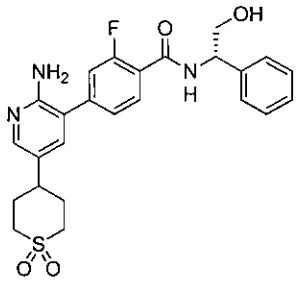
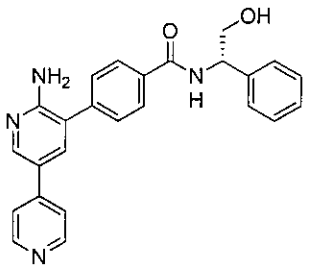
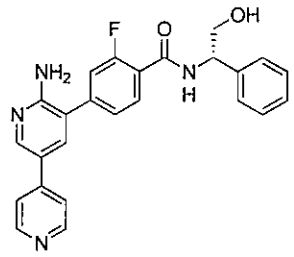
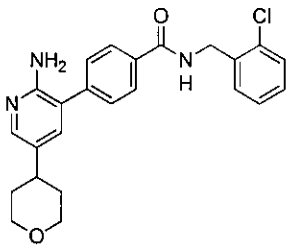
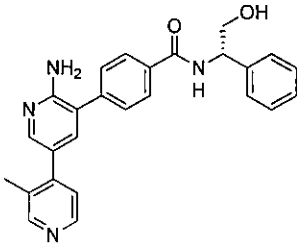
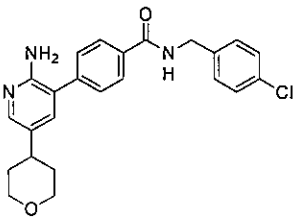
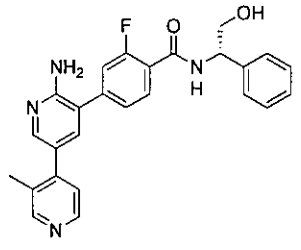
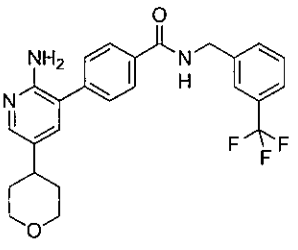
	
	
	
	

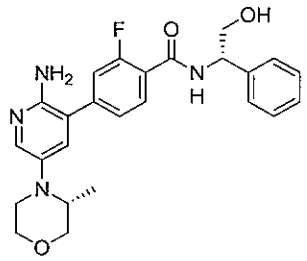
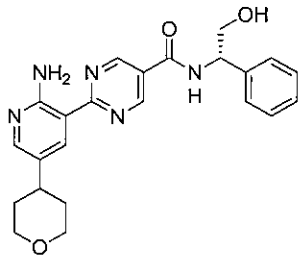
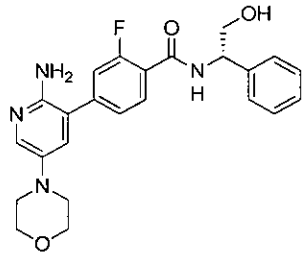
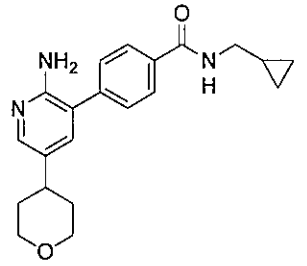
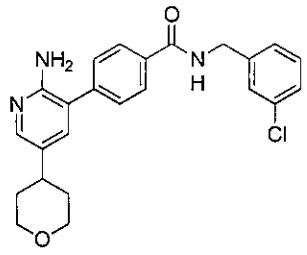
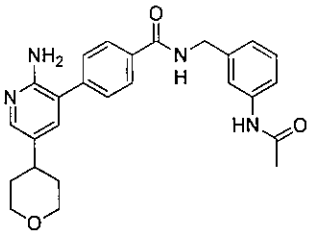
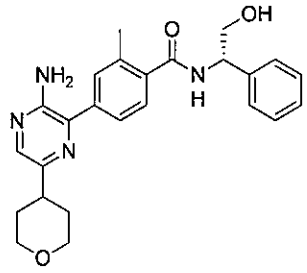
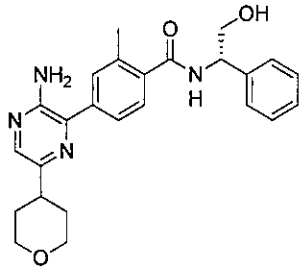
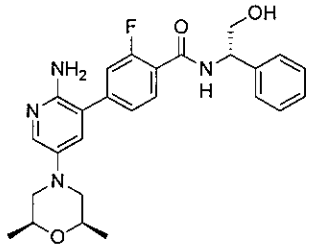
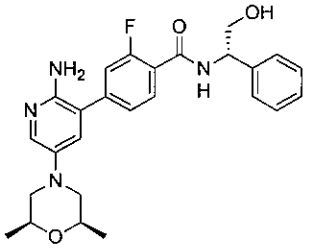
	
	
	
	

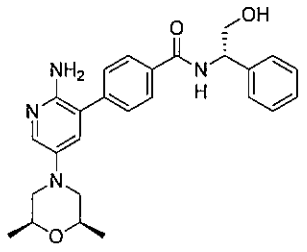
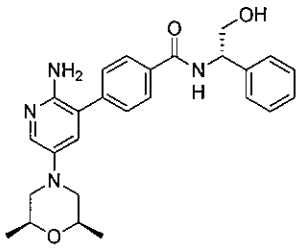
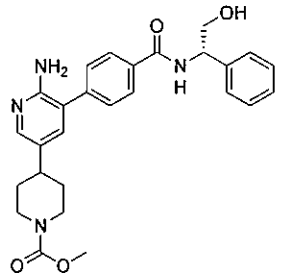
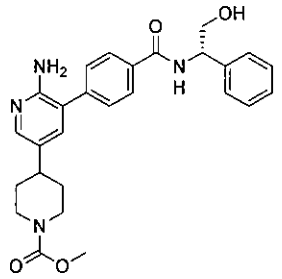
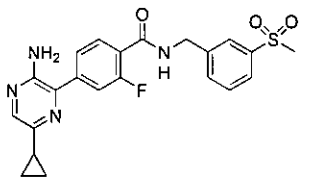
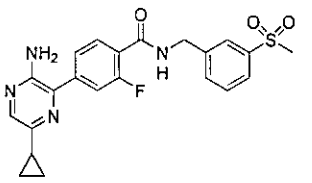
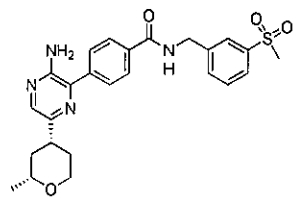
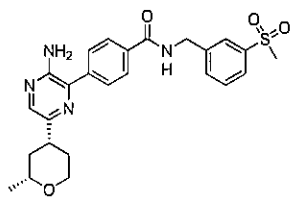
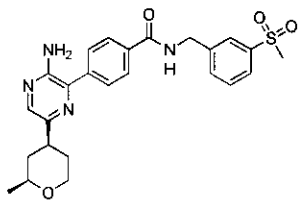
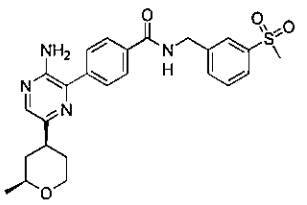
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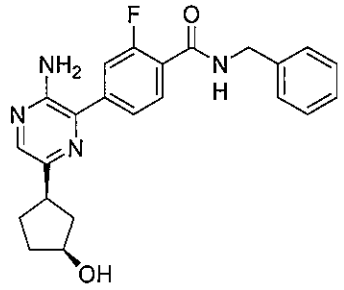
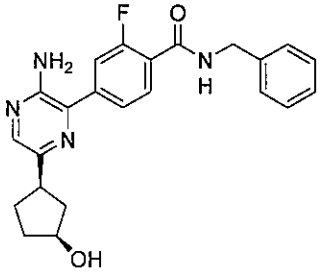
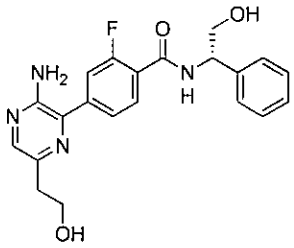
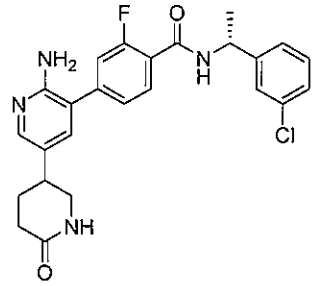
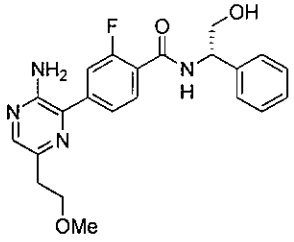
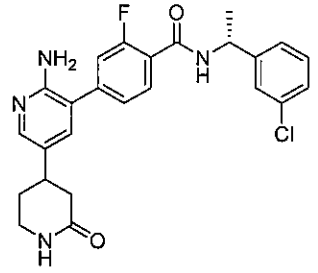
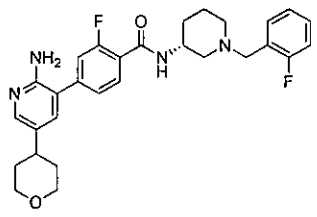
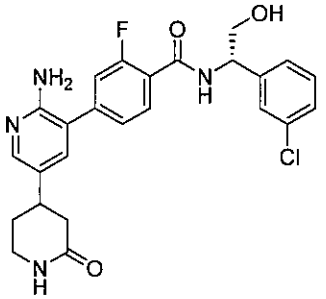
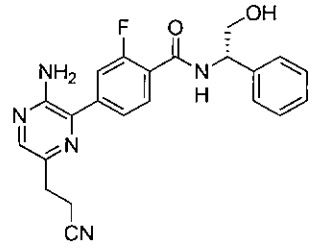
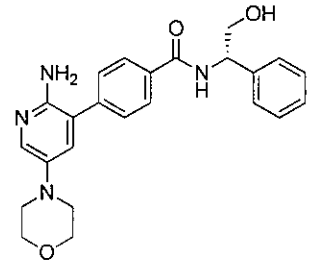
	
	
	
	

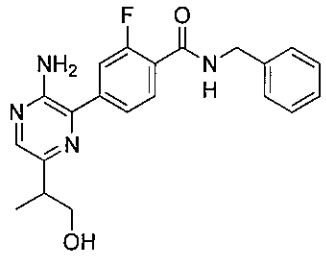
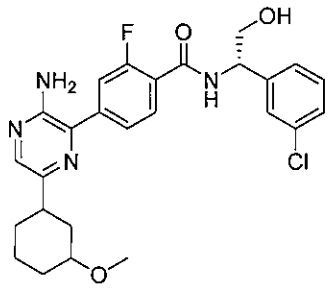
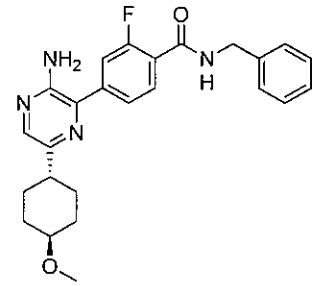
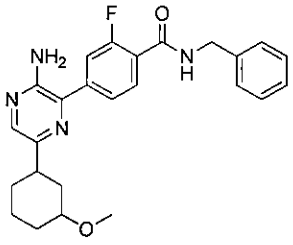
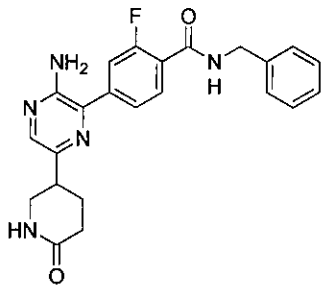
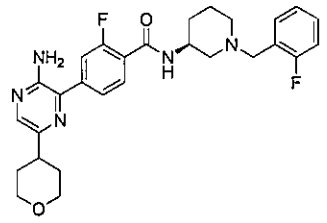
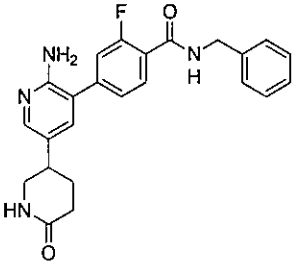
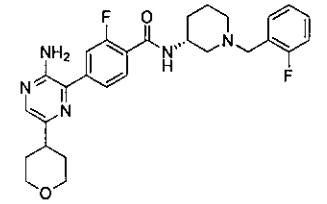
	
	
	
	

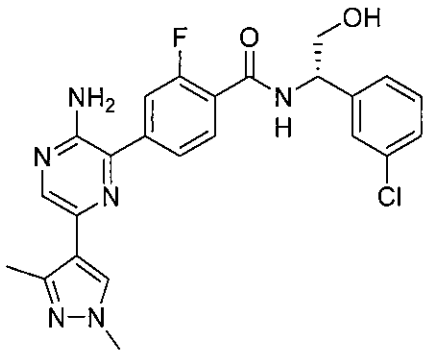
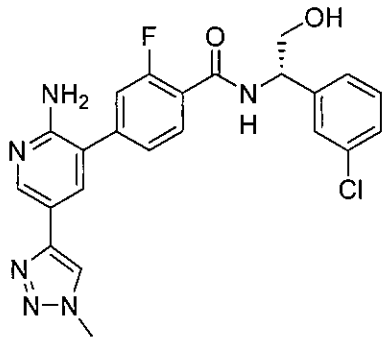
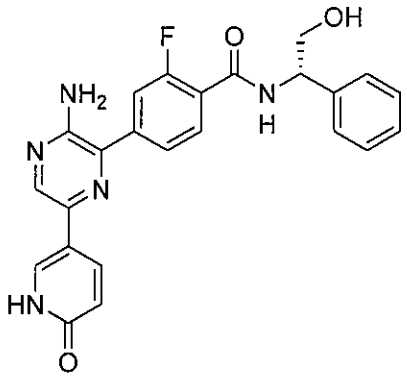
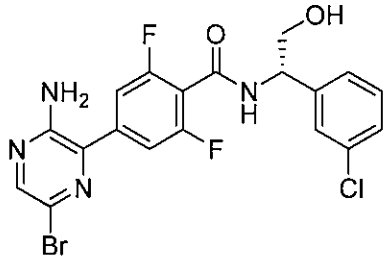
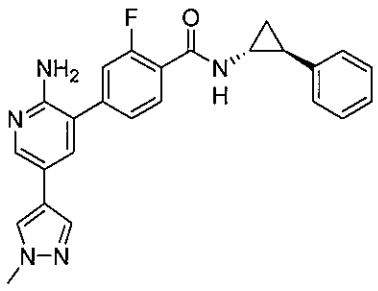
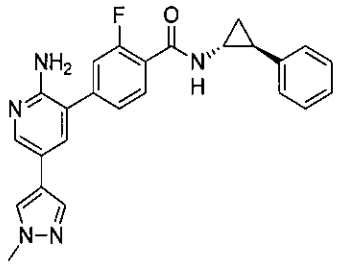
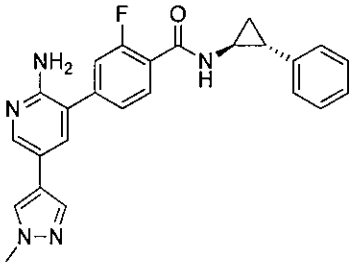
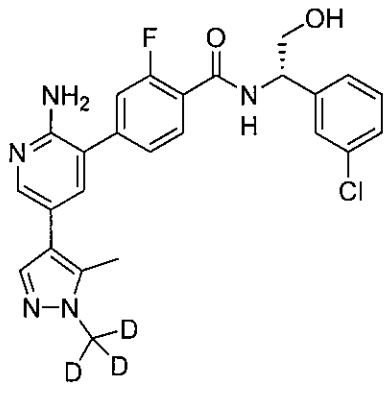
	
	
	
	
	

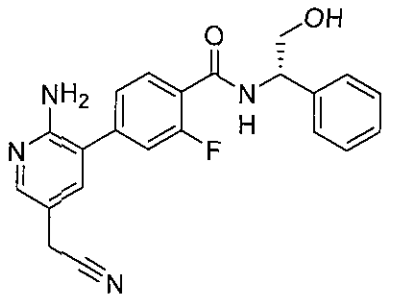
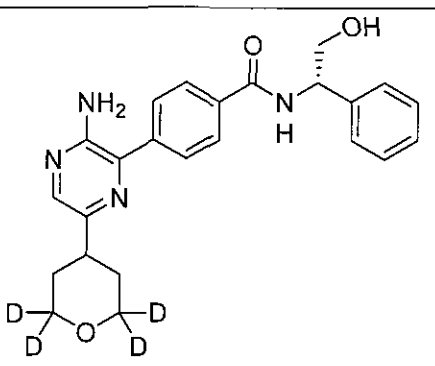
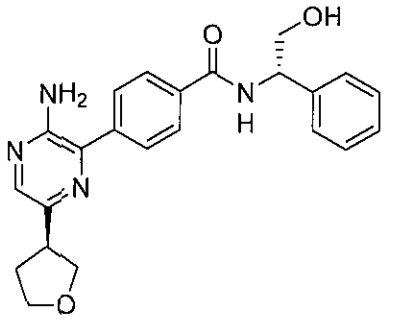
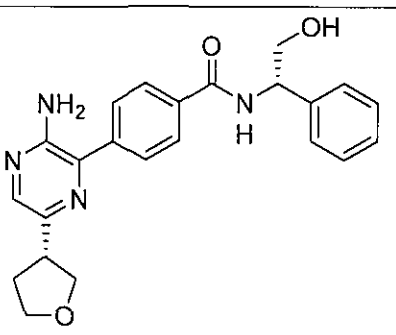
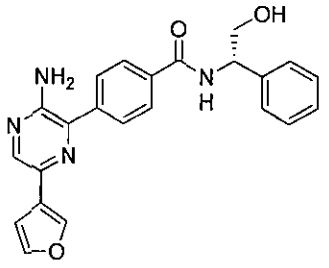
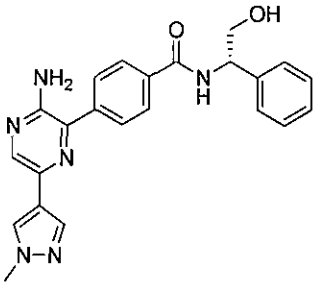
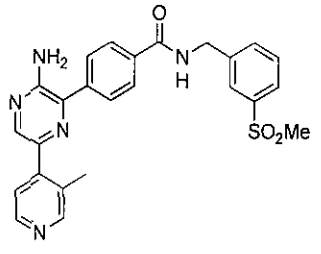
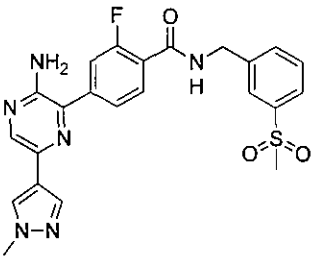
	
	
	
	
	

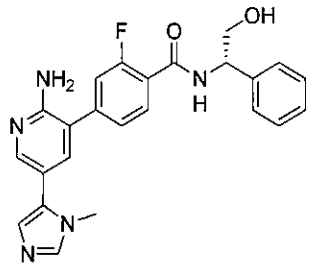
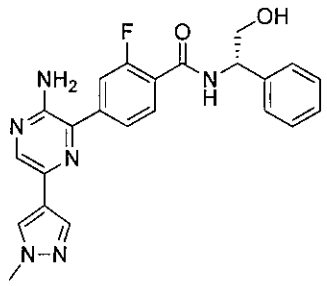
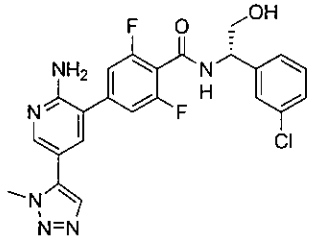
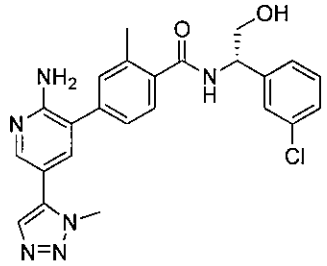
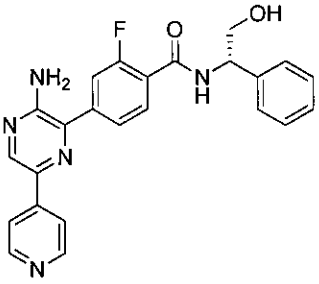
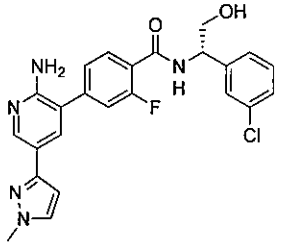
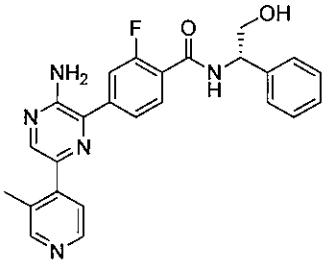
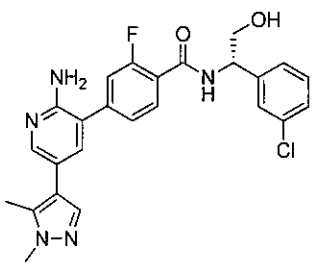
	
	
	
	
	

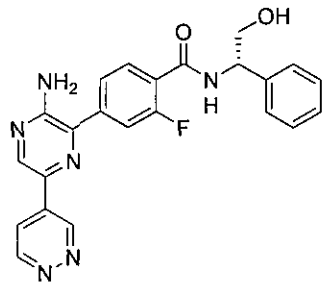
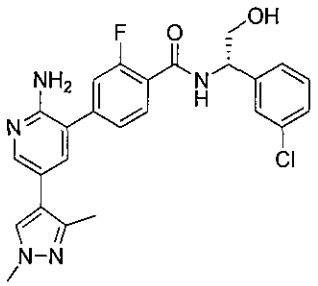
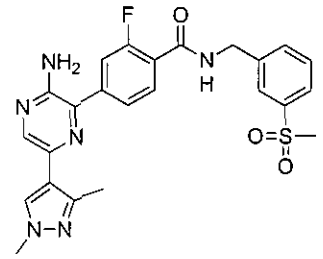
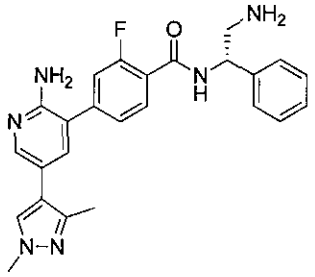
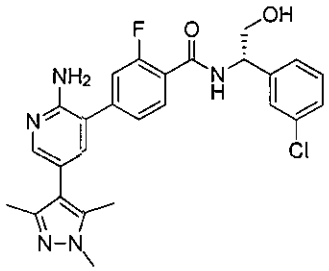
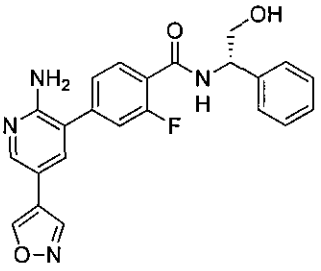
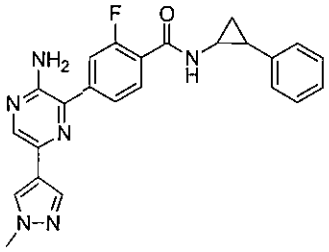
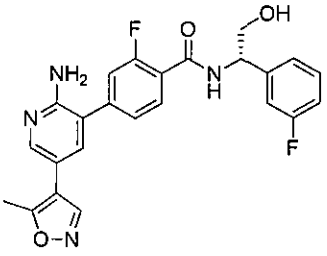
	
	
	
	
	

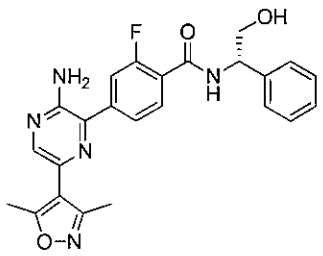
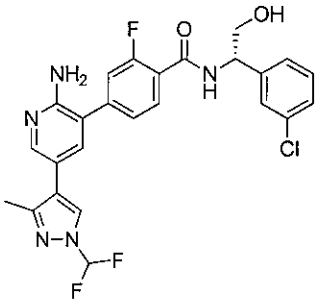
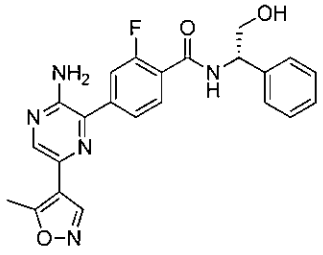
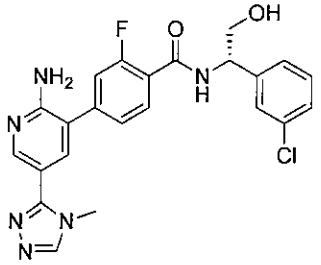
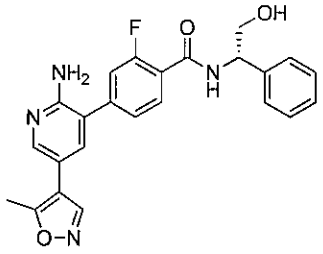
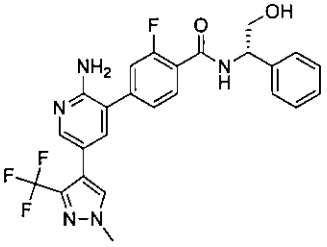
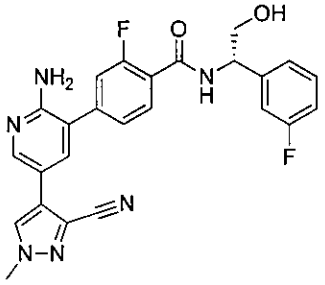
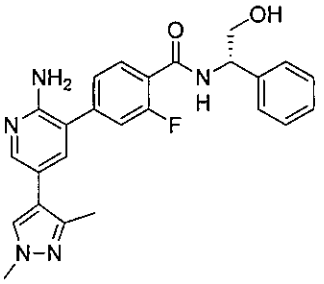
	
	
	
	

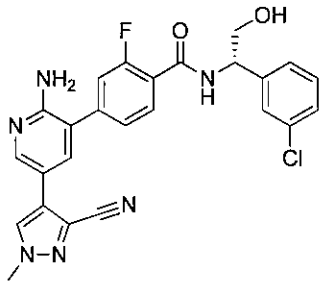
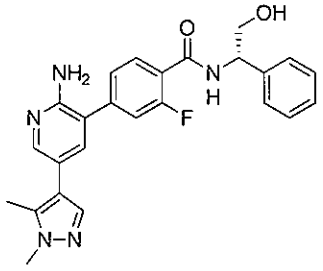
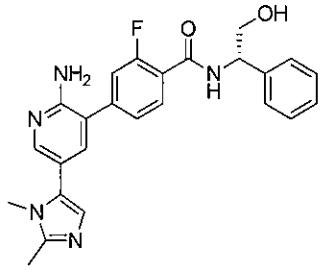
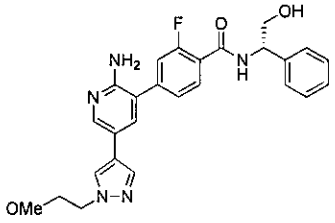
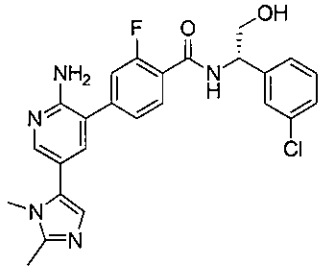
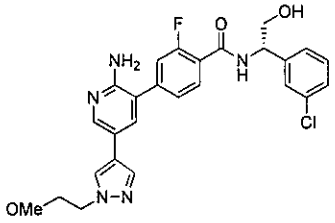
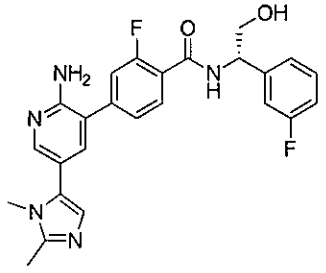
	
	
	
	

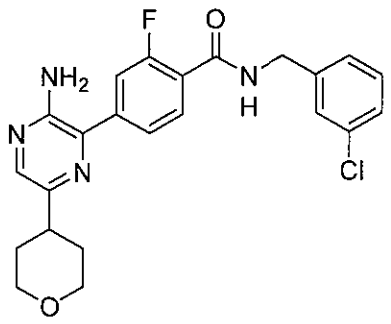
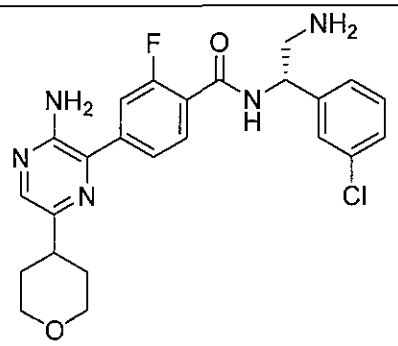
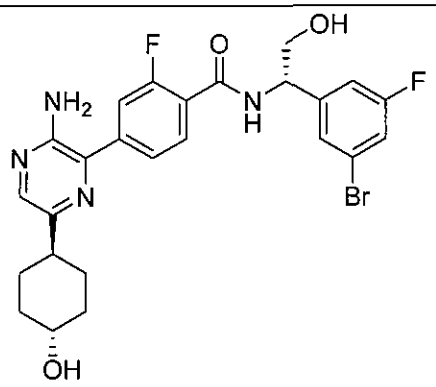
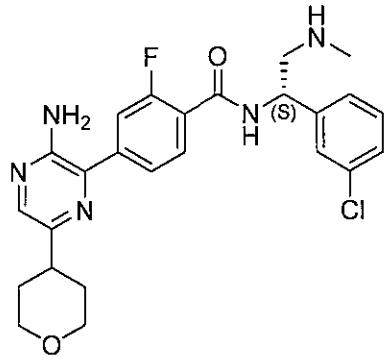
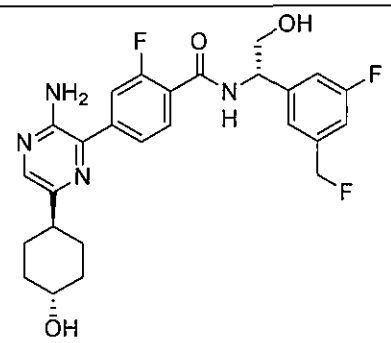
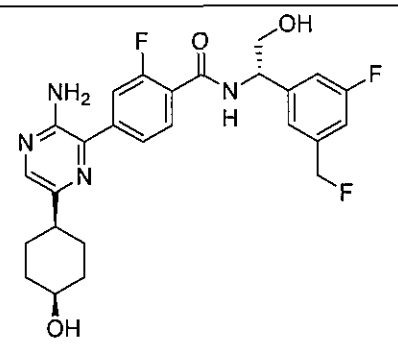
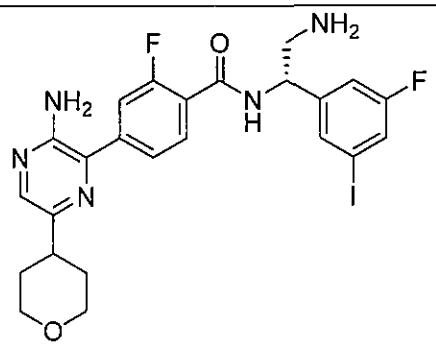
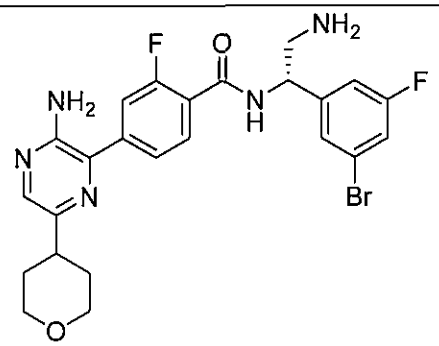
	
	
	
	

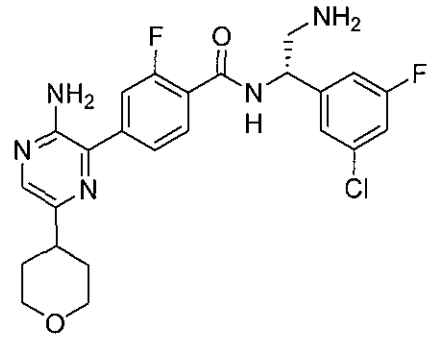
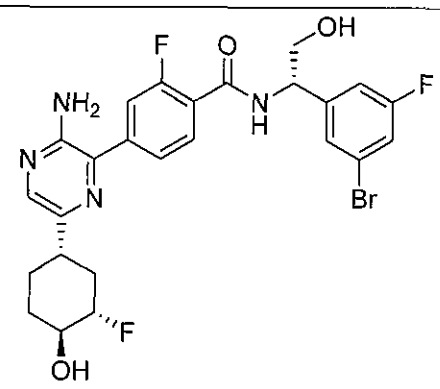
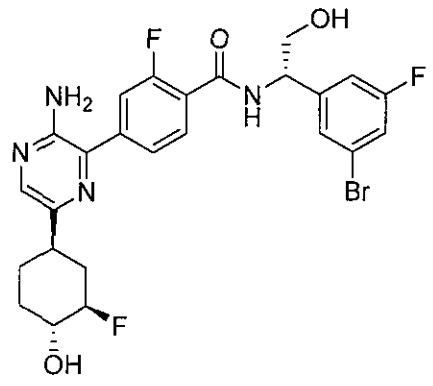
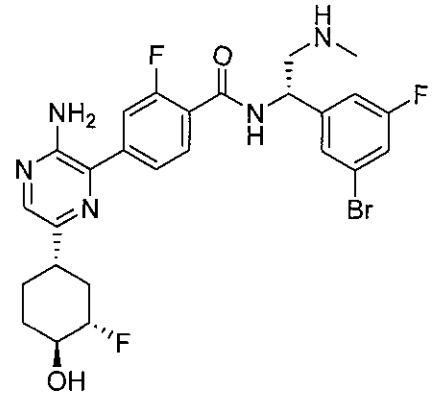
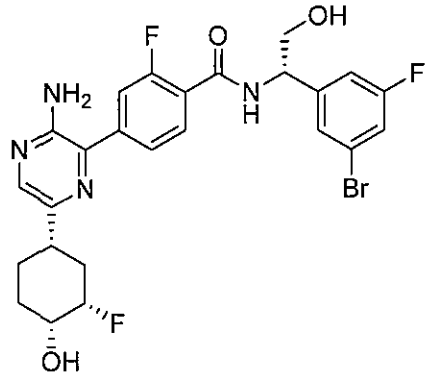
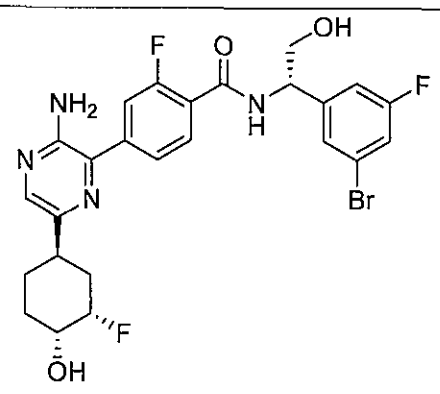
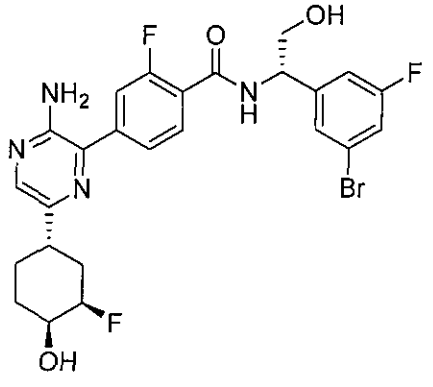
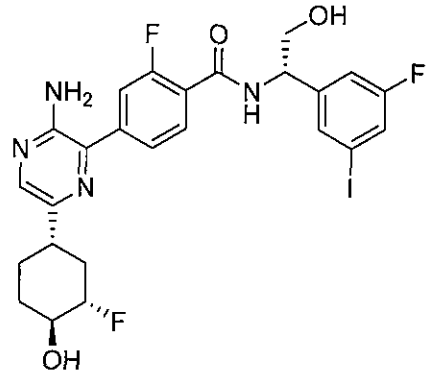
	
	
	
	

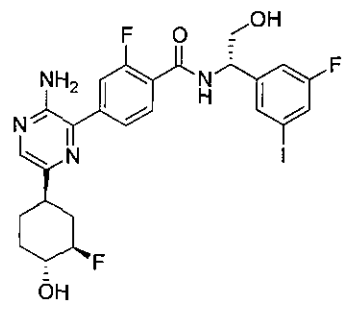
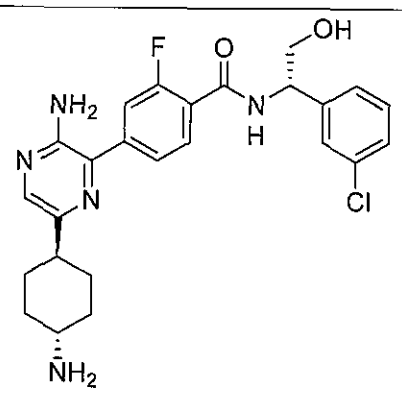
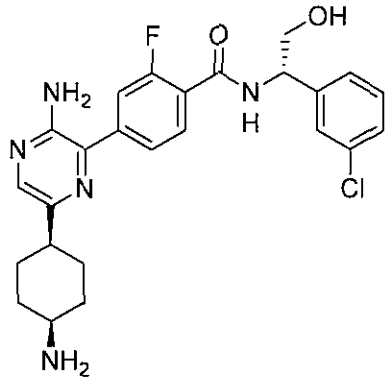
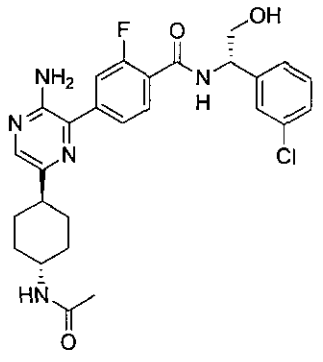
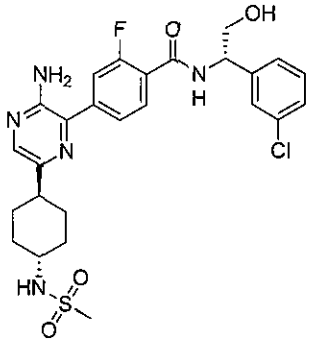
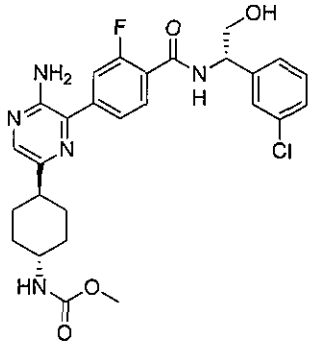
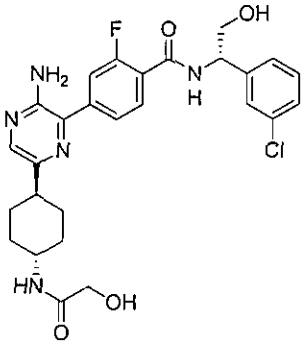
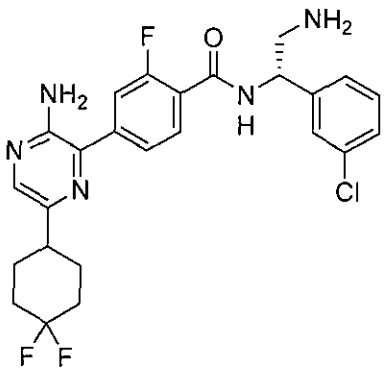
	
	
	
	

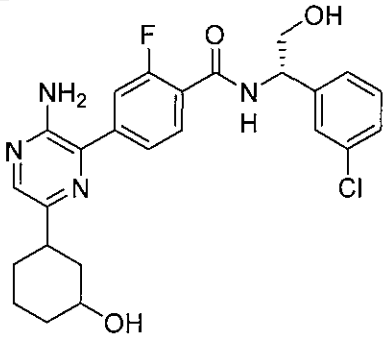
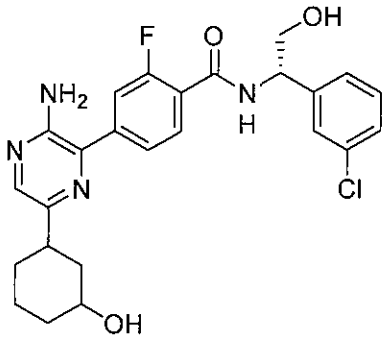
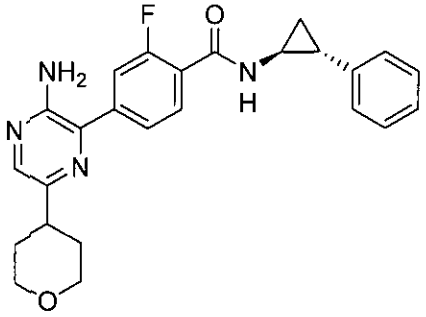
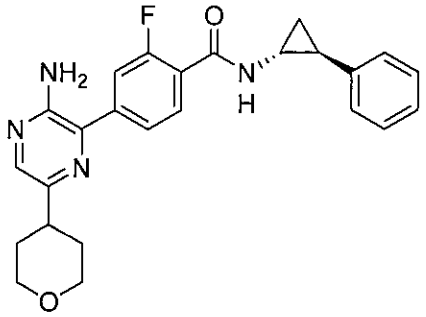
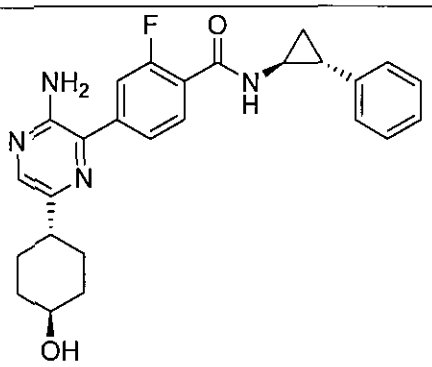
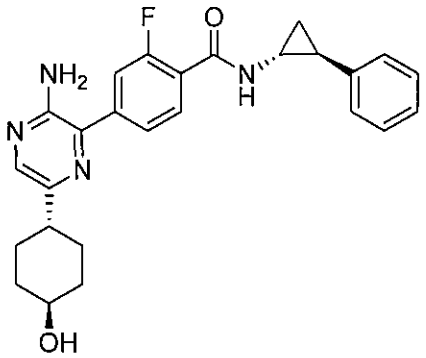
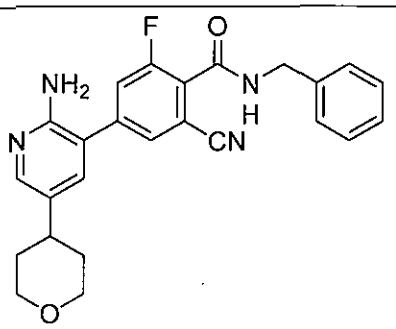
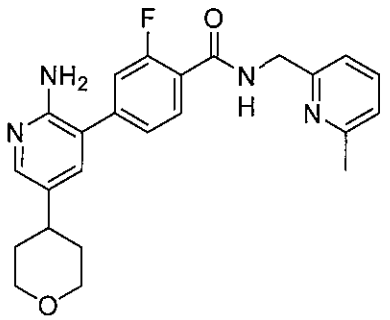
	
	
	
	

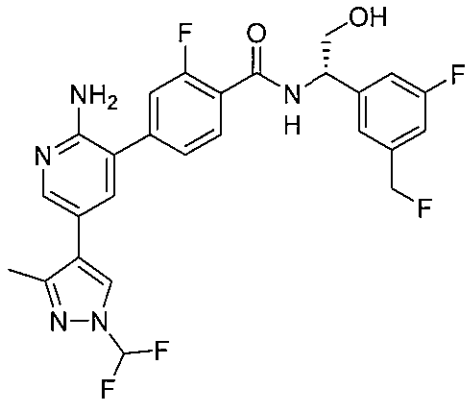
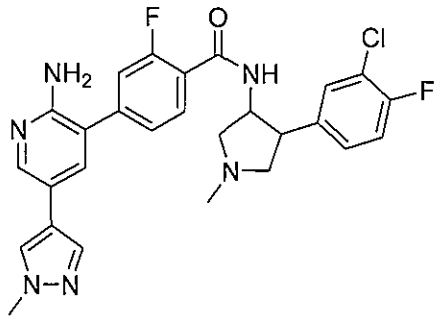
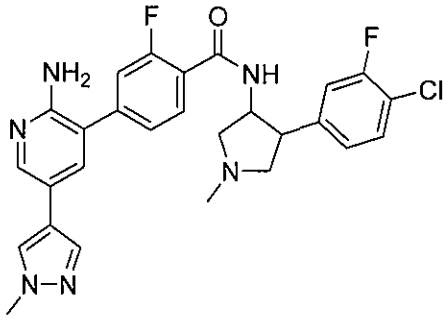
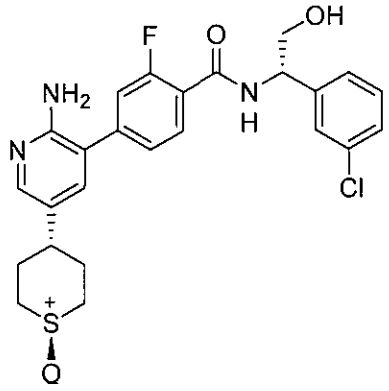
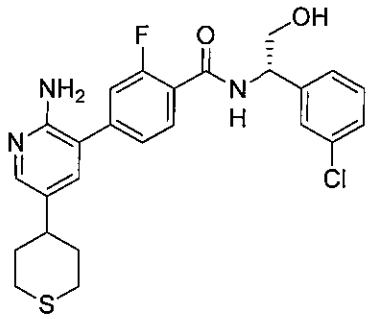
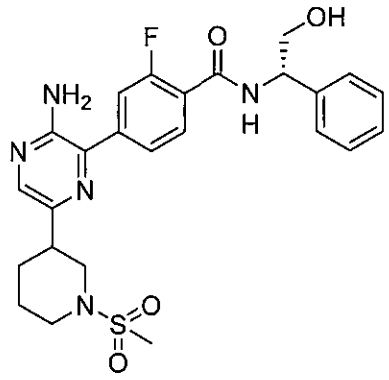
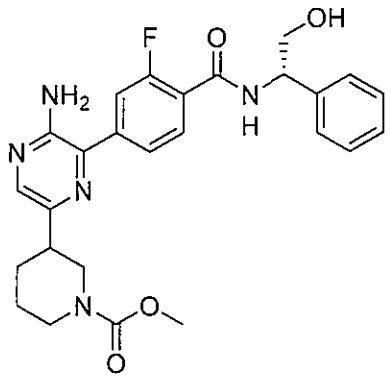
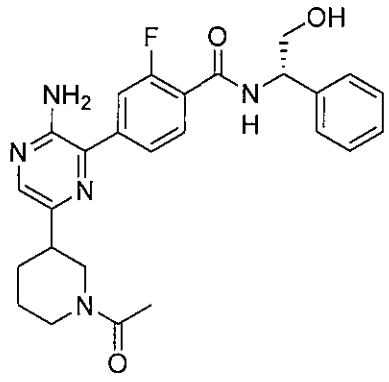
	
	
	
	

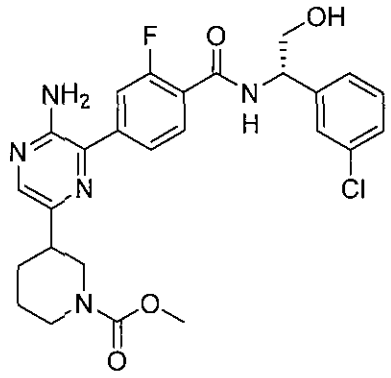
	
	
	
	

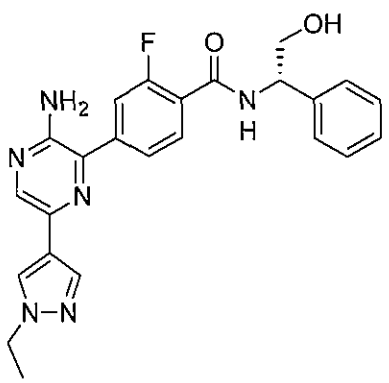
	
	
	
	

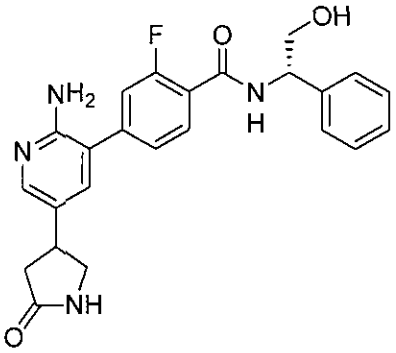
	
	
	
	

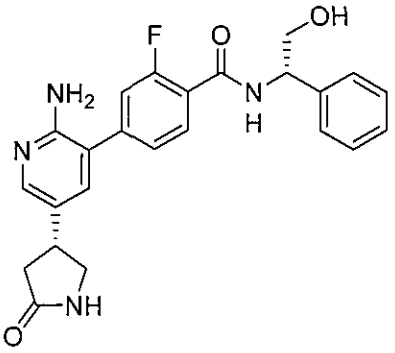
	
	
	
	

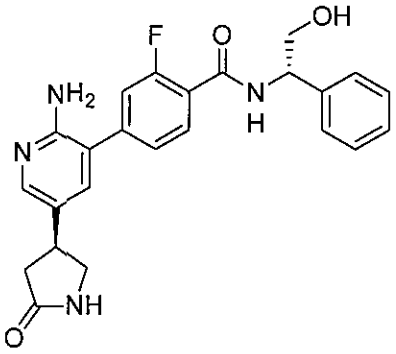
	
	
	
	

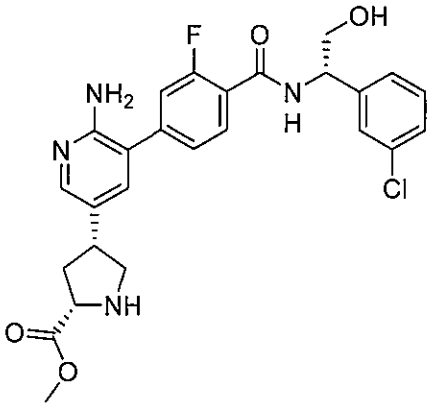


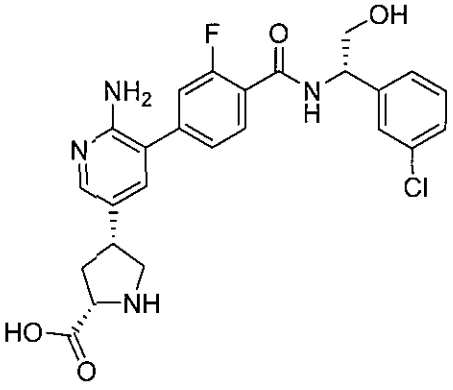


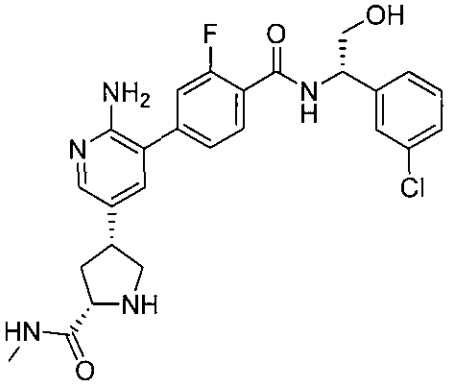


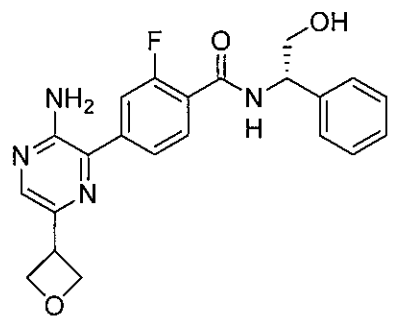
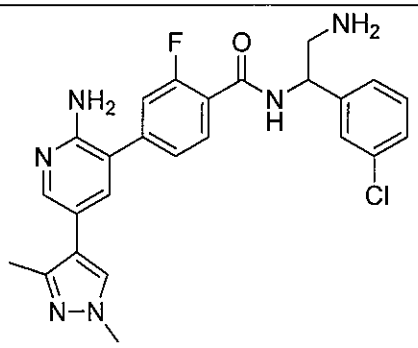
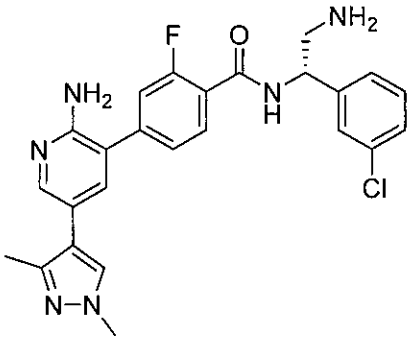
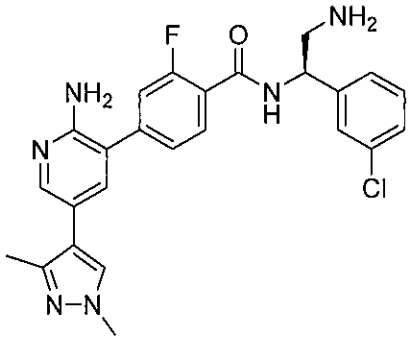
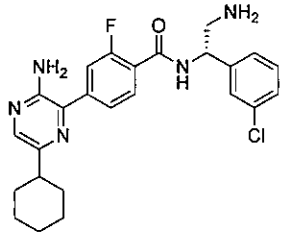
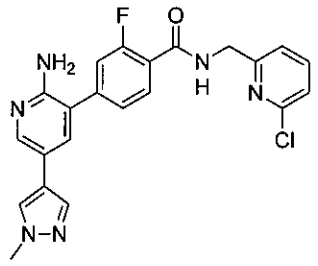
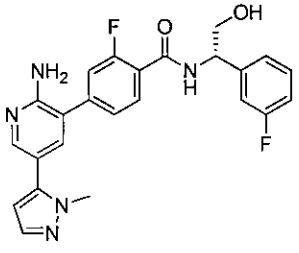
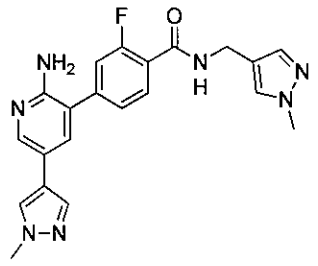


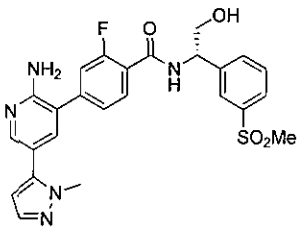
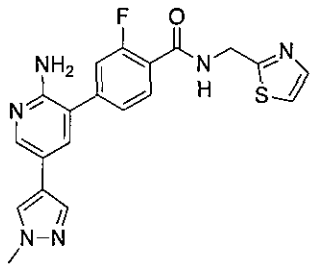
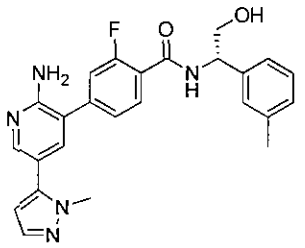
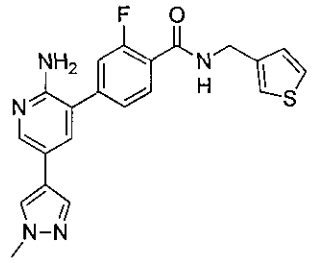
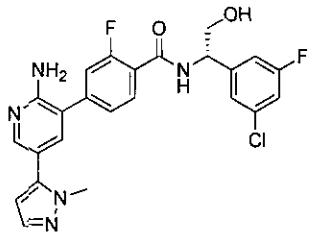
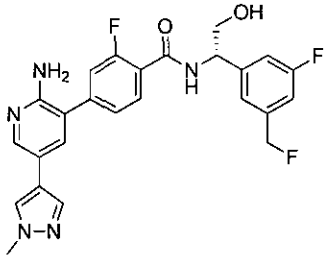
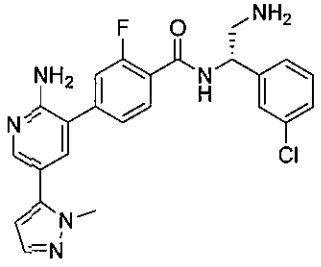
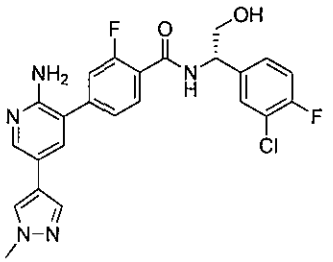
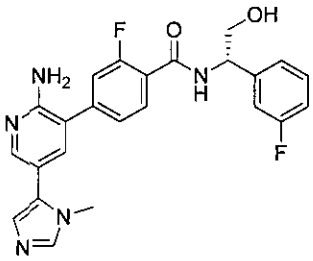
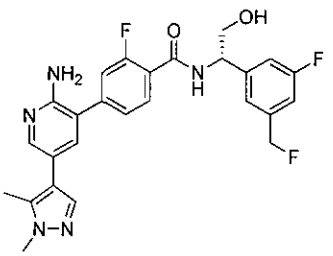


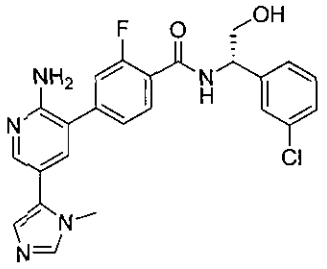
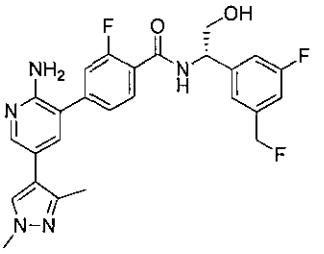
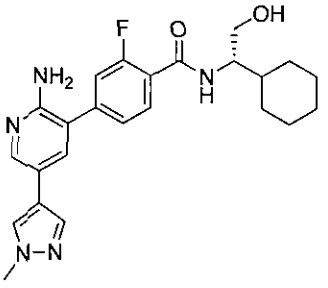
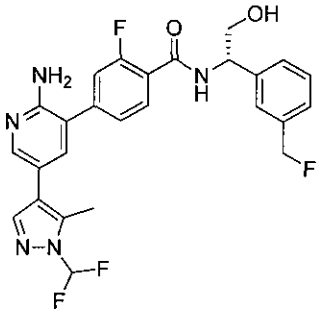
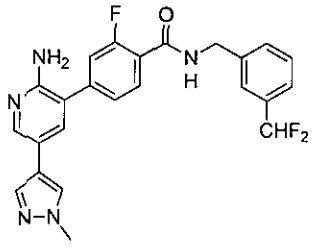
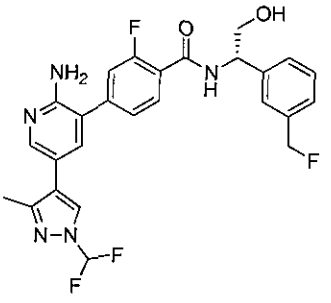
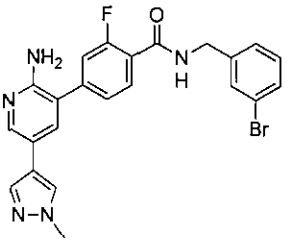
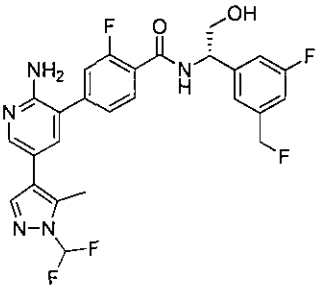


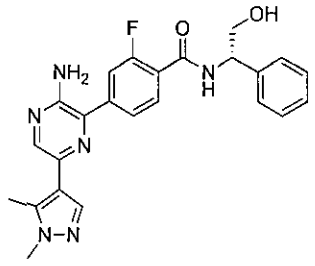
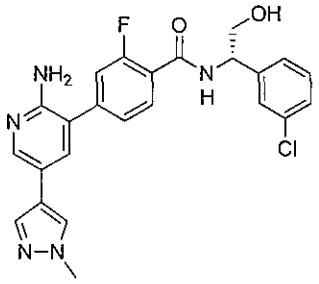
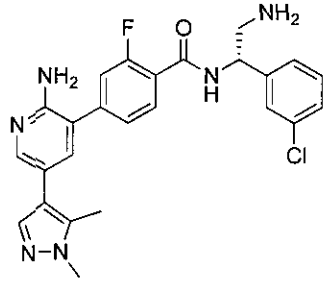
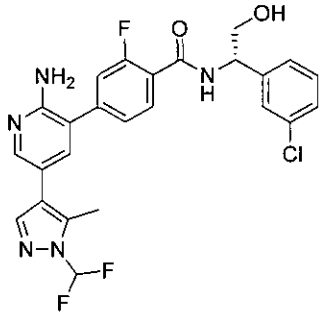
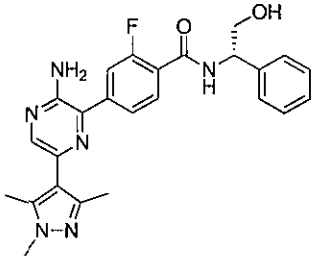
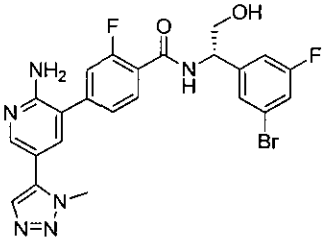
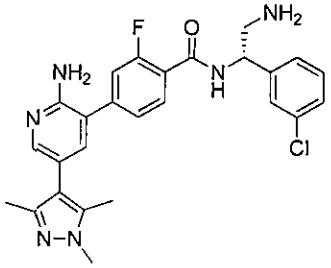
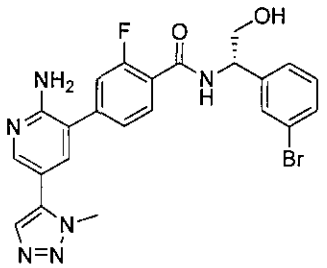


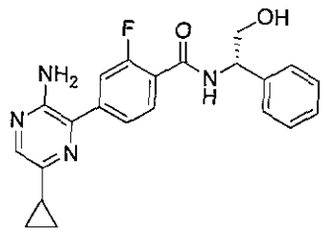
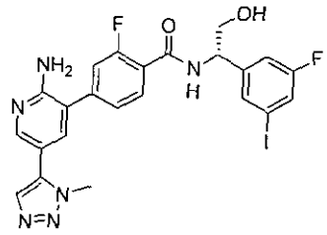
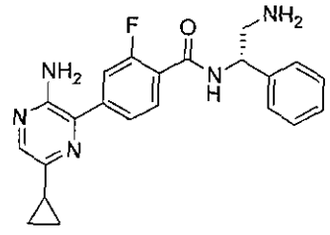
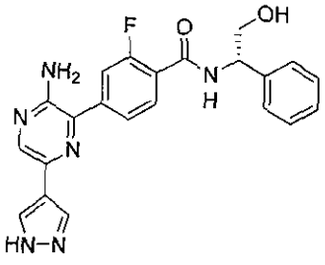
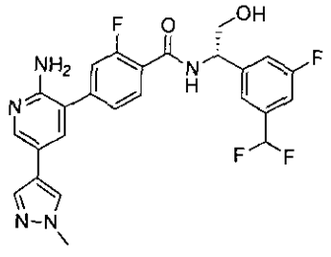
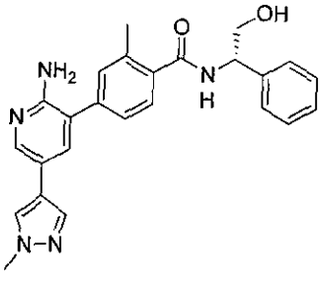
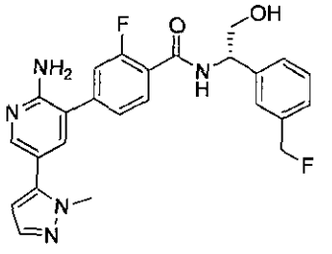
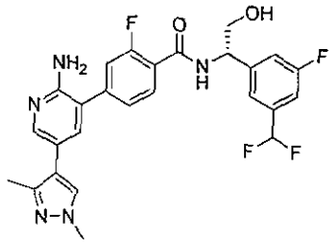


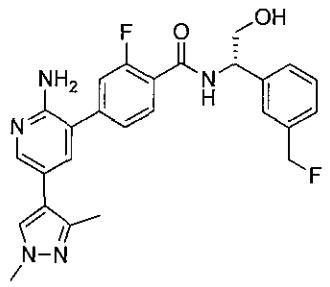
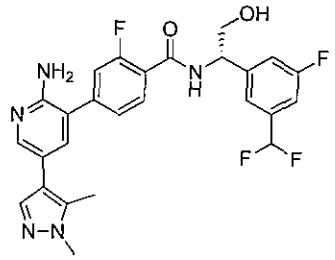
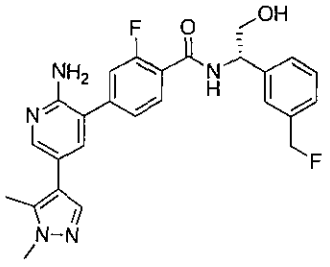
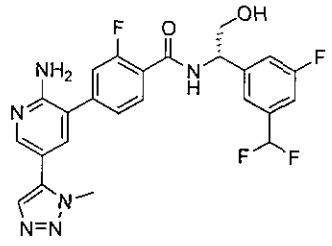
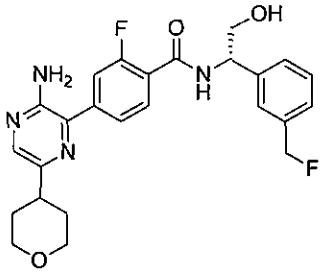
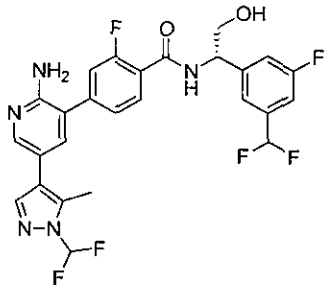
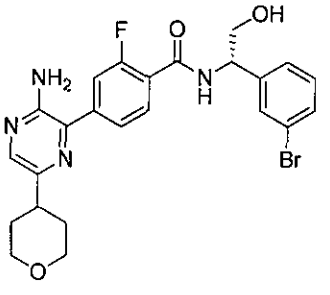
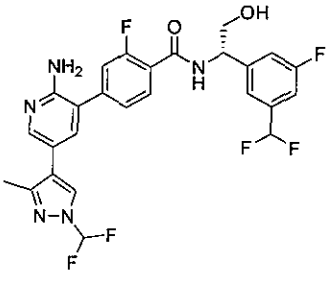
	
	
	
	

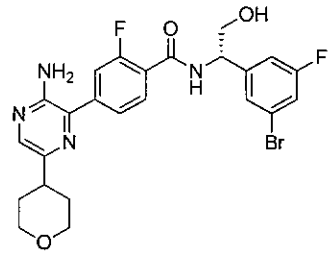
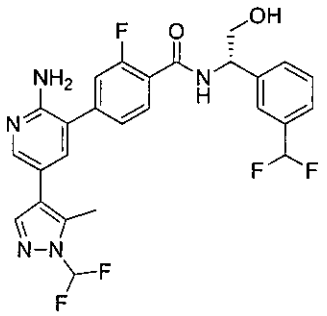
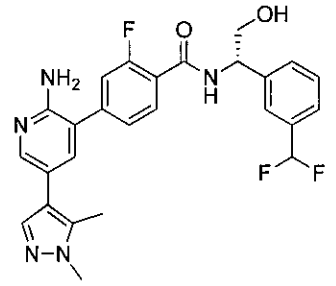
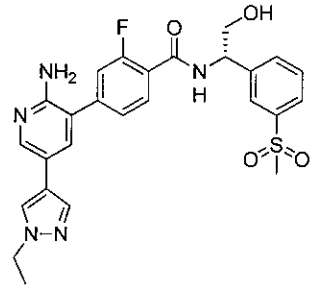
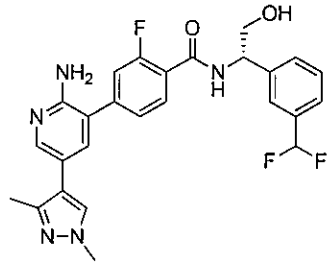
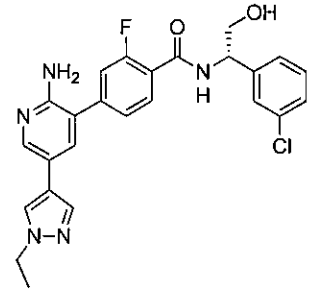
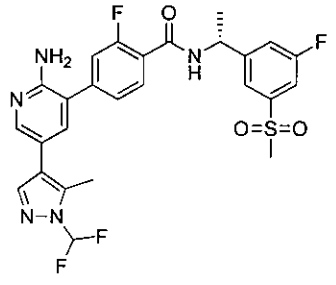
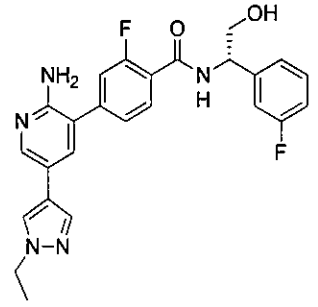
	
	
	
	
	

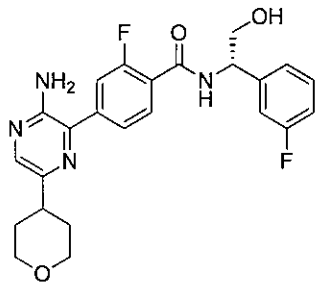
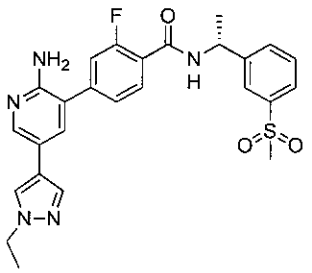
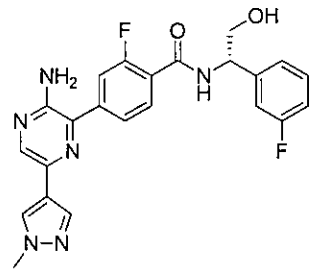
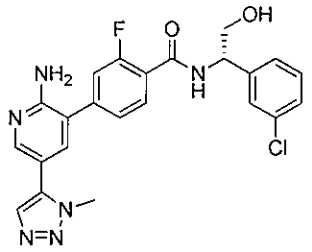
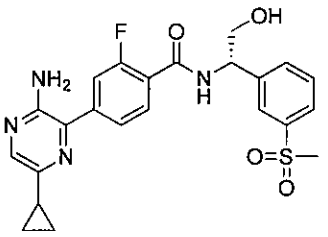
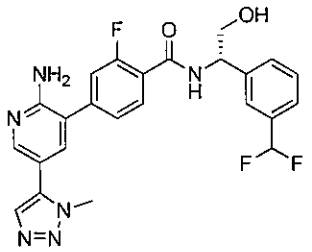
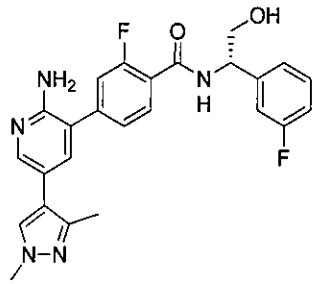
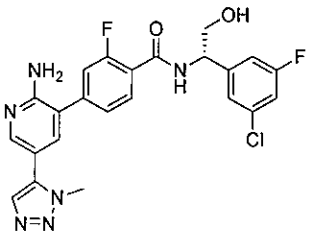
	
	
	
	

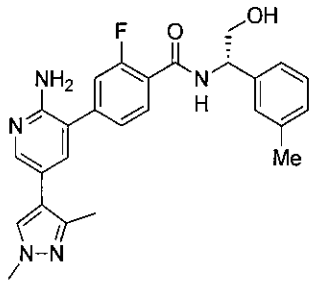
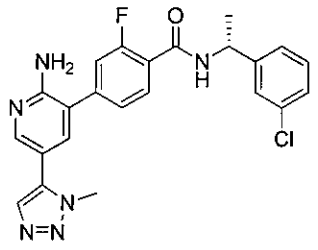
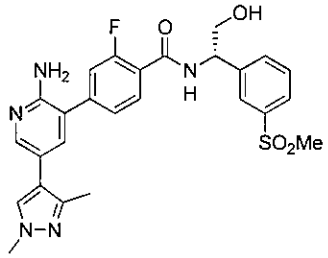
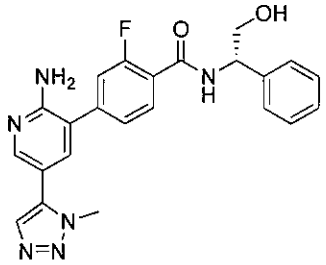
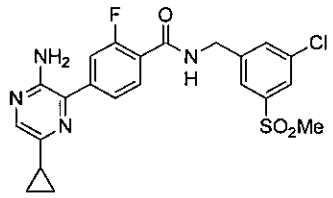
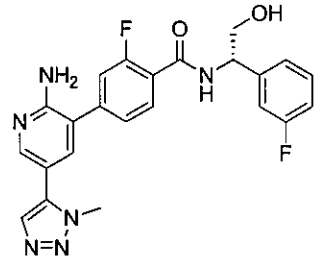
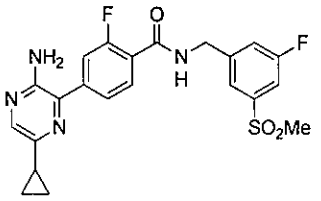
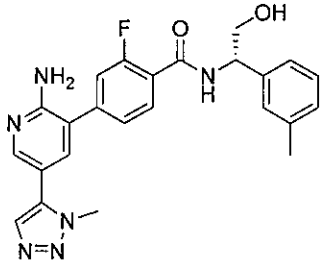
	
	
	
	

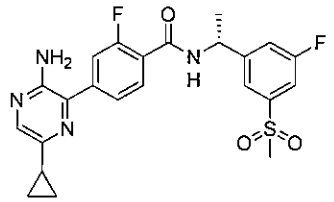
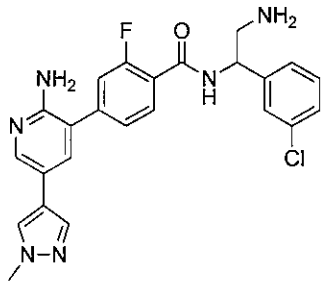
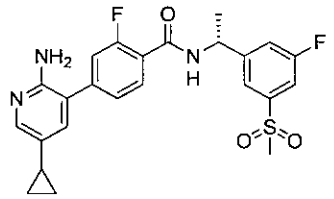
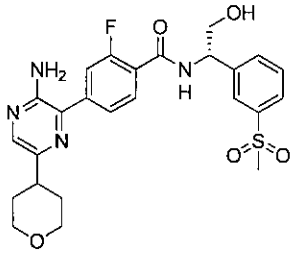
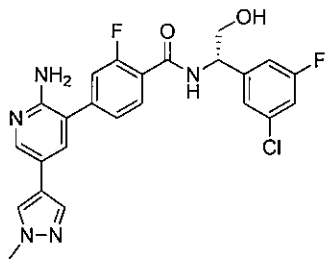
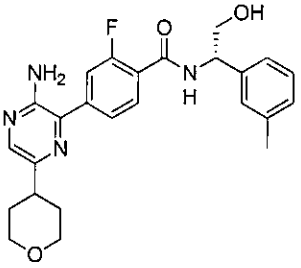
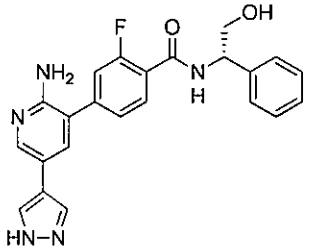
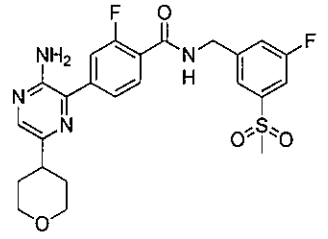
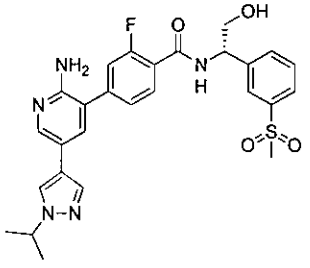
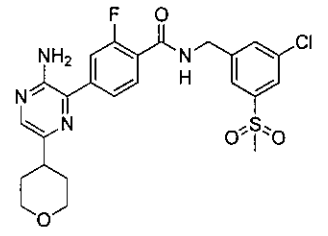
	
	
	
	

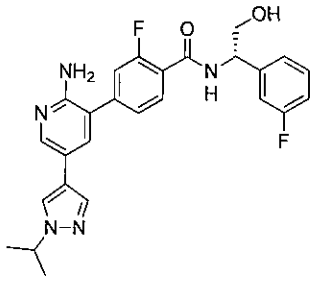
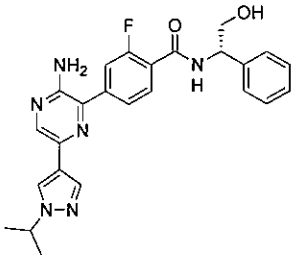
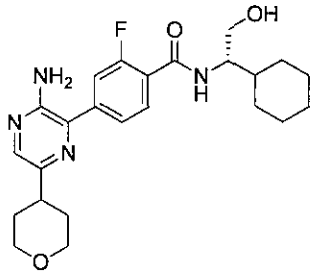
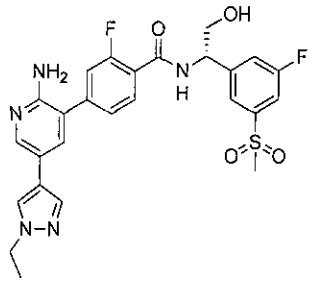
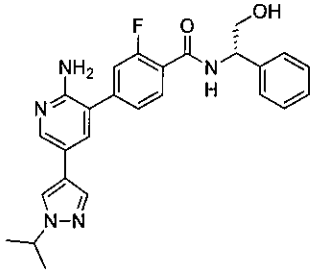
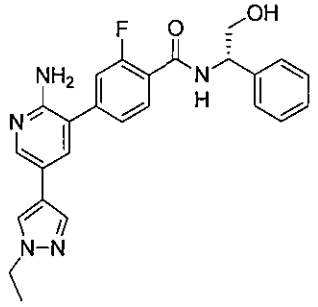
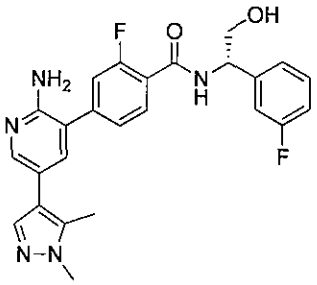
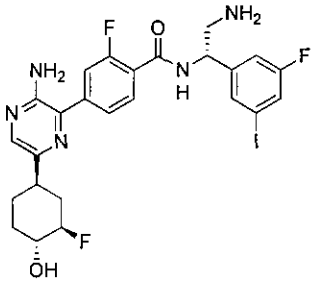
	
	
	
	

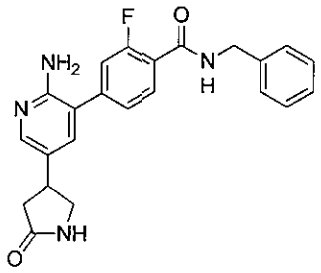
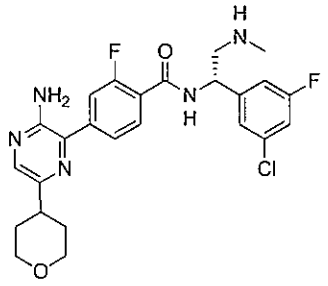
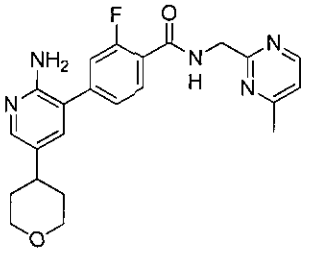
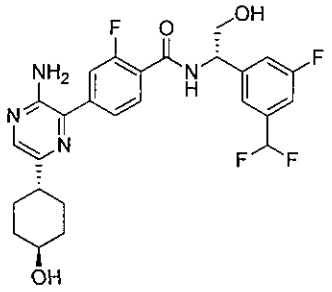
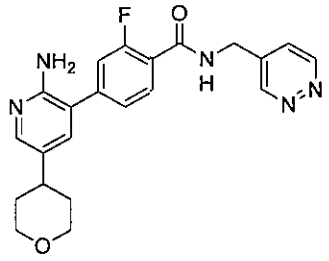
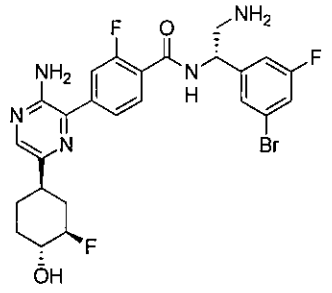
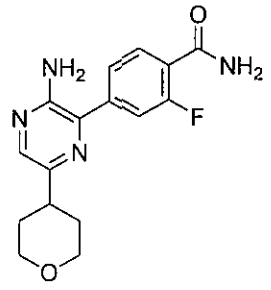
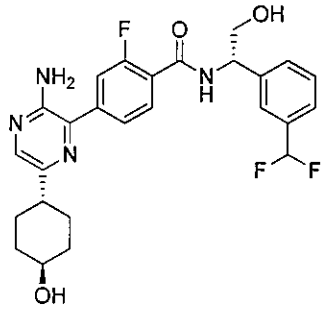
	
	
	
	

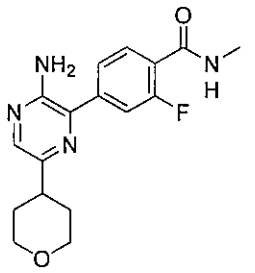
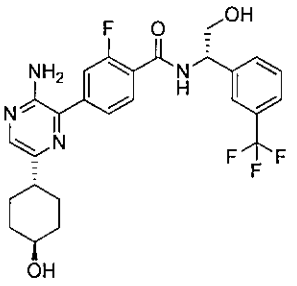
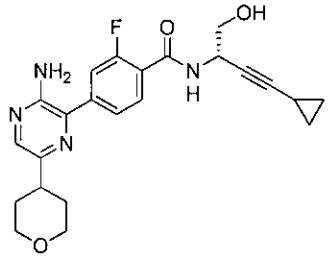
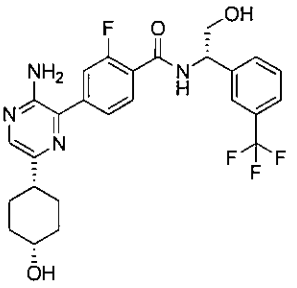
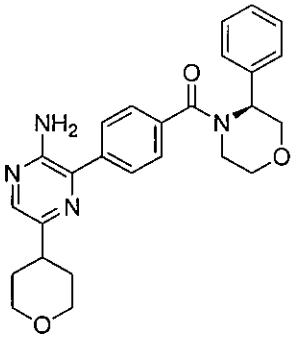
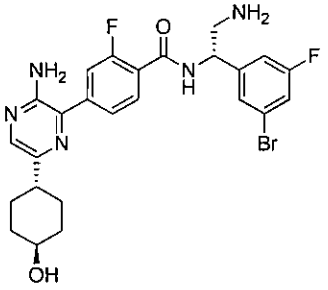
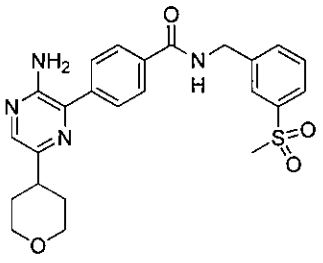
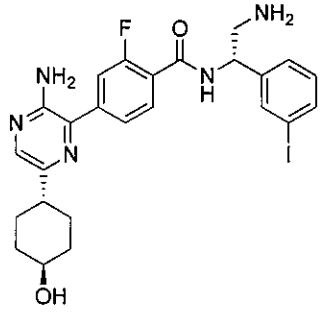
	
	
	
	

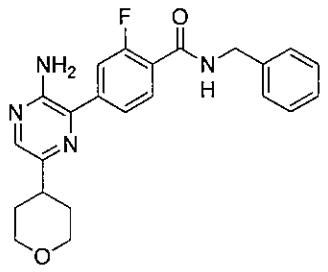
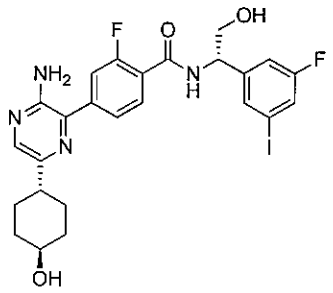
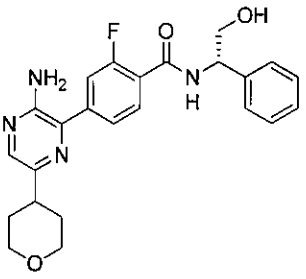
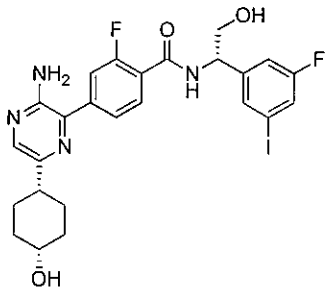
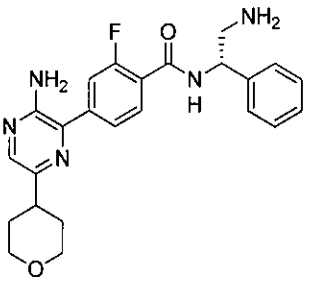
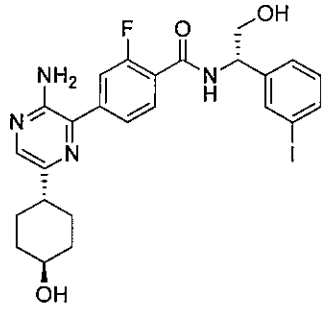
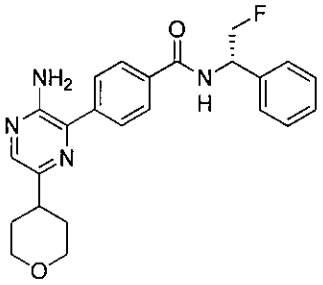
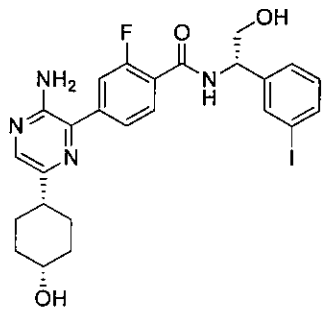
	
	
	
	

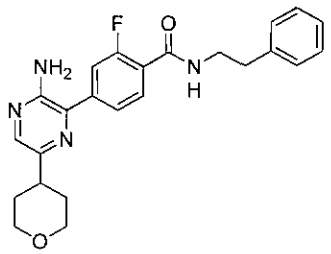
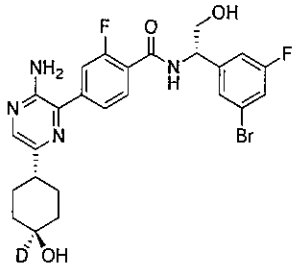
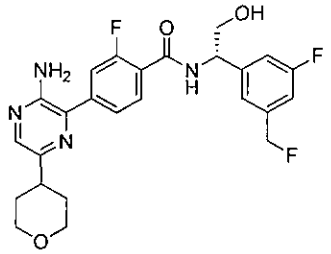
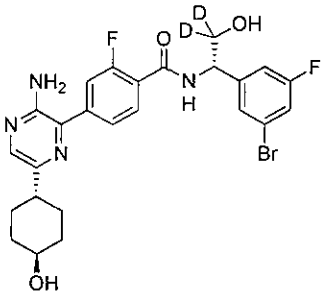
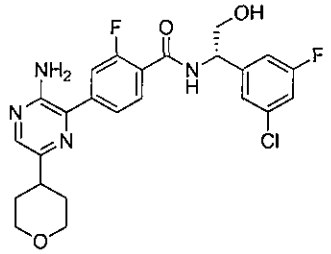
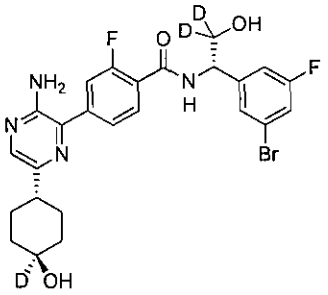
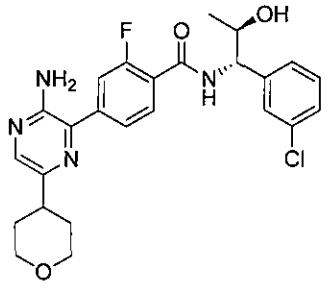
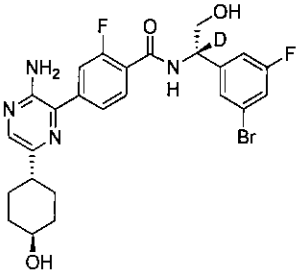
	
	
	
	
	

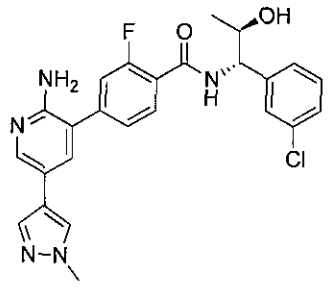
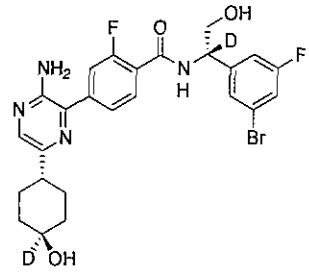
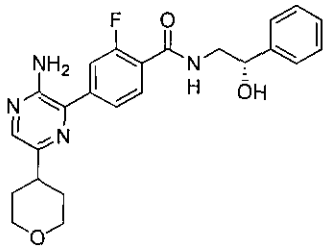
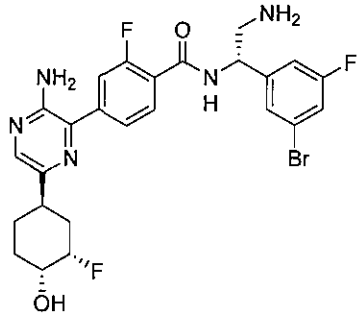
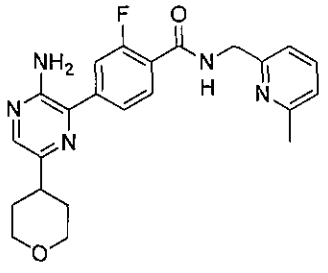
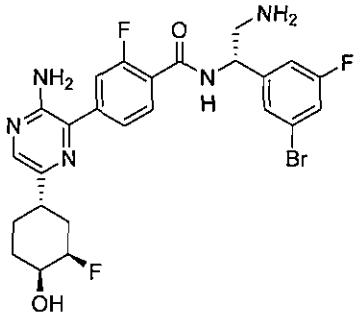
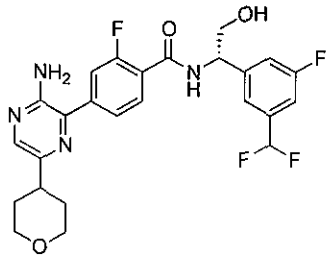
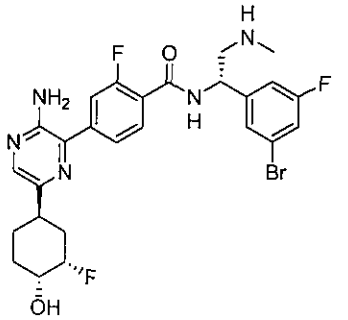
	
	
	
	

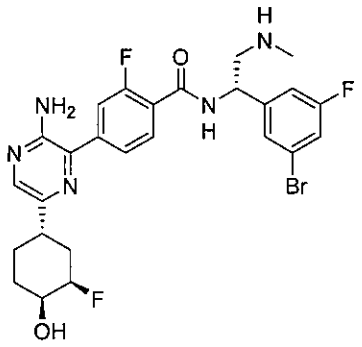
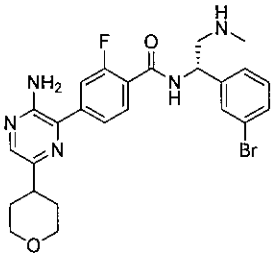
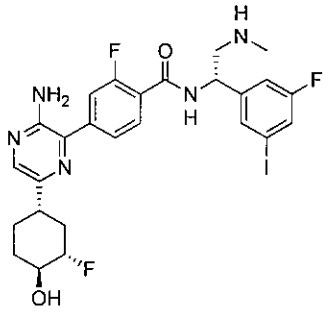
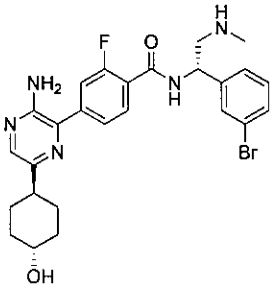
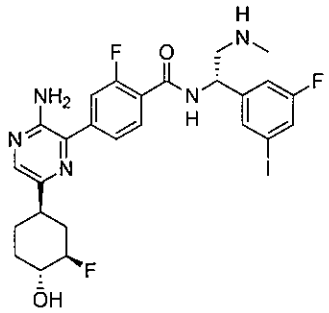
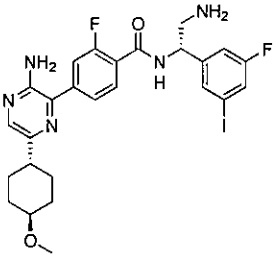
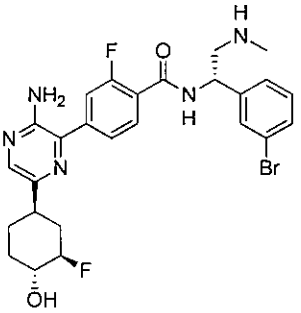
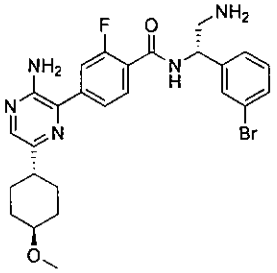
	
	
	
	

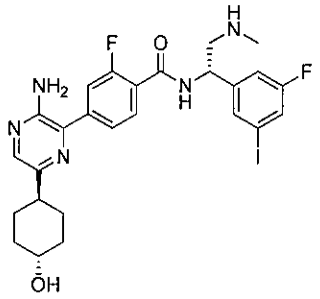
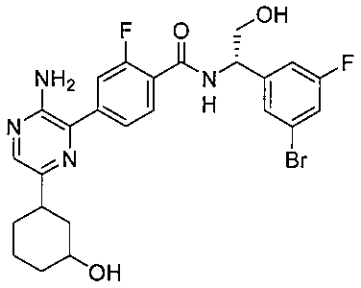
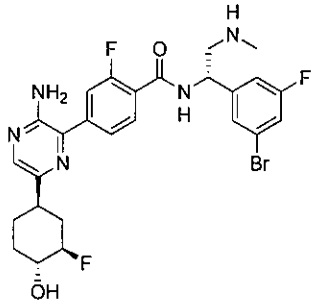
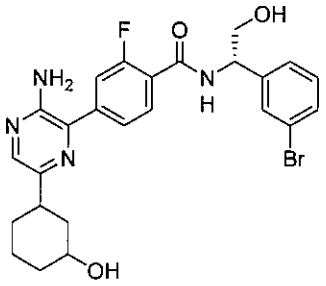
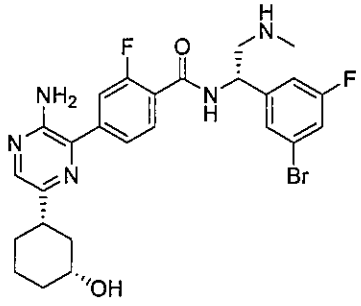
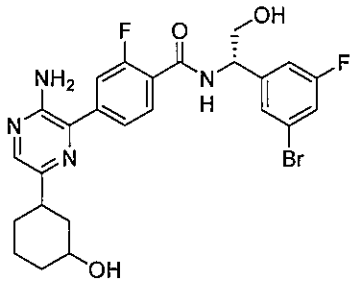
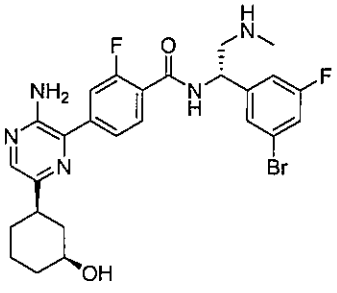
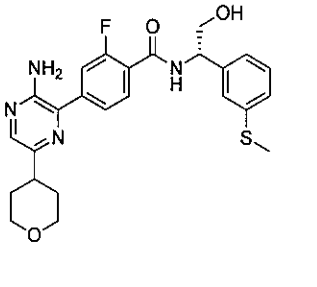
	
	
	
	

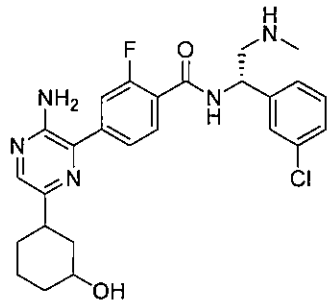
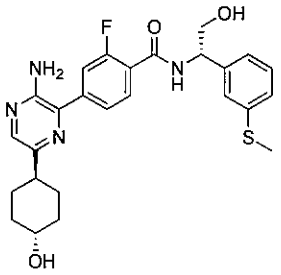
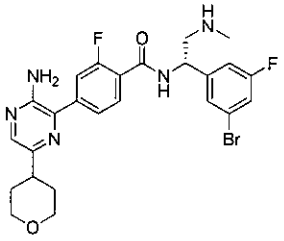
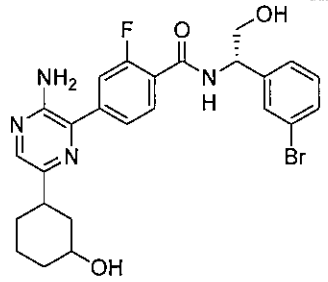
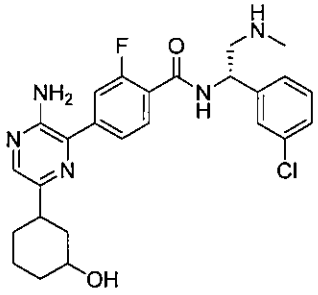
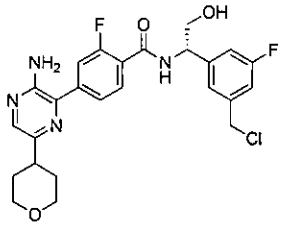
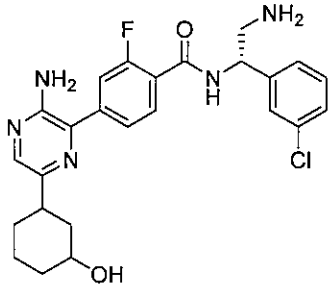
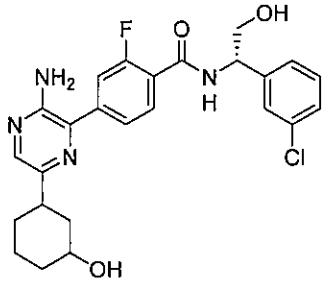
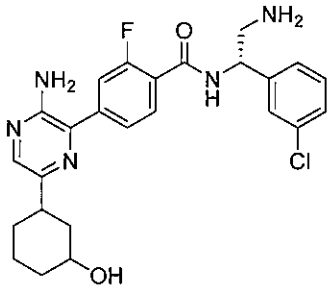
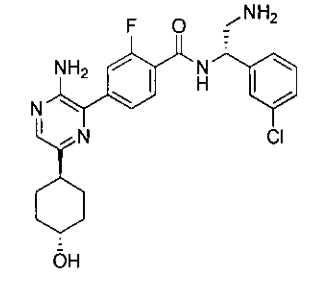
	
	
	
	

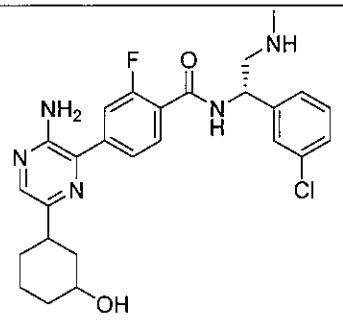
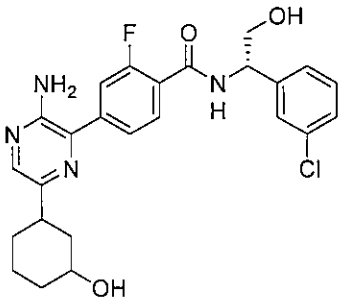
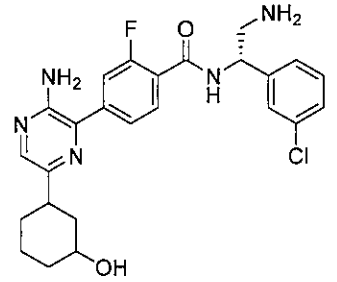
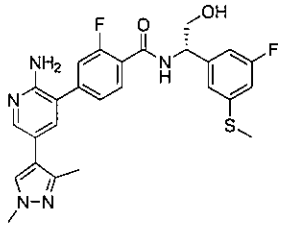
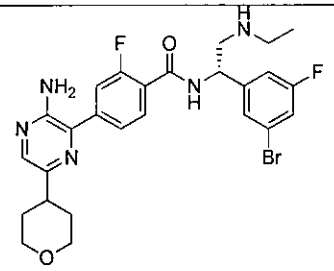
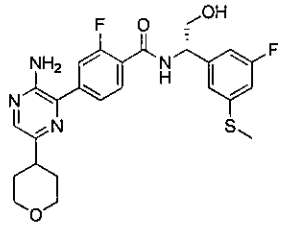
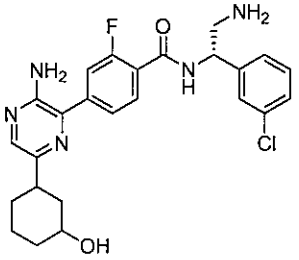
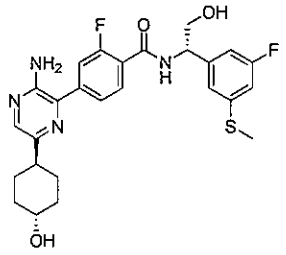
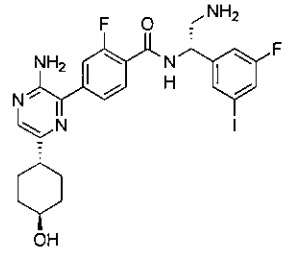
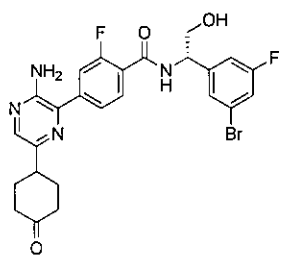
	
	
	
	

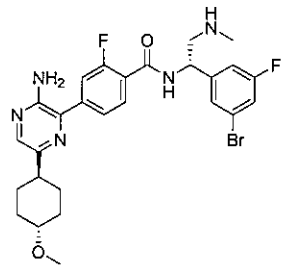
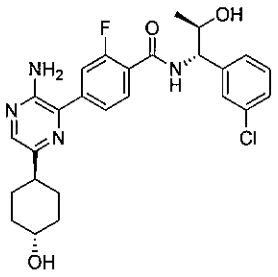
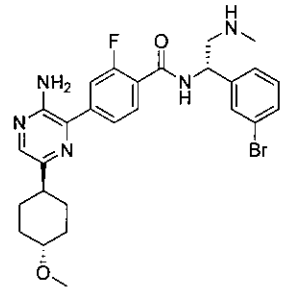
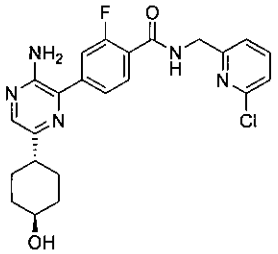
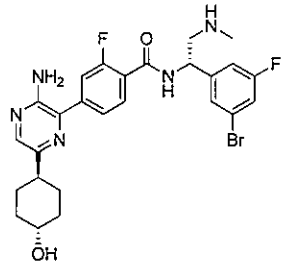
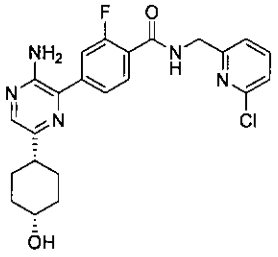
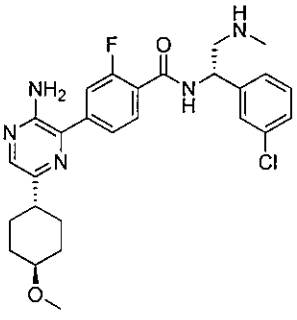
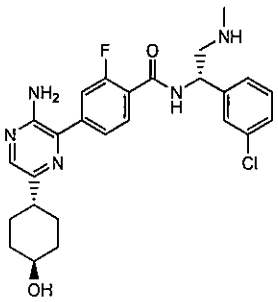
	
	
	
	

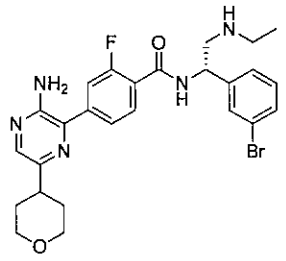
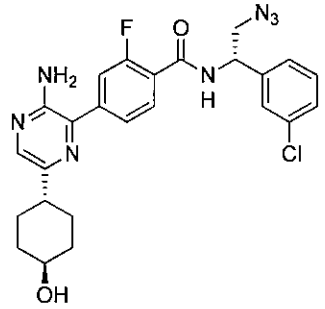
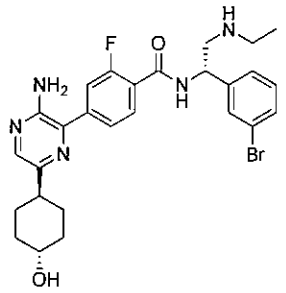
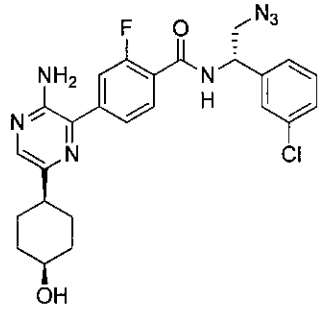
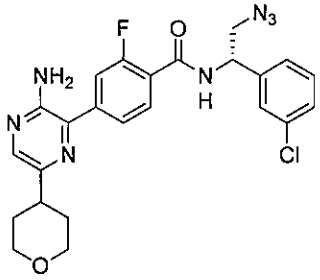
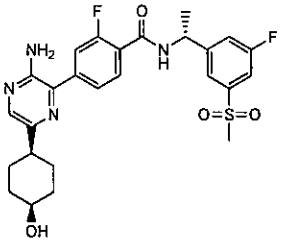
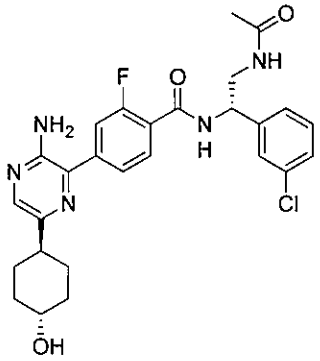
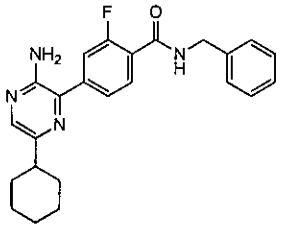
	
	
	
	

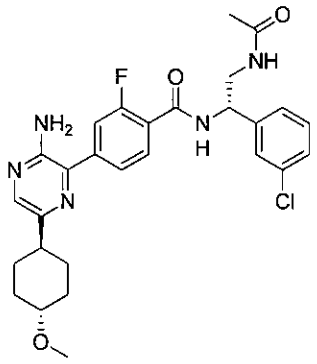
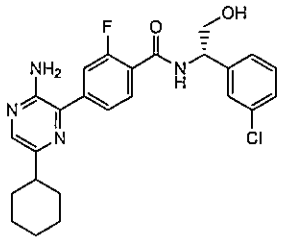
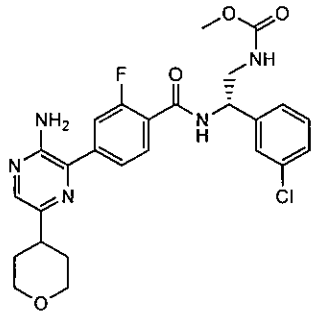
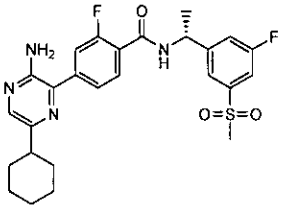
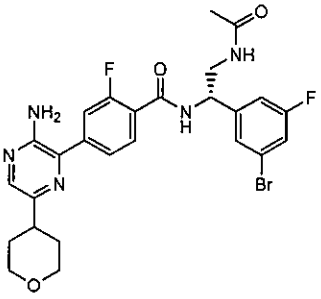
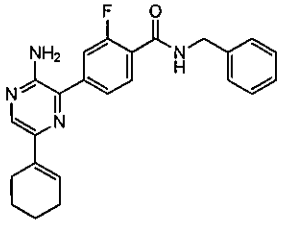
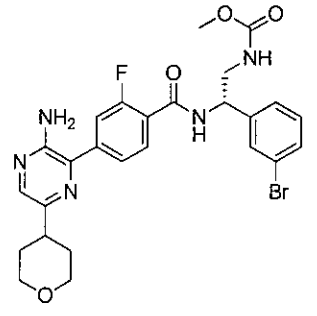
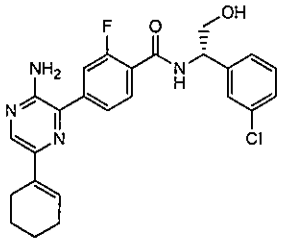
	
	
	
	

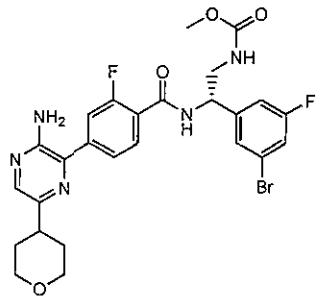
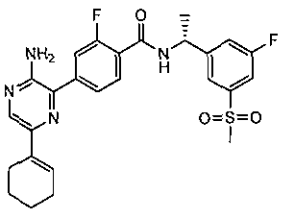
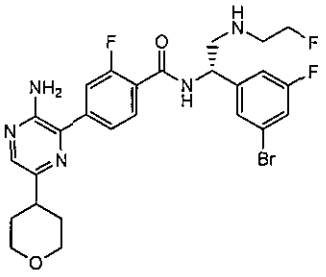
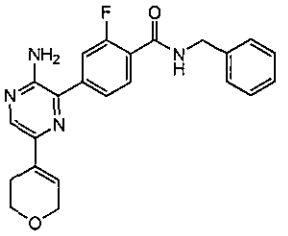
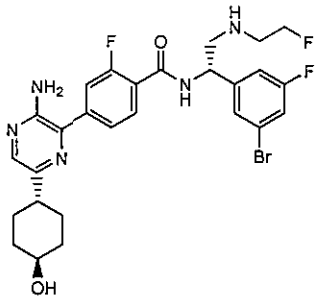
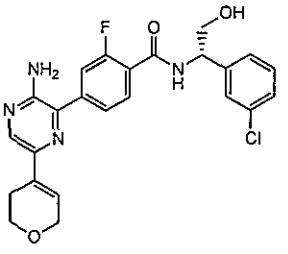
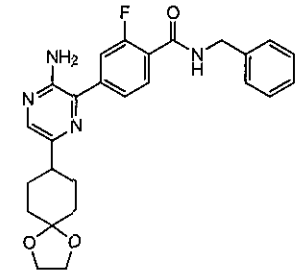
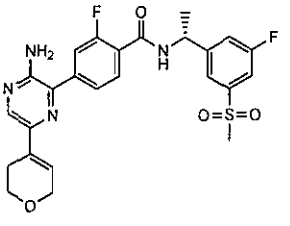
	
	
	
	
	

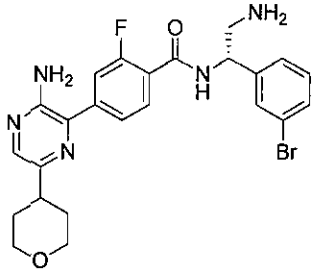
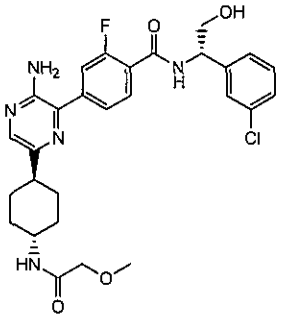
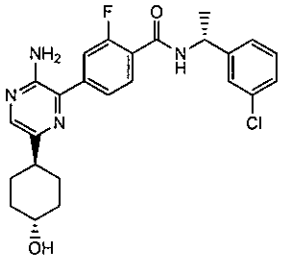
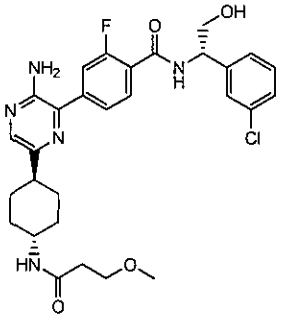
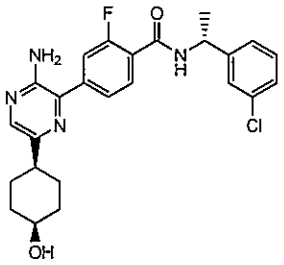
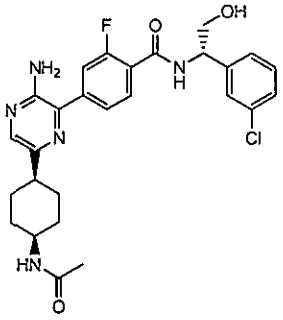
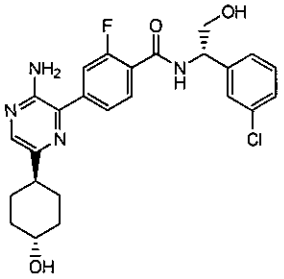
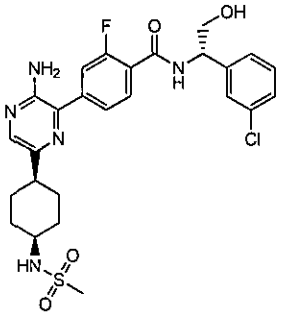
	
	
	
	
	

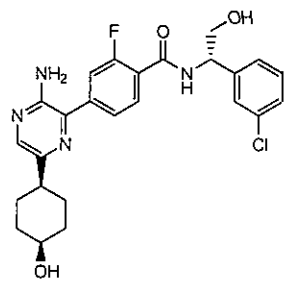
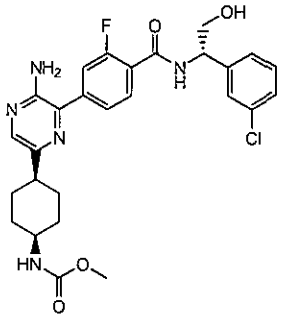
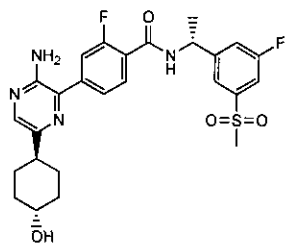
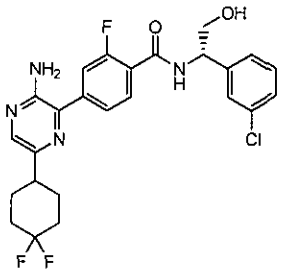
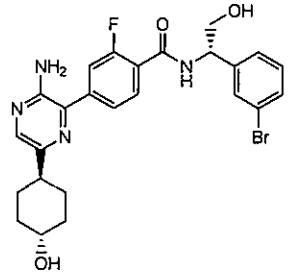
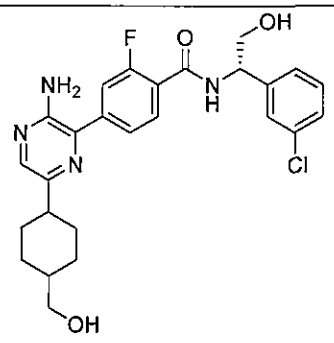
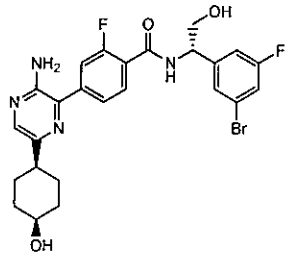
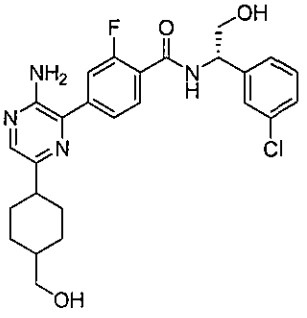
	
	
	
	

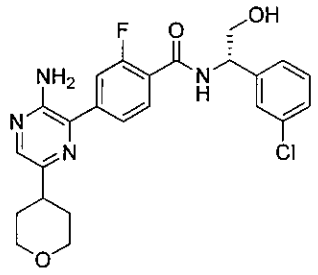
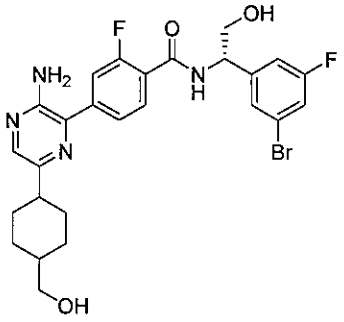
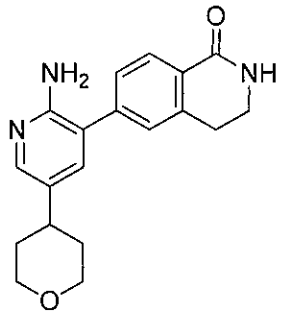
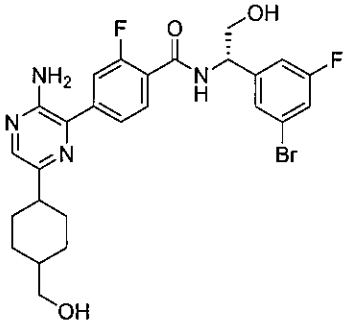
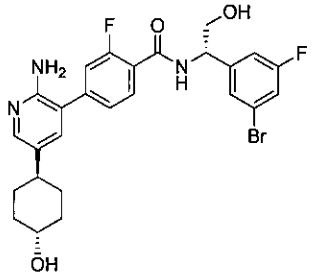
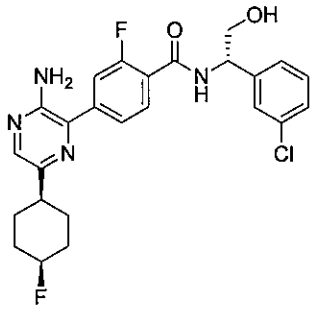
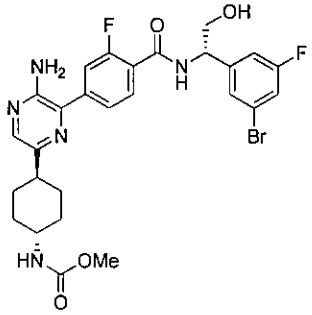
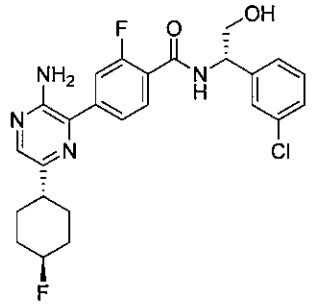
	
	
	
	

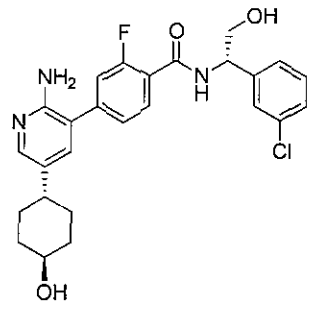
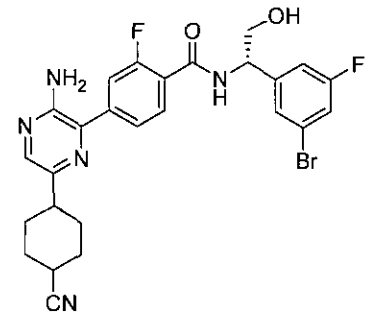
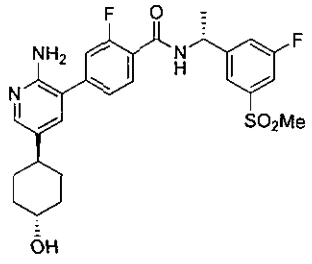
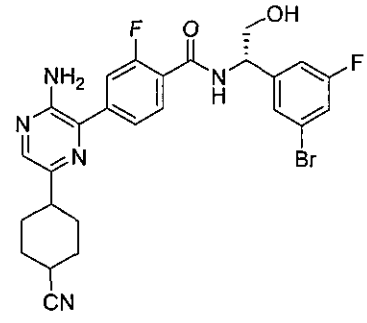
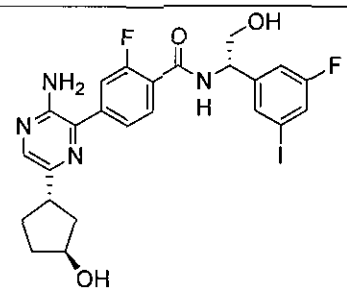
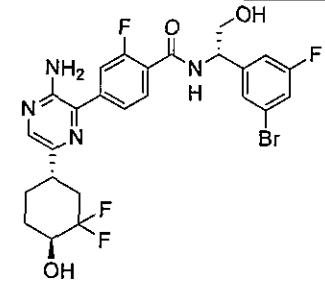
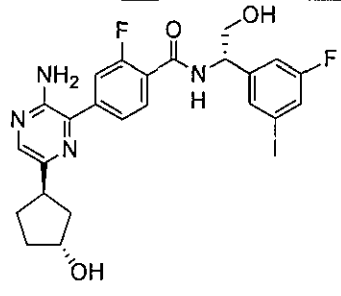
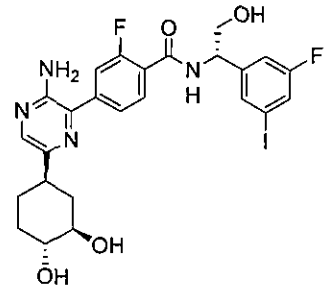
	
	
	
	

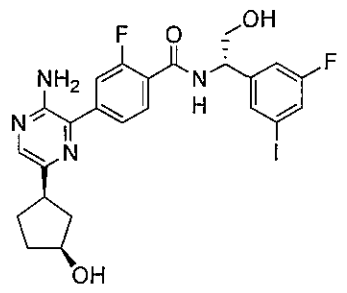
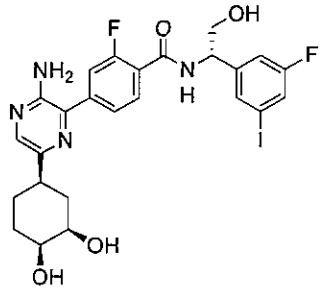
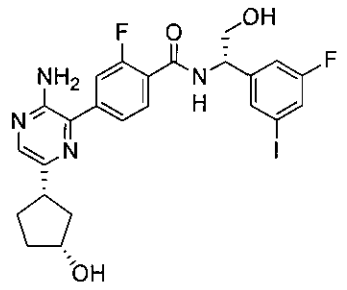
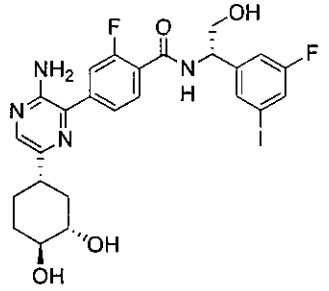
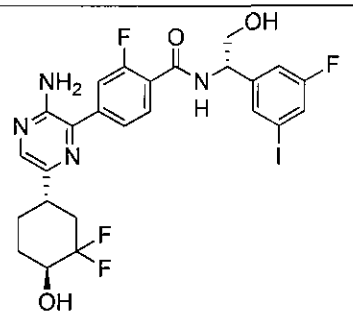
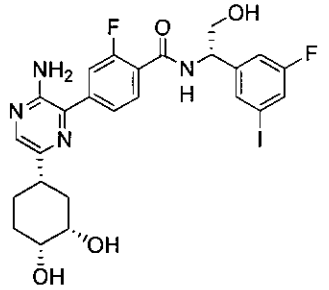
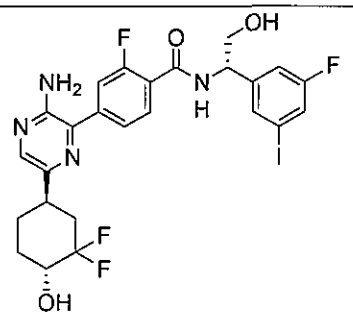
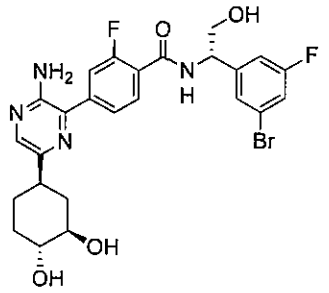
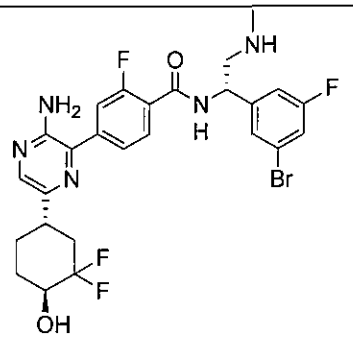
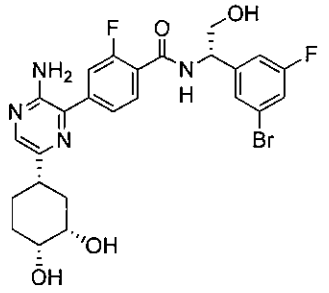
	
	
	
	

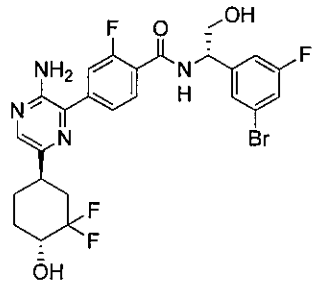
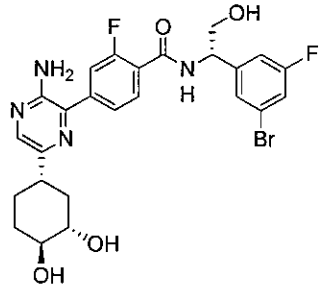
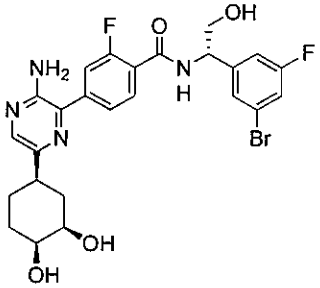
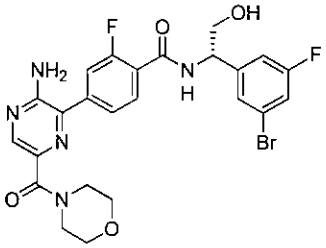
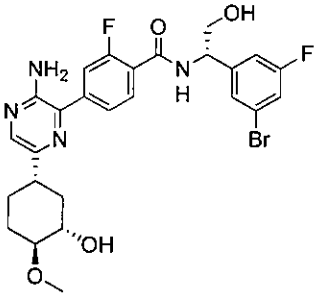
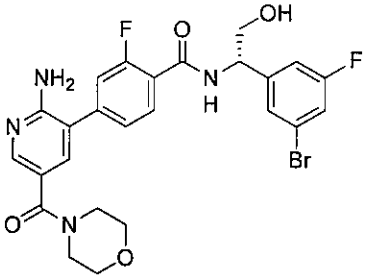
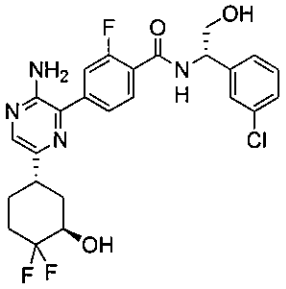
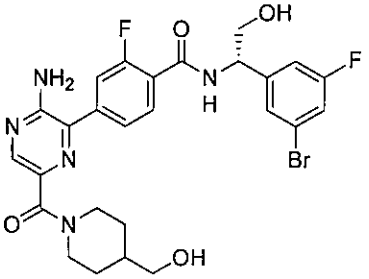
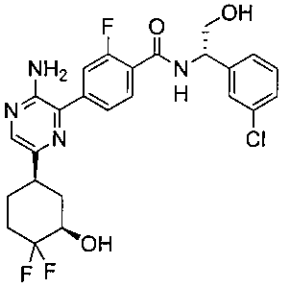
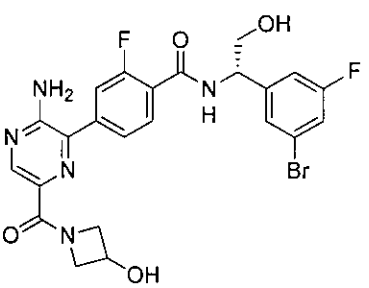
	
	
	
	

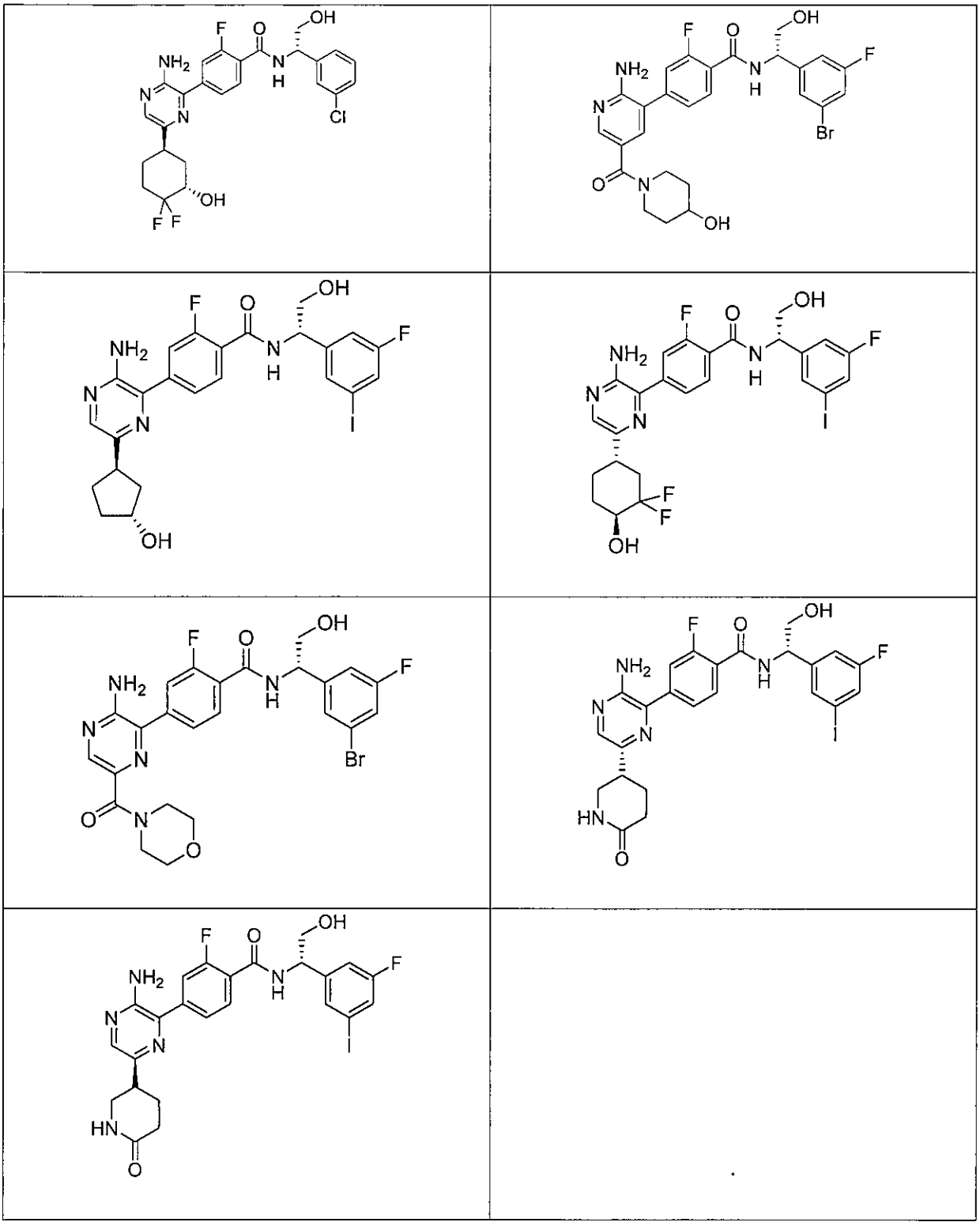
	
	
	
	

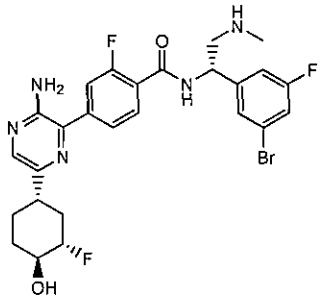
	
	
	
	
	

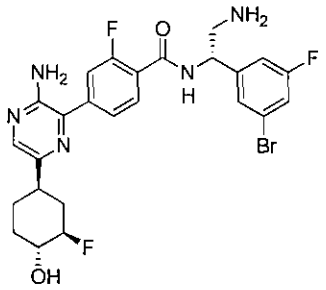


18. A pharmaceutical composition comprising a compound of claim 1 admixed with at least one pharmaceutically acceptable excipient and further comprising a therapeutic co-agent selected from anticancer compounds, analgesics, and anti-inflammatory compounds.

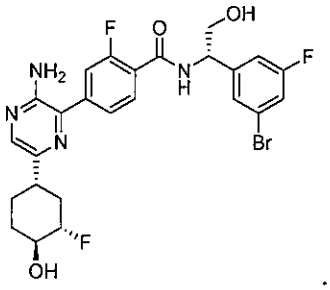
19. A compound, or a pharmaceutically acceptable salt thereof, selected from:



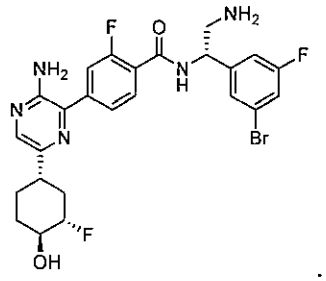
20. A compound, or a pharmaceutically acceptable salt thereof, selected from:



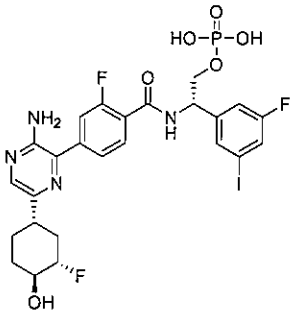
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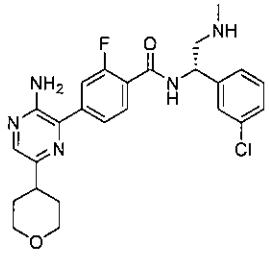
22. A compound, or a pharmaceutically acceptable salt thereof, selected from:



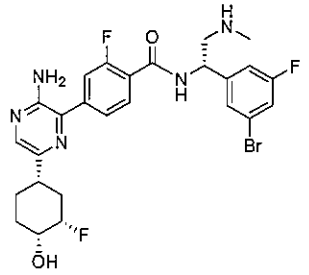
23. A compound, or a pharmaceutically acceptable salt thereof, selected from:



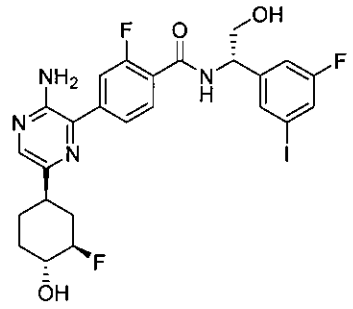
24. A compound, or a pharmaceutically acceptable salt thereof, selected from:



25. A compound, or a pharmaceutically acceptable salt thereof, selected from:



26. A compound, or a pharmaceutically acceptable salt thereof, selected from:



27. A compound, or a pharmaceutically acceptable salt thereof, selected from:

