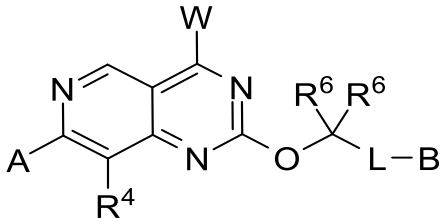
WHAT IS CLAIMED IS:

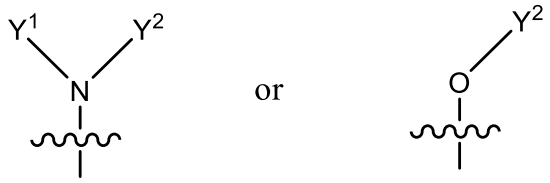
1. A compound of Formula (I):



Formula (I)

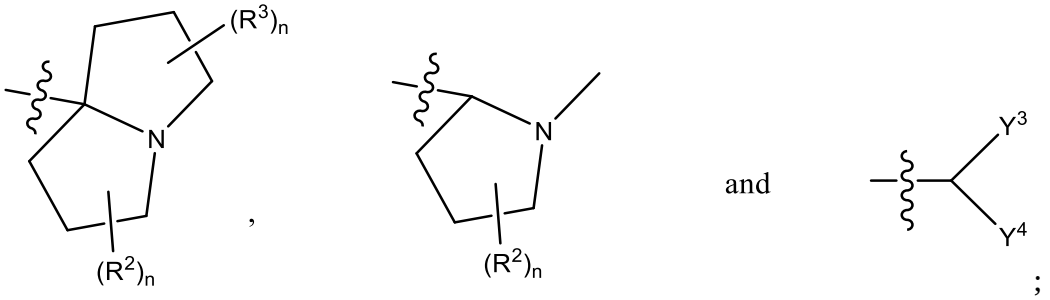
or a pharmaceutically acceptable salt thereof, wherein:

W is:



A is aryl or heteroaryl, wherein the aryl or the heteroaryl is optionally substituted with 1-4 R^1;

B is selected from:



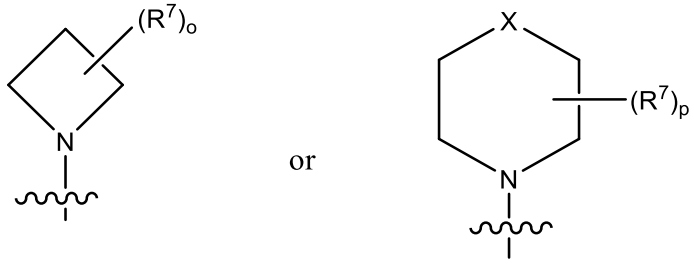
;

Y^1 is hydrogen, L-hydroxy optionally substituted with 1-4 R^8, L-alkoxy optionally substituted with 1-4 R^8, halogen, L-C3-C6 cycloalkyl optionally substituted with 1-4 R^9, L-heteroaryl optionally substituted with 1-4 R^8, L-aryl optionally substituted with 1-4 R^8, L-C(O)-NH_2, and L-heterocycle

substituted with 1-2 oxo (=O) or oxo-containing substituent, and optionally further substituted with 1-2 R^8;

Y^2 is hydrogen or C1-C4 alkyl;

or Y^1 and Y^2 join to form:

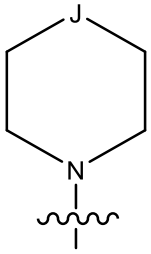


where X is selected from: a bond, -S-, -O-, -N< bound to a fused ring, $-CH_2-$, $-CH_2-N-$, $-CH_2-N-CH_2-$, $-CH_2-CH_2-CH_2-$, $-CH_2-CH_2-$, $-O-CH_2-$ and $-S-CH_2-$;

Y^3 is hydrogen or C1-C4 alkyl;

Y^4 is hydrogen or C1-C4 alkyl;

or Y^3 and Y^4 join to form:



where J is selected from: a bond, -O-, -NH-, $-CH_2-$, $-C(C1-C3\ alkyl)_2-$, -CH(C1-C3alkyl)- and -N(C1-C3 alkyl)-;

each R^1 is independently halogen, cyano, hydroxy, C1-C4 alkyl, -S-C1-C3 alkyl, C2-C4 alkenyl, C2-C4 alkynyl, C2-C4 hydroxyalkynyl, C1-C3 cyanoalkyl , triazolyl, C1-C3 haloalkyl, -O-C1-C3 haloalkyl, -S-C1- C3 haloalkyl, C1-C3 alkoxy, hydroxyC1-C3 alkyl, $-CH_2C(=O)N(R^5)_2$, -C3-C4 alkynyl$(NR^5)_2$, $-N(R^5)_2$, deuteroC2-C4 alkynyl, (C1-C3 alkoxy)haloC1-C3 alkyl-, or C3-C6 cycloalkyl wherein said C3-C6 cycloalkyl is optionally substituted with halogen or C1-C3 alkyl;

each R^2 is independently hydrogen, hydroxy, halogen, cyano, C1-C3 alkyl, C1-C3 cyanoalkyl, C1-C3 hydroxyalkyl, HC(=O)-, -L-OC(O)N(R^5)$_2$, -CO_2R^5, or -CO_2N(R^5)$_2$;

each R^3 is independently hydrogen, hydroxy, halogen, cyano, C1-C3 alkyl, C1-C3 cyanoalkyl, C1-C3 hydroxyalkyl, HC(=O)-, -L-OC(O)N(R^5)$_2$, -CO_2R^5, or -CO_2N(R^5)$_2$;

each R^4 is independently hydrogen, halogen or C1 – C3 alkyl;

each R^5 is independently hydrogen or C1-C3 alkyl, or two R^5 join to form cycloalkyl or heterocycle;

each R^6 is independently hydrogen, hydroxy, C1-C4 hydroxyalkyl or heteroaryl,

or two R^6 join to form C3-C6 cycloalkyl or heterocycle;

each R^7 is independently hydrogen, C1-C3 alkyl, hydroxy, halogen, C1-C3 haloalkyl, -L-NH_2, -NH(C1-C3 alkyl), -N(C1-C3 alkyl)$_2$, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)N(R^{10})$_2$, -NHC(O)H , -CN, aryl, -(CH_2)$_{1-2}$S(O)$_2$N(R^{10})$_2$, -NH-S(O)$_2$N(R^{10})$_2$, -O-S(O)$_2$N(R^{10})$_2$, S(O)$_2R^{10}$,or heteroaryl or heterocycle optionally independently substituted with 1-2 substituents independently selected from C1-C3 alkyl, -CN and C(O)NH_2,

two R^7 on the same atom optionally join to form a spirocyclic ring selected from C3-C6 cycloalkyl and heterocycle, where said spirocyclic ring is optionally substituted with 1-4 substituents independently selected from oxo (=O), halogen, hydroxy, C1-C3 alkyl and -O-(C1-C3 alkyl),

two R^7 on adjacent atoms optionally join to form a bond or a fused ring selected from C3-C6 cycloalkyl optionally substituted with 1-4 R^8, heteroaryl optionally substituted with 1-4 R^8, aryl optionally substituted with 1-4 R^8, and heterocycle optionally substituted with 1-4 R^8, and

two R^7 on non-adjacent atoms optionally join to form a 1-2 carbon bridge;

each R^8 is independently C1-C3 alkyl, hydroxy, halogen, -N(R10)$_2$, -N(R10)C(O)R10, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)N(R10)$_2$, heteroaryl or -CN;

each R^9 is independently C1-C3 alkyl, hydroxy, halogen, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)NH_2, -C(O)NH(C1-C3 alkyl), -C(O)N(C1-C3 alkyl)$_2$ or -CN;

each R^{10} is independently hydrogen, halogen, C1-C3 alkyl, or two R^{10} join to form cycloalkyl or heterocycle optionally substituted with 1-2 C1-C3 alkyl;

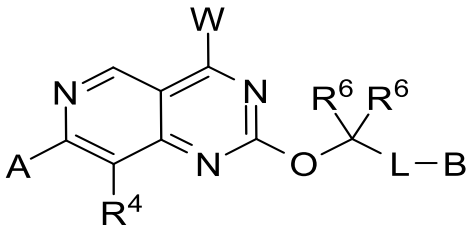
each L is independently a bond, -C1-C4 alkyl-, -C1-C4 alkyl-NH-, -NH-, -N(C1-C3 alkyl)- or cyclopropyl-CH_2-;

each n is 0-3;

o is 1-6; and

p is 1-8.

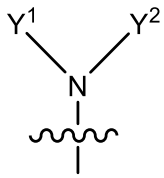
2. A compound of Formula (I):



Formula (IA)

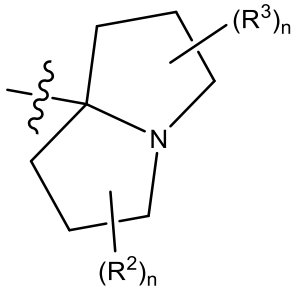
or a pharmaceutically acceptable salt thereof, wherein:

W is:



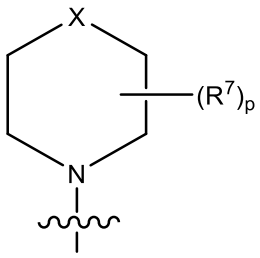
A is naphthyl optionally substituted with 1-4 R^1;

B is from :



;

Y^1 and Y^2 join to form:



where X is selected from: $-CH_2-$, $-CH_2-CH_2-$ and $-O-CH_2-$;

each R^1 is independently halogen, cyano, hydroxy, C1-C4 alkyl, -S-C1-C3 alkyl, C2-C4 alkenyl, C2-C4 alkynyl, C2-C4 hydroxyalkynyl, C1-C3 cyanoalkyl , triazolyl, C1-C3 haloalkyl, -O-C1-C3 haloalkyl, -S-C1- C3 haloalkyl, C1-C3 alkoxy, hydroxyC1-C3 alkyl, $-CH_2C(=O)N(R^5)_2$, -C3-C4 alkynyl$(NR^5)_2$, $-N(R^5)_2$, deuteroC2-C4 alkynyl, (C1-C3 alkoxy)haloC1-C3 alkyl-, or C3-C6 cycloalkyl wherein said C3-C6 cycloalkyl is optionally substituted with halogen or C1-C3 alkyl;

each R^2 is independently hydrogen, hydroxy, halogen, cyano, C1-C3 alkyl, C1-C3 cyanoalkyl, C1-C3 hydroxyalkyl, HC(=O)-, -L-$OC(O)N(R^5)_2$, $-CO_2R^5$, or $-CO_2N(R^5)_2$;

each R^3 is independently hydrogen, hydroxy, halogen, cyano, C1-C3 alkyl, C1-C3 cyanoalkyl, C1-C3 hydroxyalkyl, HC(=O)-, -L-$OC(O)N(R^5)_2$, $-CO_2R^5$, or $-CO_2N(R^5)_2$;

each R^4 is independently hydrogen, halogen or C1 – C3 alkyl;

each R^5 is independently hydrogen or C1-C3 alkyl, or two R5 join to form cycloalkyl or heterocycle;

each R^6 is independently hydrogen, hydroxy, C1-C4 hydroxyalkyl or heteroaryl,

or two R^6 join to form C3-C6 cycloalkyl or heterocycle;

each R^7 is independently hydrogen, C1-C3 alkyl, hydroxy, halogen, C1-C3 haloalkyl, -L-NH_2, -NH(C1-C3 alkyl), -N(C1-C3 alkyl)$_2$, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)N(R^{10})$_2$, -NHC(O)H , -CN, aryl, -(CH_2)$_{1-2}$S(O)$_2$N(R^{10})$_2$, -NH-S(O)$_2$N(R^{10})$_2$, -O-S(O)$_2$N(R^{10})$_2$, S(O)$_2$$R^{10}$,or heteroaryl or heterocycle optionally independently substituted with 1-2 substituents independently selected from C1-C3 alkyl, -CN and C(O)NH_2,

two R^7 on the same atom optionally join to form a spirocyclic ring selected from C3-C6 cycloalkyl and heterocycle, where said spirocyclic ring is optionally substituted with 1-4 substituents independently selected from oxo (=O), halogen, hydroxy, C1-C3 alkyl and -O-(C1-C3 alkyl),

two R^7 on adjacent atoms optionally join to form a bond or a fused ring selected from C3-C6 cycloalkyl optionally substituted with 1-4 R^8, heteroaryl optionally substituted with 1-4 R^8, aryl optionally substituted with 1-4 R^8, and heterocycle optionally substituted with 1-4 R^8, and

two R^7 on non-adjacent atoms optionally join to form a 1-2 carbon bridge;

each R^8 is independently C1-C3 alkyl, hydroxy, halogen, -N(R10)$_2$, -N(R10)C(O)R10, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)N(R10)$_2$, heteroaryl or -CN;

each R^9 is independently C1-C3 alkyl, hydroxy, halogen, oxo (=O), -O-(C1-C3 alkyl), -(C1-C3 alkyl)-OH, -C(O)OH, -C(O)O(C1-C3 alkyl), -C(O)NH_2, -C(O)NH(C1-C3 alkyl), -C(O)N(C1-C3 alkyl)$_2$ or -CN;

each R^{10} is independently hydrogen, halogen, C1-C3 alkyl, or two R^{10} join to form cycloalkyl or heterocycle optionally substituted with 1-2 C1-C3 alkyl;

each L is independently a bond, -C1-C4 alkyl-, -C1-C4 alkyl-NH-, -NH-, -N(C1-C3 alkyl)- or cyclopropyl-CH_2-;

each n is 0-3;

o is 1-6; and

p is 1-8.

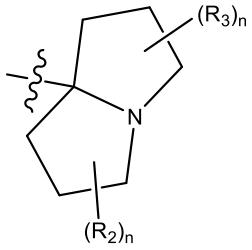
3. The compound or salt of claim 2, wherein each R1 is independently selected from halogen, hydroxy, C1-C3 alkoxy and C1-C4 alkyl.

4. The compound or salt of claim 2, wherein each R2, if present, is selected from hydrogen and halogen, and wherein each R3, if present, is selected from hydrogen and halogen.

5. The compound or salt of claim 2, wherein each R7 is independently selected from hydrogen, C1-C4 alkyl, hydroxy, C1-C3 alkoxy, and wherein two R7 on non-adjacent atoms optionally join to form a 1-2 carbon bridge.

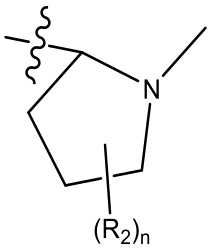
6. The compound or salt of claim 2, wherein each R6 is independently hydrogen or hydroxy.

7. The compound or salt of claim 1, wherein B is:



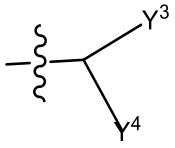
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8. The compound or salt of claim 1, wherein B is:



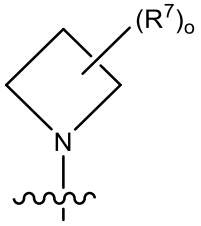
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9. The compound or salt of claim 1, wherein B is:

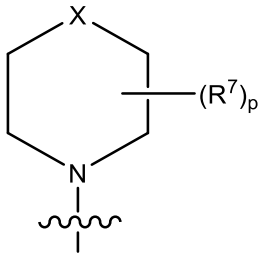


.

10. The compound or salt of any of claims 1-3, wherein Y^1 and Y^2 join to form:

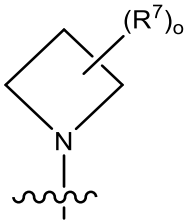


or



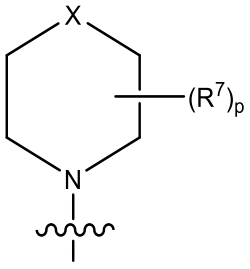
.

11. The compound or salt of claim 4, wherein Y^1 and Y^2 join to form:



.

12. The compound or salt of claim 4, wherein Y^1 and Y^2 join to form:



.

13. The compound or salt of any of claims 1-6, wherein A is naphthyl.

14. The compound or salt of any of claims 1-6, wherein A is indazolyl.

15. The compound or salt of any of claims X, wherein A is phenyl.

16. The compound or salt of any of claims X, wherein A is pyridyl.

17. The compound or salt of any of claims 1-6, wherein at least one R^1 is C1-C4 alkyl.

18. The compound or salt of any of claims 1-6, wherein at least one R^1 is halogen

19. The compound or salt of claim 10, wherein said halogen is a fluorine.

20. The compound or salt of any of claims 1-6, wherein at least one R^1 is hydroxy.

21. The compound or salt of any of claims 1-6, wherein one R^2 is C1-C4 alkyl.

22. The compound or salt of any of claims 1-6, wherein at least one R^2 is halogen.

23. The compound or salt of claim 14, wherein said halogen is a fluorine.

24. The compound or salt of any of claims 1-6, wherein at least one R^2 is hydroxy.

25. The compound or salt of any of claims 1-6, wherein at least one R^3 is C1-C4 alkyl.

26. The compound or salt of any of claims 1-6, wherein at least one R^3 is halogen.

27. The compound or salt of claim 18, wherein said halogen is fluorine.

28. The compound or salt of any of claims 1-6, wherein at least one R^3 is hydroxy.

29. The compound or salt of any of claims 1-6, wherein R^4 is halogen.

30. The compound or salt of claim 21, wherein said halogen is fluorine.

31. The compound or salt of any of claims 1-6, wherein at least one R^5 is C1-C4 alkyl.

32. The compound or salt of any of claims 1-6, wherein at least one R^5 is hydrogen.

33. The compound or salt of any of claims 1-6, wherein one or both R^6 are C1-C4 alkyl.

34. The compound or salt of any of claims 1-6, wherein one or both R^6 are hydrogen.

35. The compound or salt of any of claims 1-6, wherein two R^6 join to form C3-C6 cycloalkyl or heterocycle.

36. The compound or salt of any of claims 1-6, wherein Y^1 is L-C3-C6 cycloalkyl, L-heteroaryl, L-aryl, or L-heterocycle, where L is a bond, C1-C4 alkyl, NH or N(C1-C3) alkyl.

37. The compound or salt of claim 27, wherein Y^1 is L-heteroaryl, where said heteroaryl is thietane dioxide, iso-thiazolidine dioxide, imidazopyrazine, pyridine or pyrimidine.

38. The compound or salt of claim 27, wherein Y^1 is L-C3-C6 cycloalkyl.

39. The compound or salt of claim 30, wherein the cycloalkyl is cyclobutane, cyclopentane, cyclohexane or cycloheptane.

40. The compound or salt of claim 27, wherein Y^1 is L-heterocycle.

41. The compound or salt of claim 32, wherein the heterocycle is pyrrolidinone.

42. In certain embodiments of the invention Y^2 is hydrogen.

43. The compound or salt of any of claims 1-6, wherein Y^2 is C1-C4 alkyl;

44. The compound or salt of any of claims 1-6, wherein at least one R^8 is C1-C4 alkyl.

45. The compound or salt of any of claims 1-6, wherein at least one R^8 is hydroxy or C1-C3 alkyl-hydroxy.

46. The compound or salt of any of claims 1-6, wherein one or two R^8 are oxo (=O).

47. The compound or salt of any of claims 1-6, wherein at least one R^8 is aryl or heteroaryl.

48. The compound or salt of any of claims 1-6, wherein at least one R^8 is C(O)OH.

49. The compound or salt of any of claims 1-6, wherein at least one R^8 is $-C(O)NH_2$, -C(O)NH(C1-C3 alkyl) or $-C(O)N(C1\text{-}C3\ alkyl)_2$.

50. The compound or salt of any of claims 1-6, wherein at least one R^8 is $-NH_2$, -NH(C1-C3 alkyl); $-N(C1\text{-}C3\ alkyl)_2$.

51. The compound or salt of any of claims 1-6, wherein at least one R^9 is C1-C4 alkyl.

52. The compound or salt of any of claims 1-6, wherein at least one R^9 is hydroxy or C1-C3 alkyl-hydroxy.

53. The compound or salt of any of claims 1-6, wherein one or two R^9 is oxo (=O).

54. The compound or salt of any of claims 1-6, wherein at least one R^9 is aryl or heteroaryl.

55. The compound or salt of any of claims 1-6, wherein at least one R^9 is C(O)OH.

56. The compound or salt of any of claims 1-6, wherein at least one R^9 is -C(O)NH_2, -C(O)NH(C1-C3 alkyl) or -C(O)N(C1-C3 alkyl)$_2$.

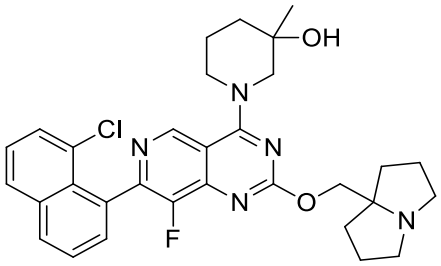
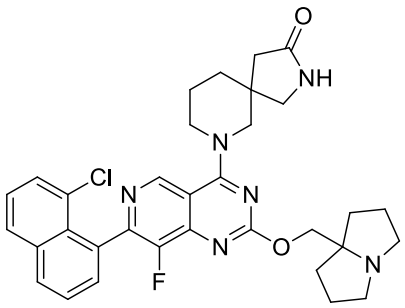
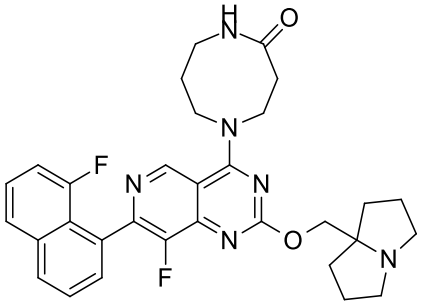
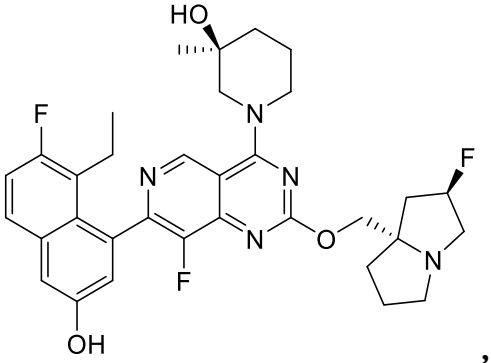
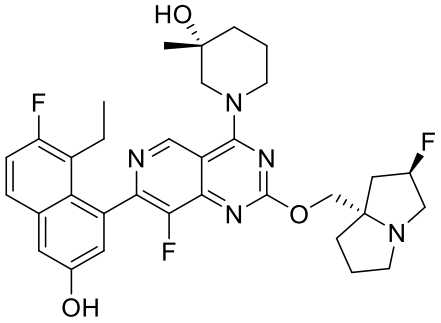
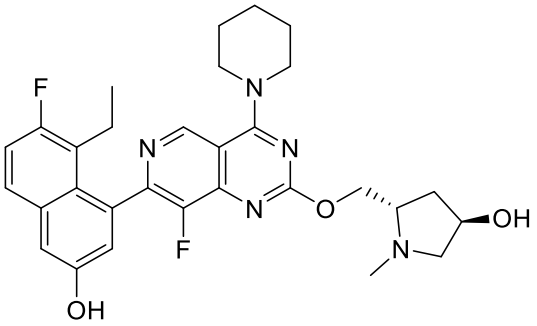
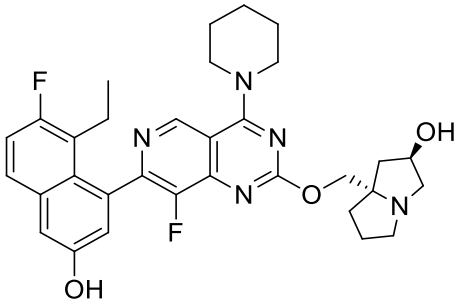
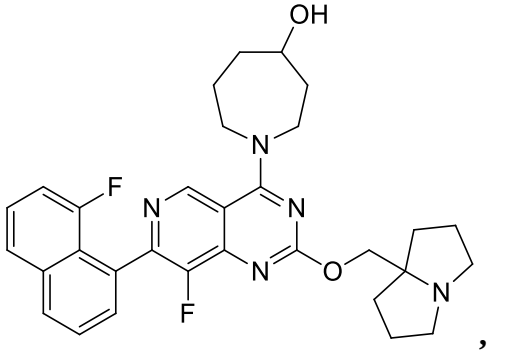
57. The compound or salt of any of claims 1-6, wherein Y^1 and Y^2 join to form piperidine, azepane, azocane, thiazepine, diazepane, oxazepane, azetidine, pyrrolidine, piperazine bound to a fused ring via nitrogen or thiomorpholine.

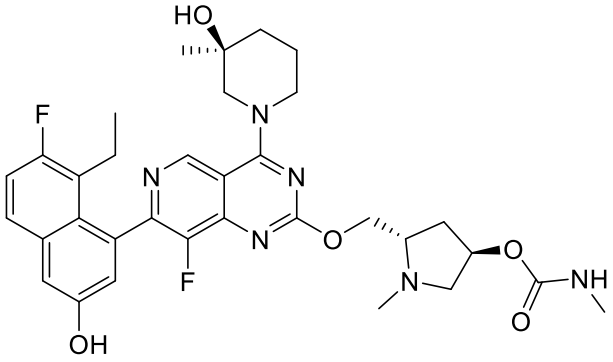
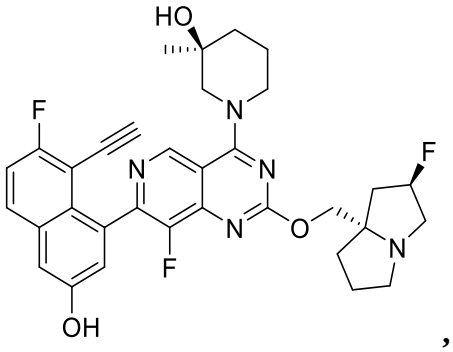
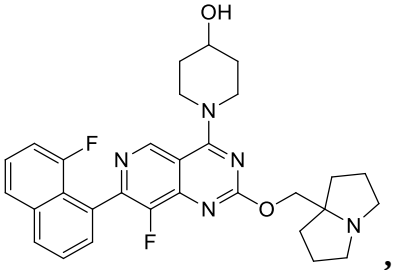
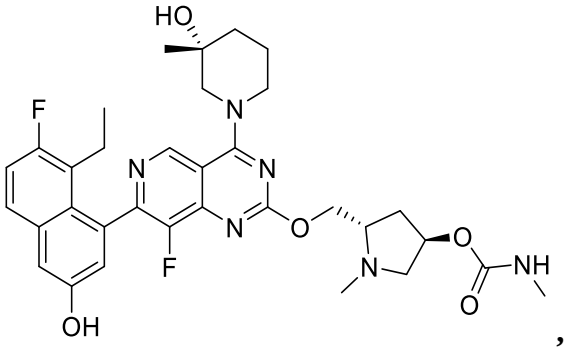
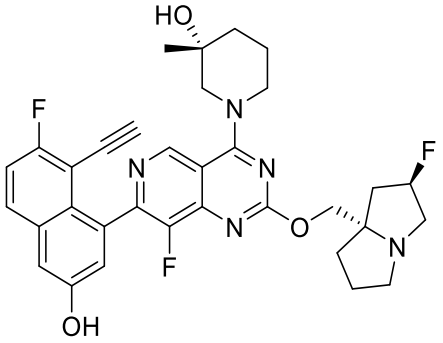
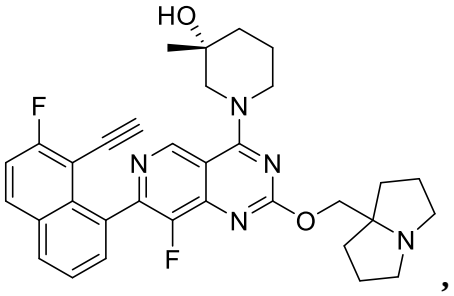
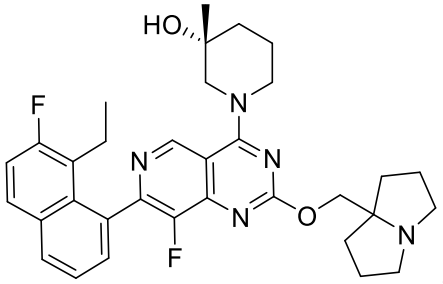
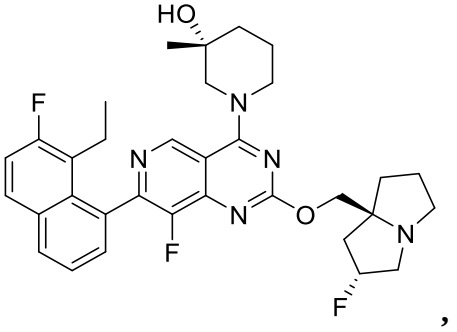
58. The compound or salt of any of claims 1-6, wherein two R^7 on the same atom join to form a spirocyclic ring selected from C3-C6 cycloalkyl and heterocycle, where said spirocyclic ring is optionally substituted with one or more substituents selected from oxo (=O), halogen, hydroxy, C1-C3 alkyl and -O-(C1-C3 alkyl).

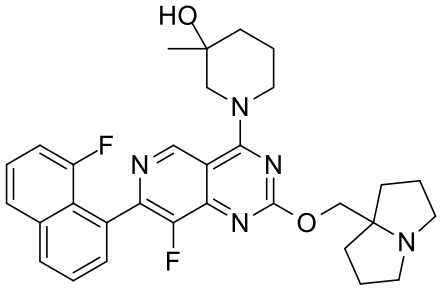
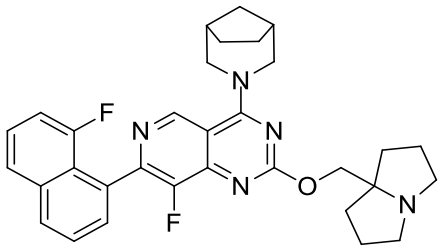
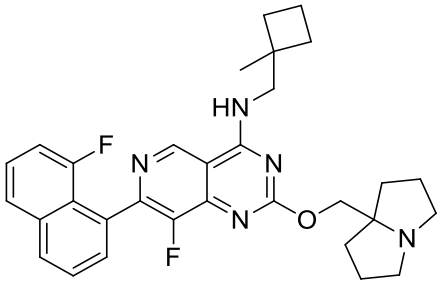
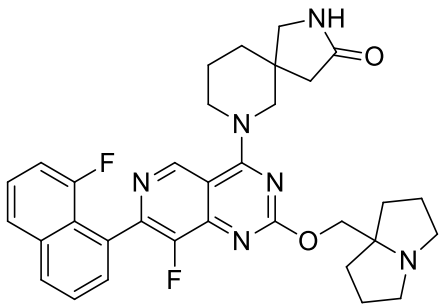
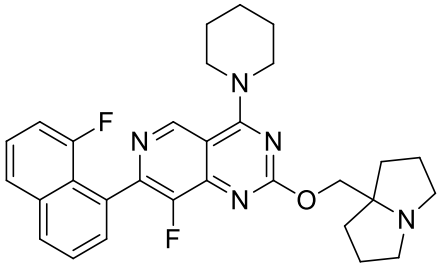
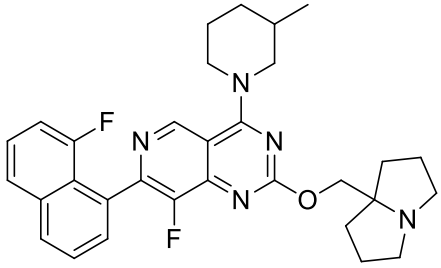
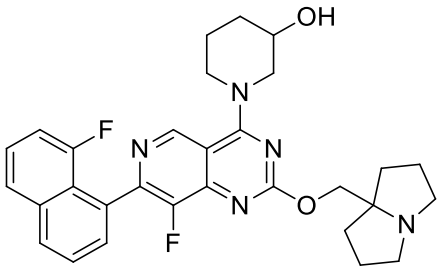
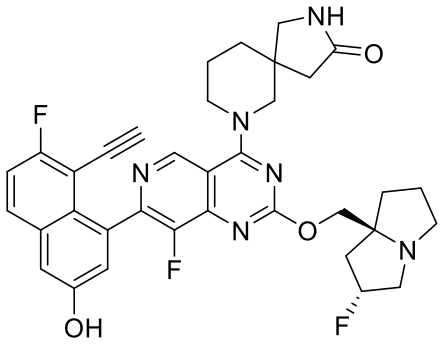
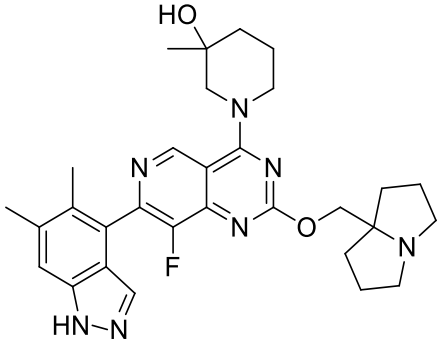
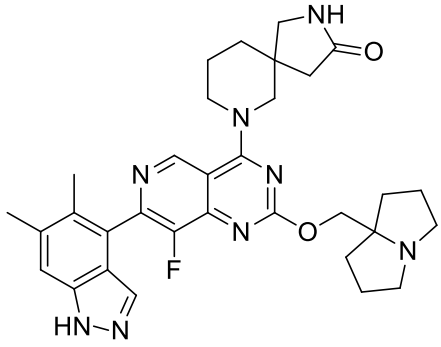
59. The compound or salt of any of claims 1-6, wherein two R^7 on adjacent atoms join to form a bond or a fused ring selected from C3-C6 cycloalkyl optionally substituted with 1-4 R^8; heteroaryl optionally substituted with 1-4 R^8; aryl optionally substituted with 1-4 R^8, and heterocycle optionally substituted with 1-4 R^8.

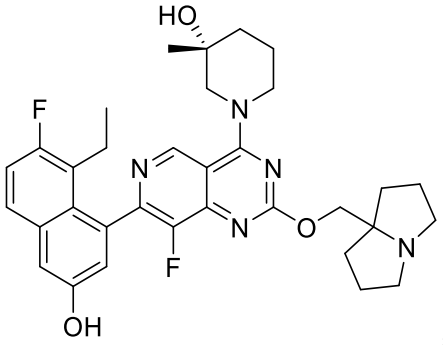
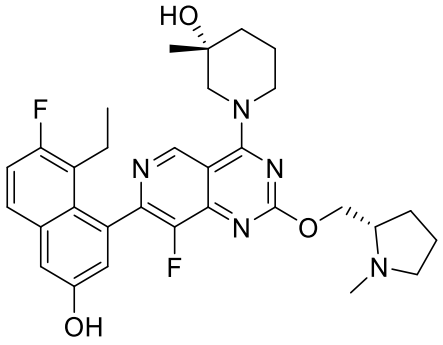
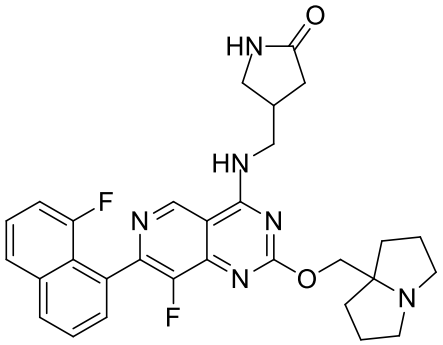
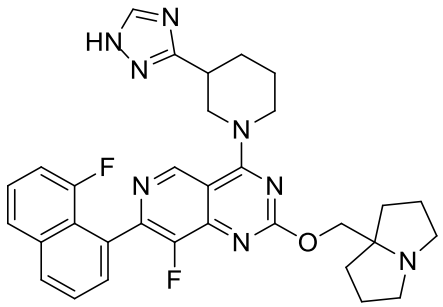
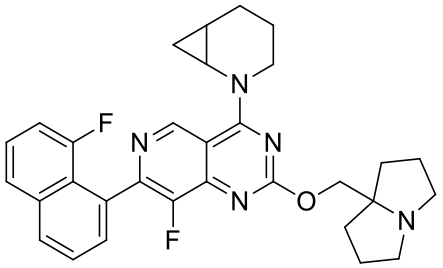
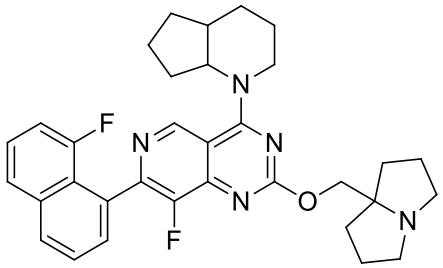
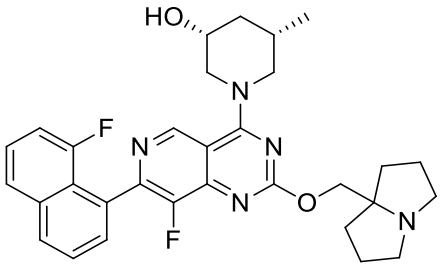
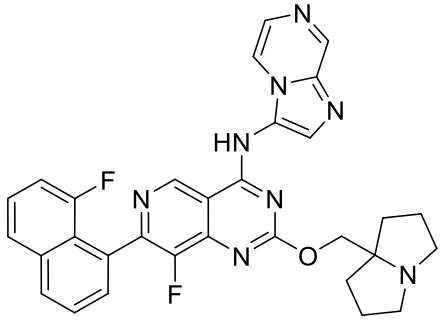
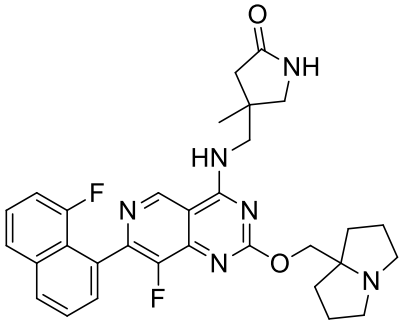
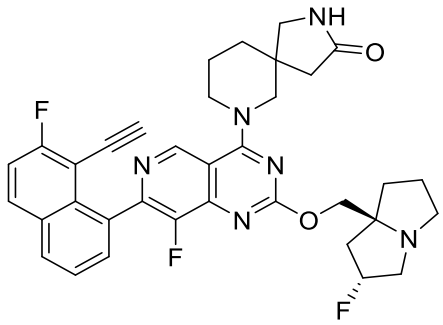
60. The compound or salt of any of claims 1-6, wherein two R^7 on non-adjacent atoms join to form a 1-2 carbon bridge.

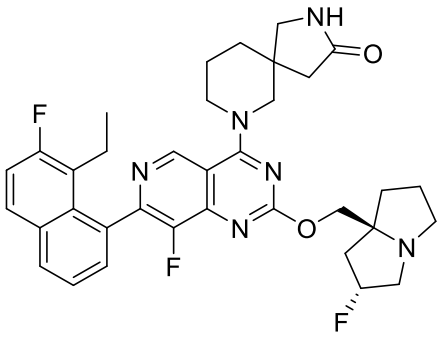
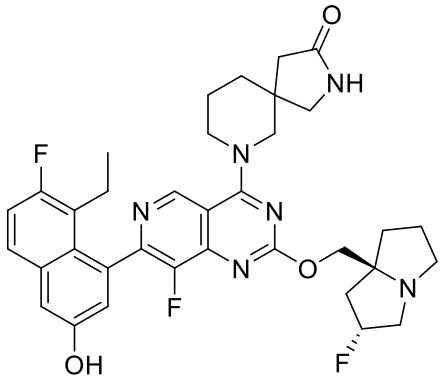
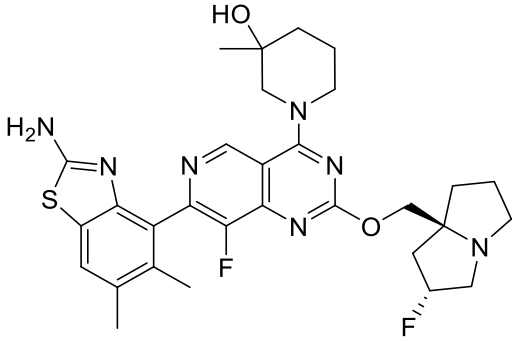
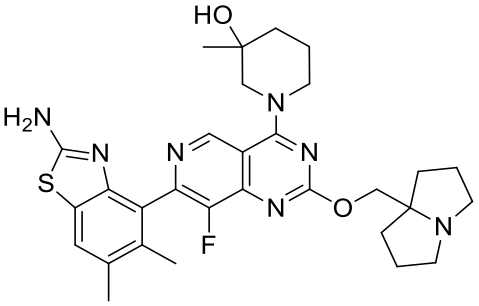
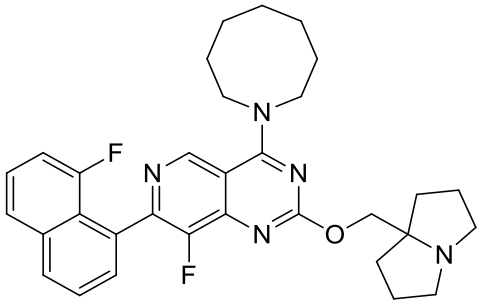
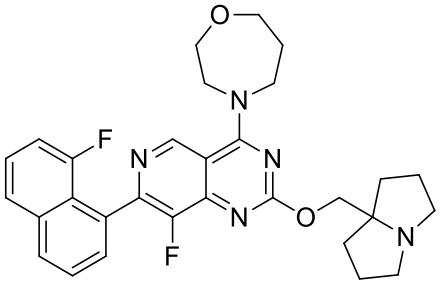
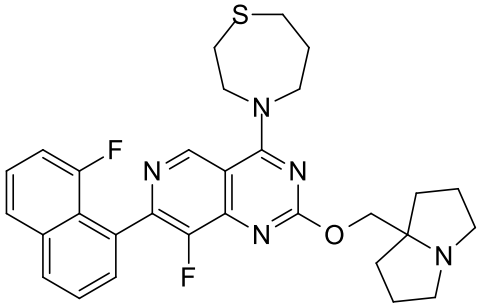
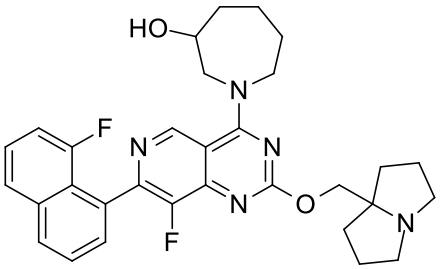
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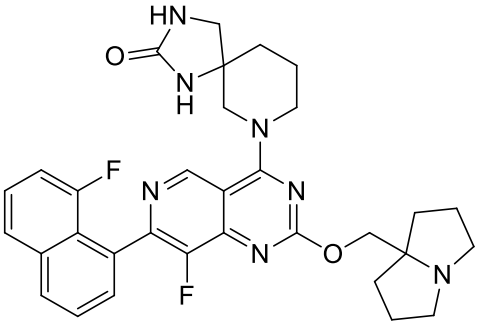
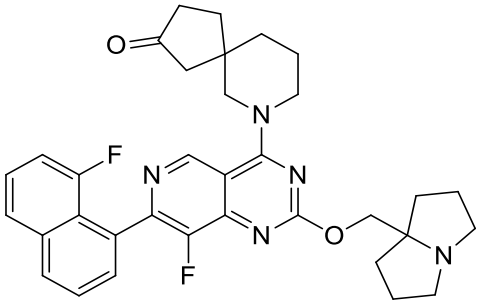
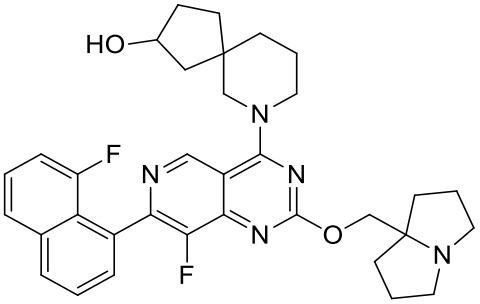
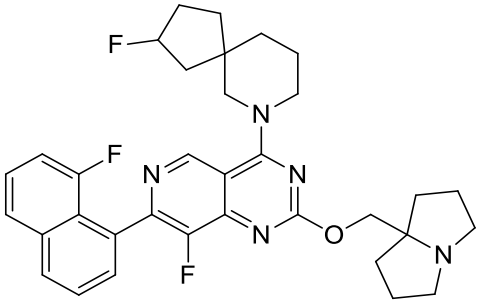
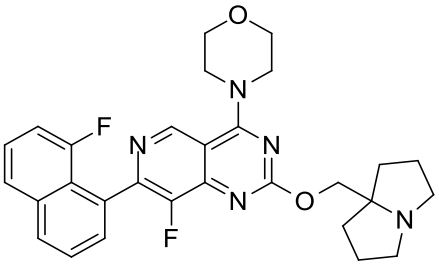
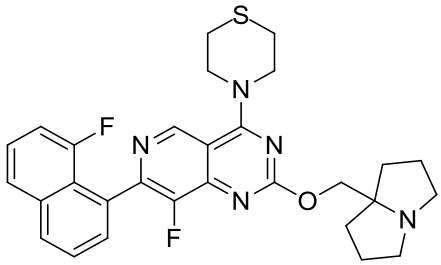
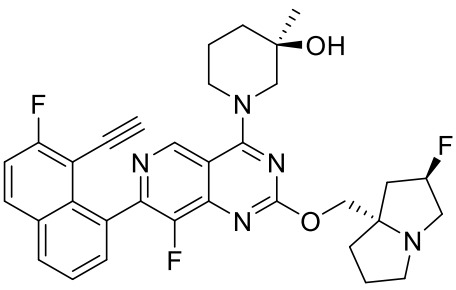
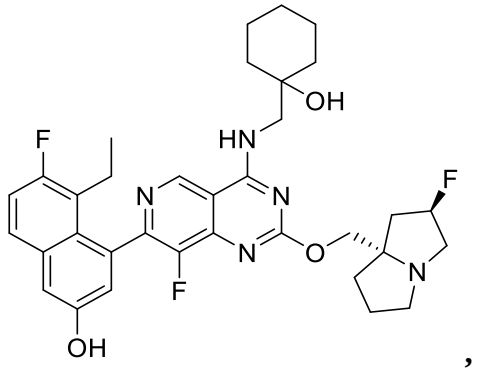
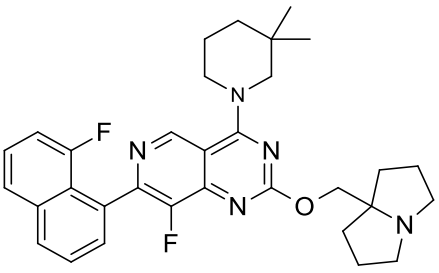
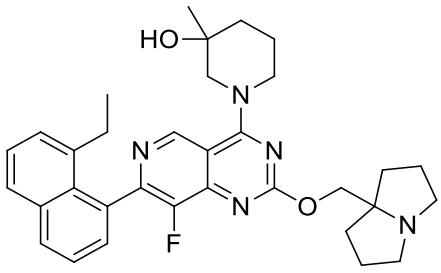









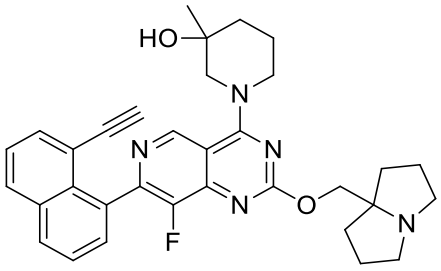
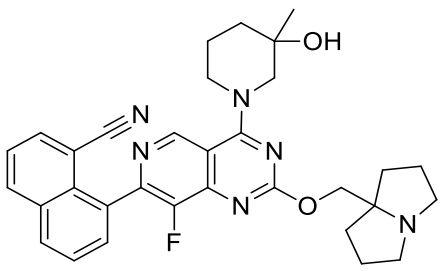
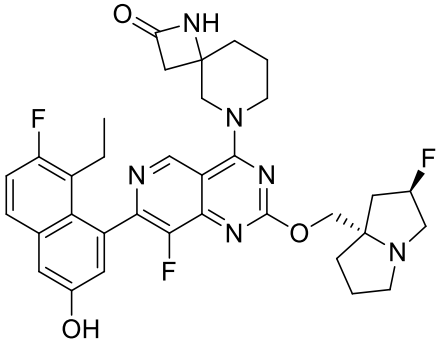
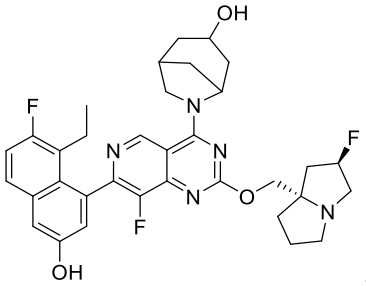
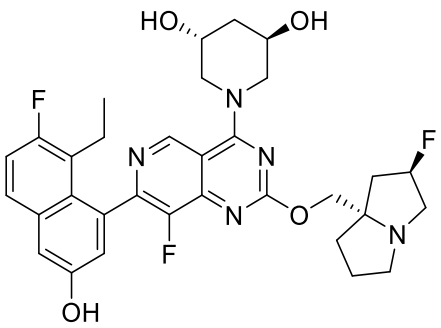
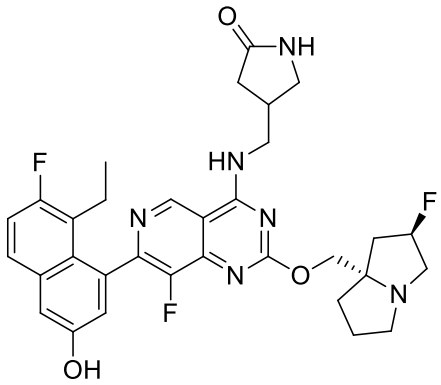
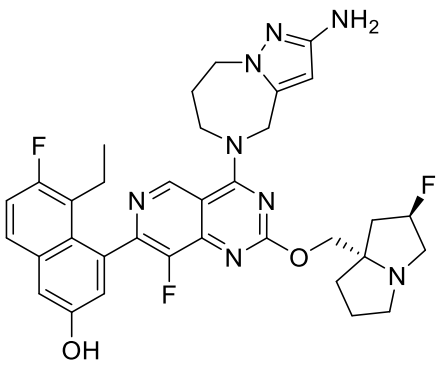
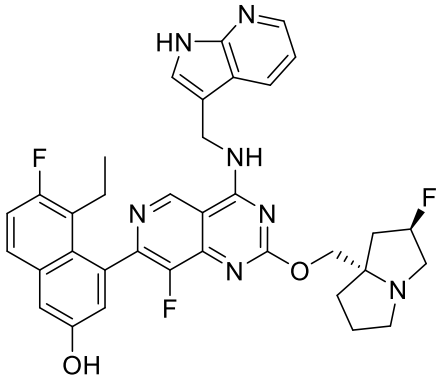

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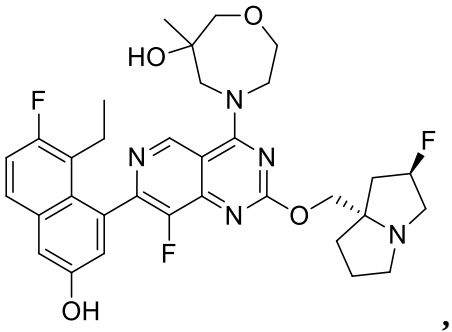
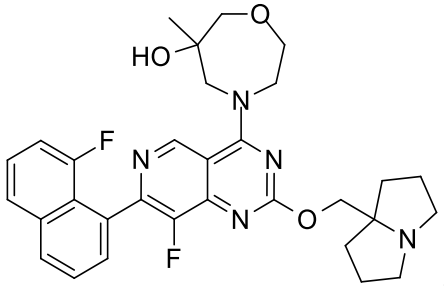
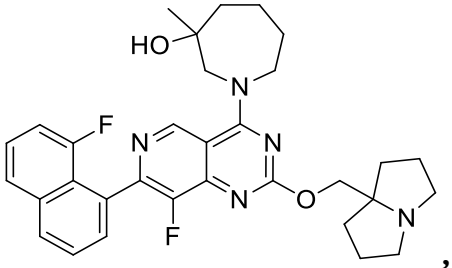
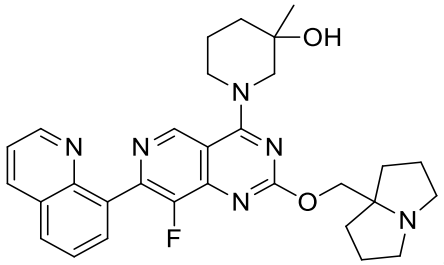
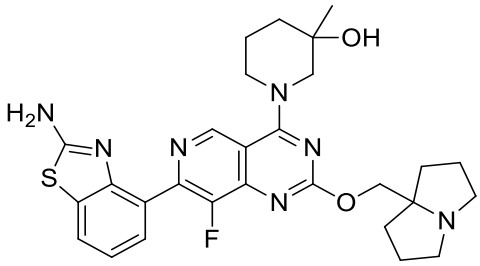
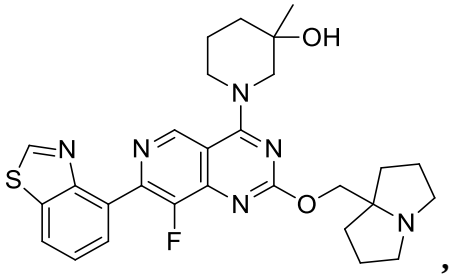
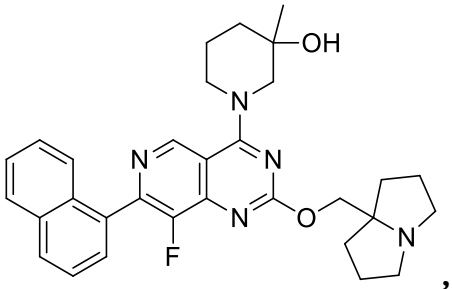
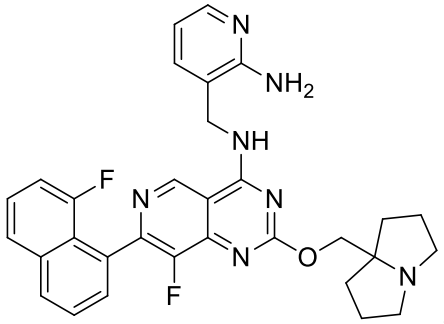
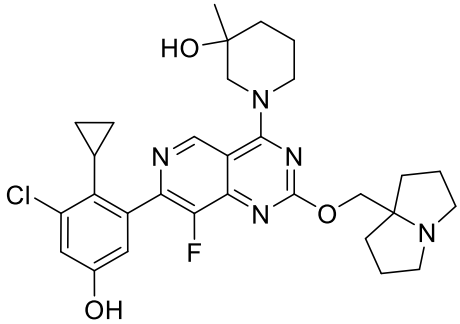
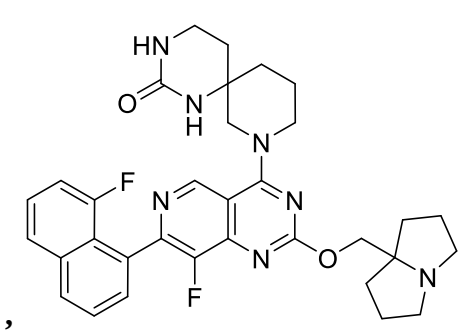

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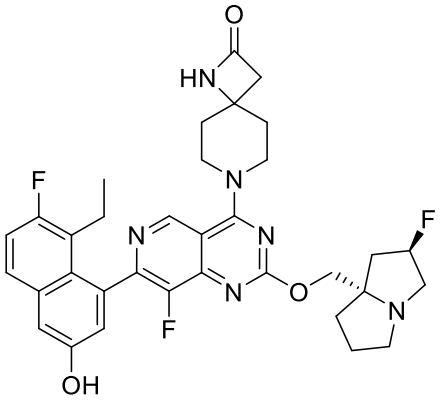
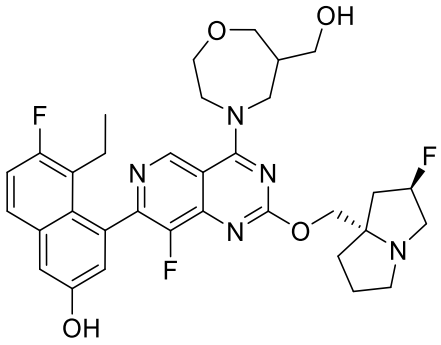
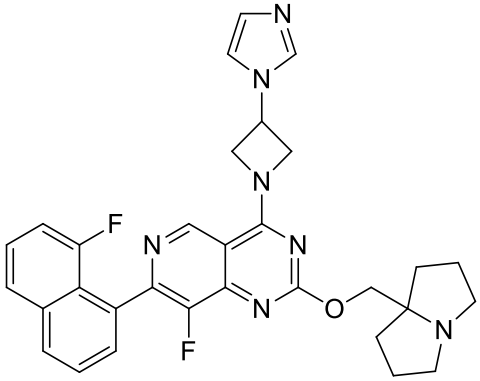
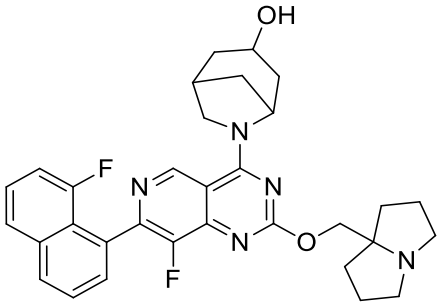
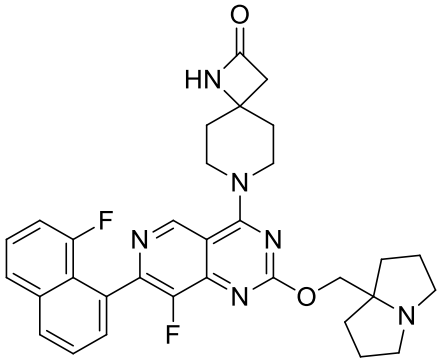
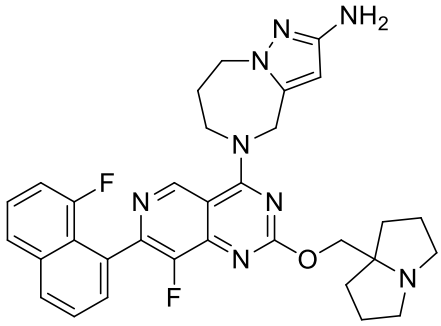
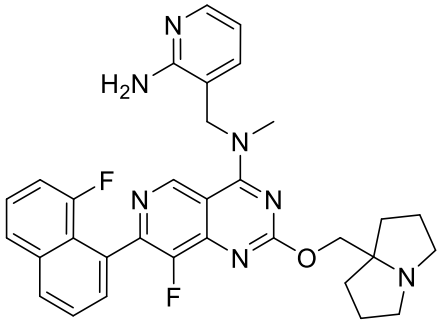
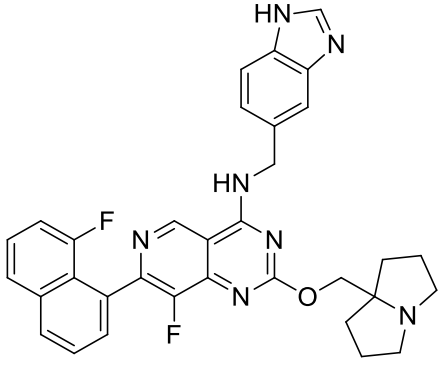

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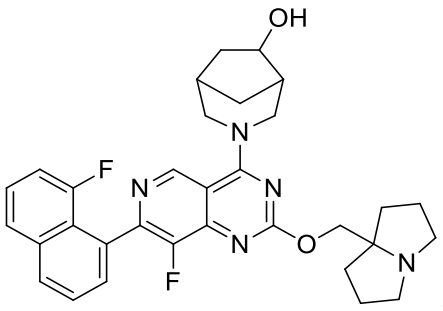
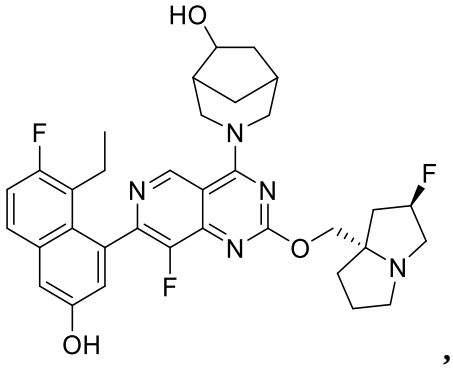
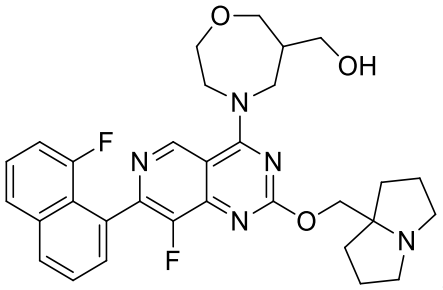
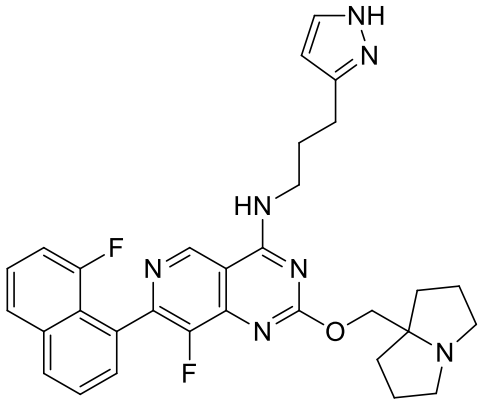
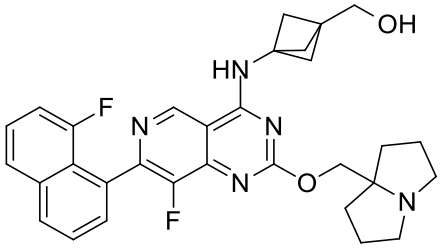
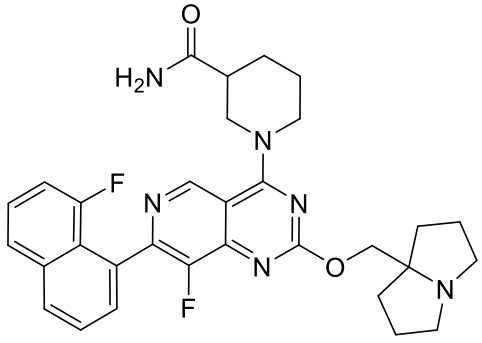
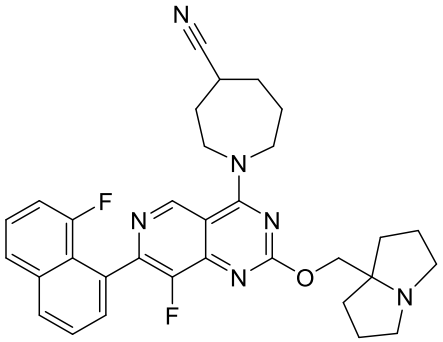
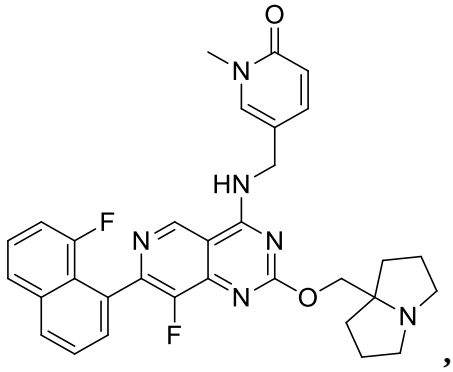









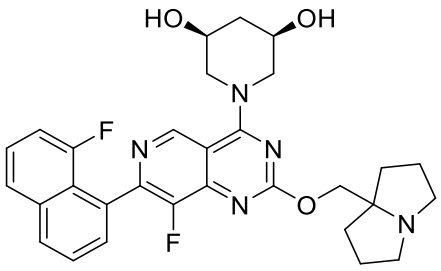
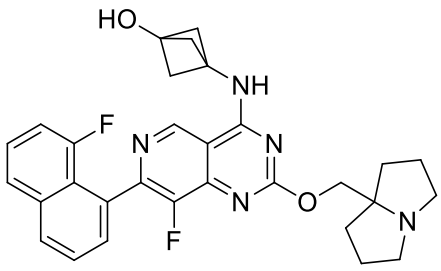
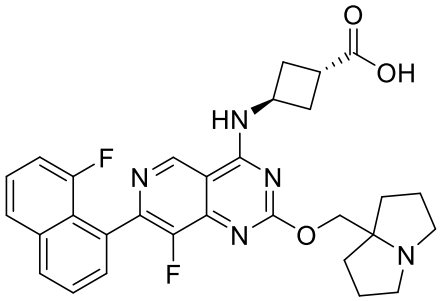
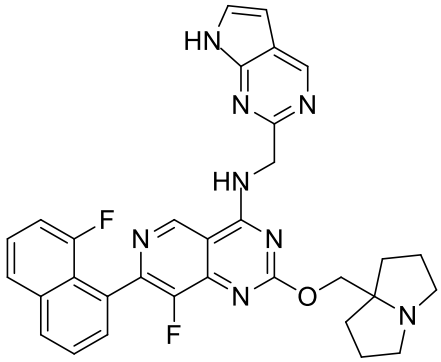
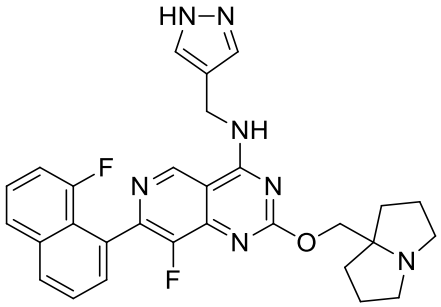
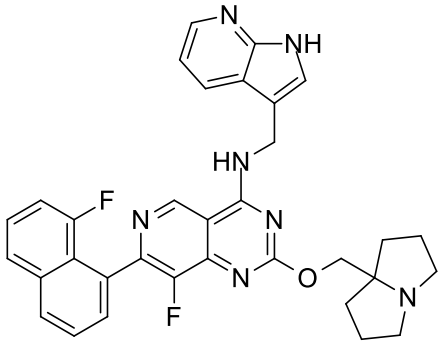
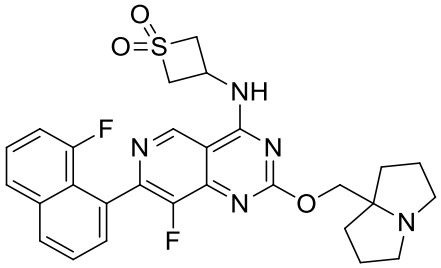
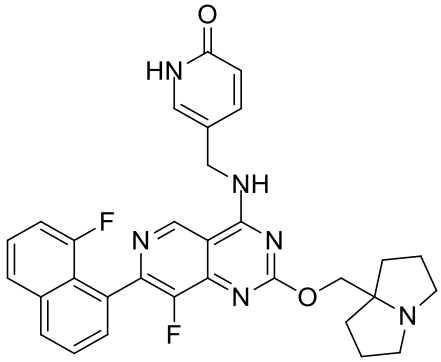
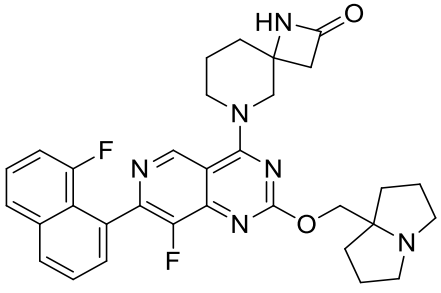
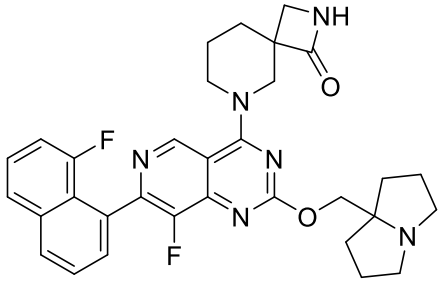

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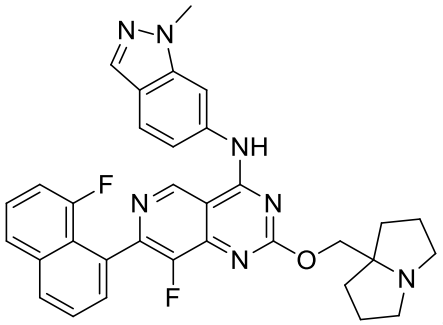
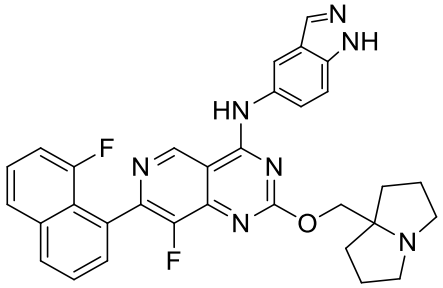
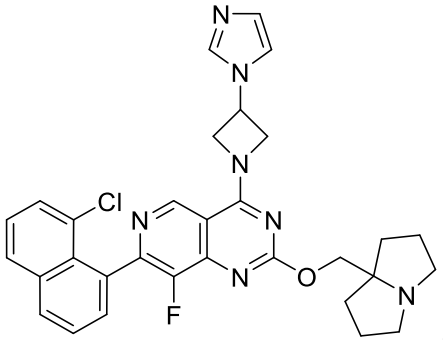
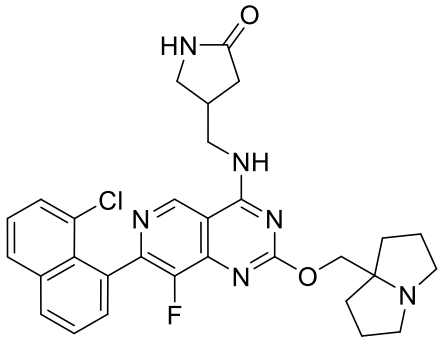
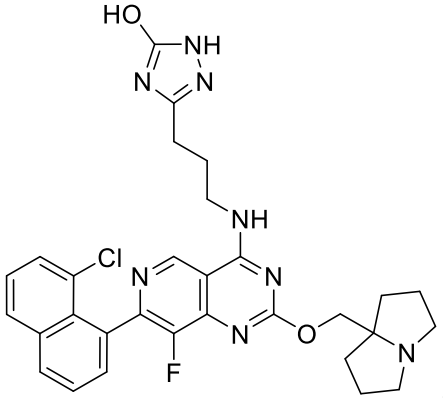
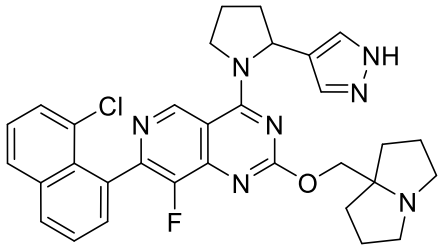
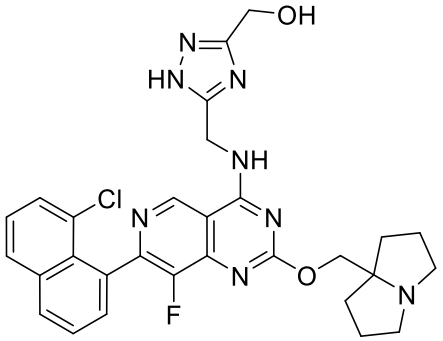
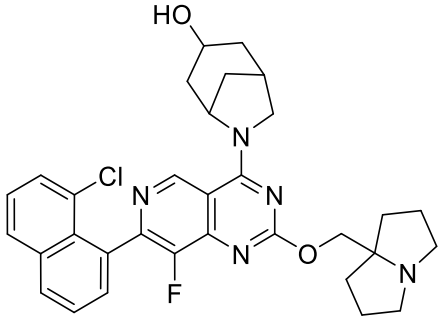









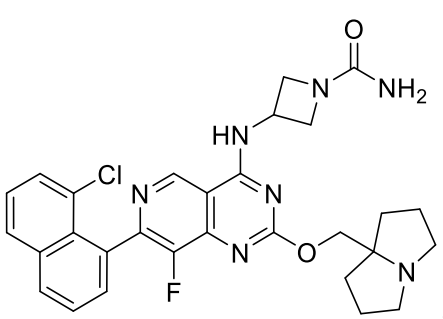
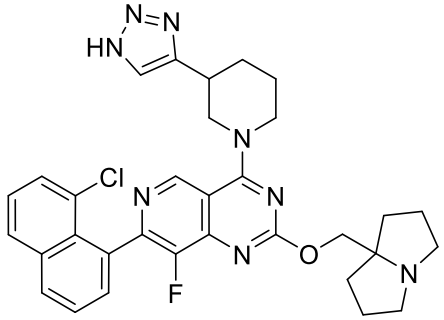
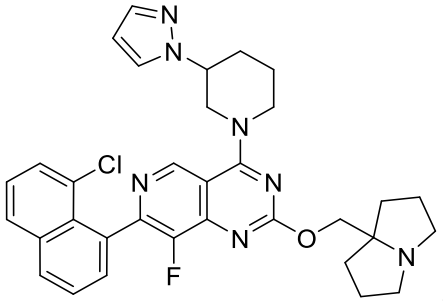
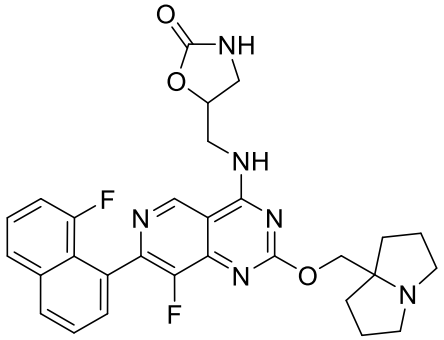
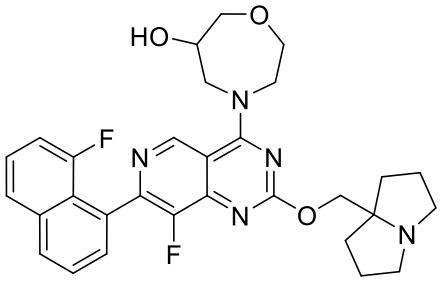
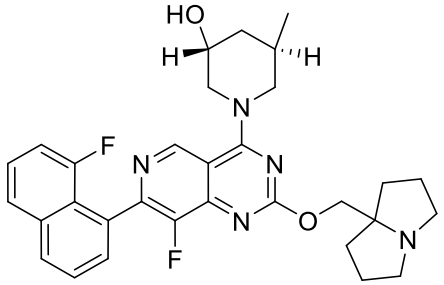
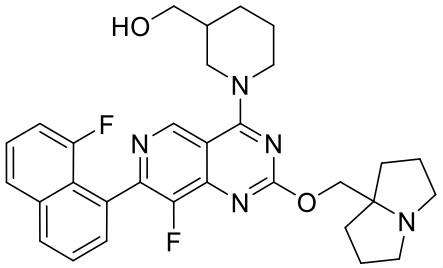
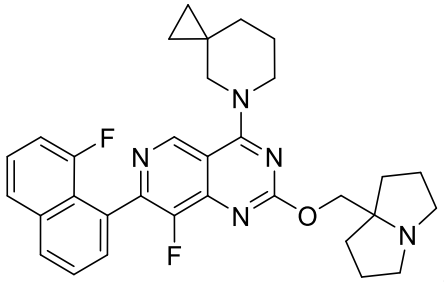
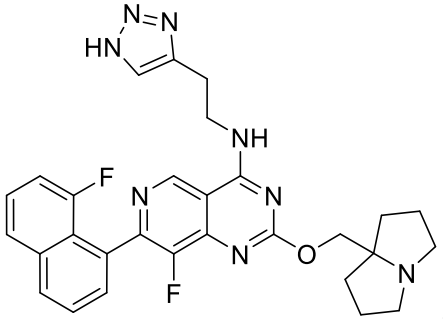
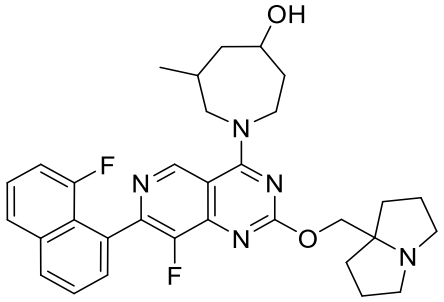











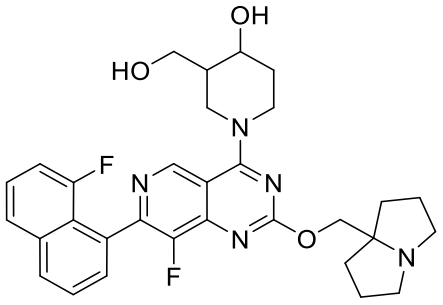
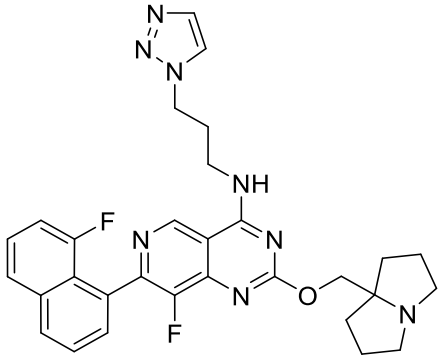
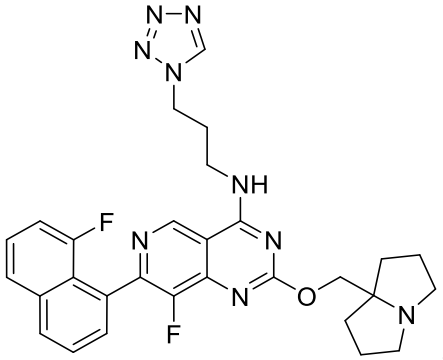
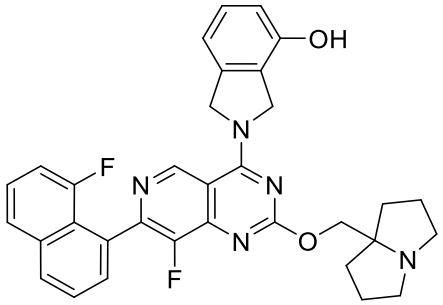
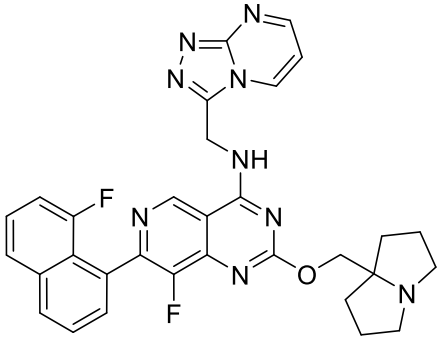
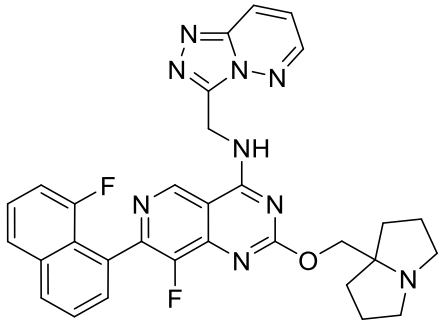
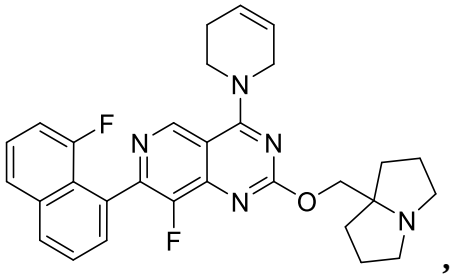
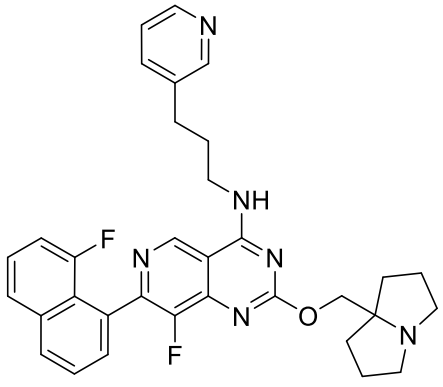









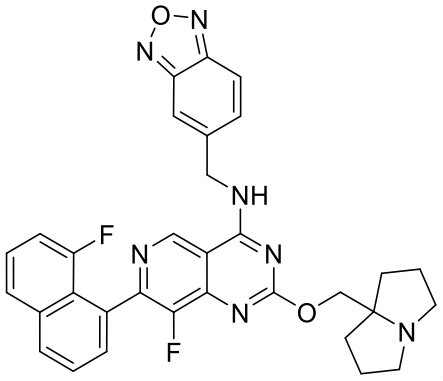
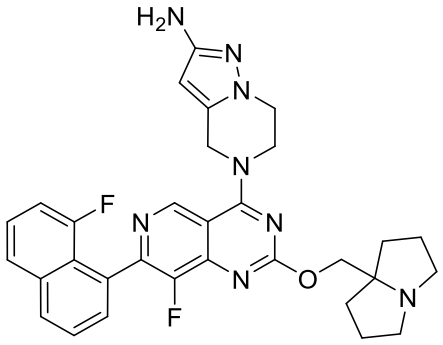
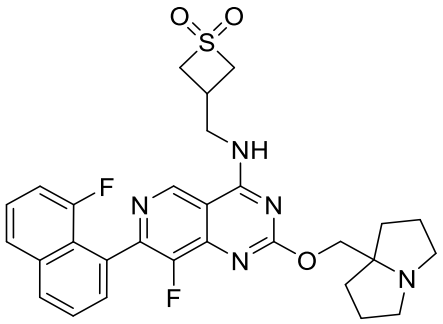
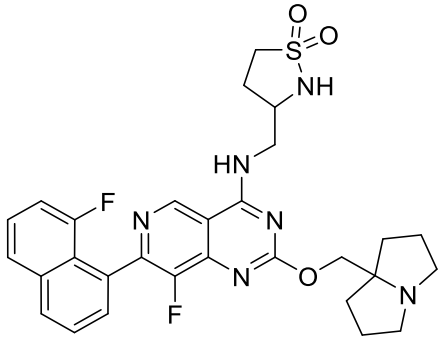
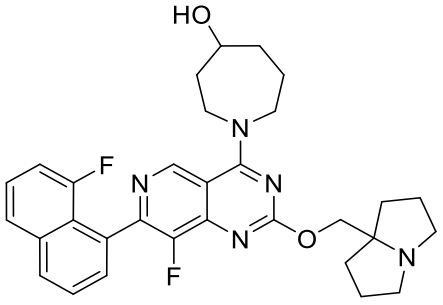
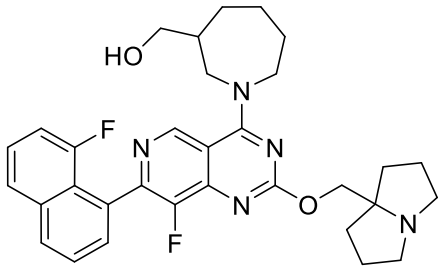
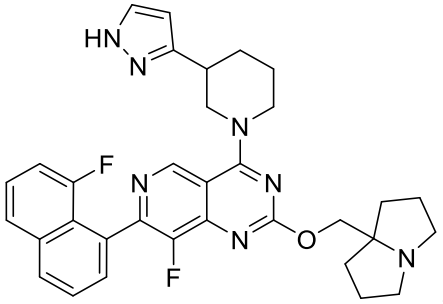
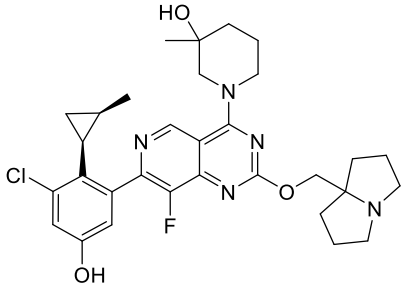









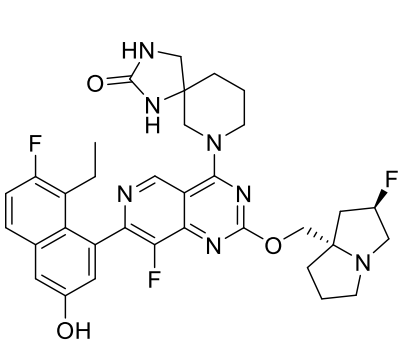
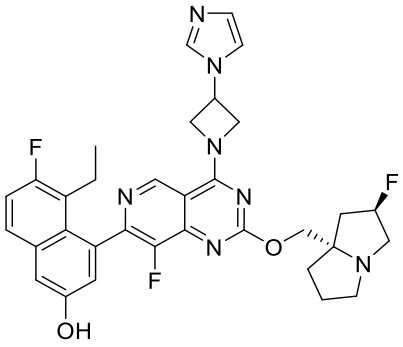
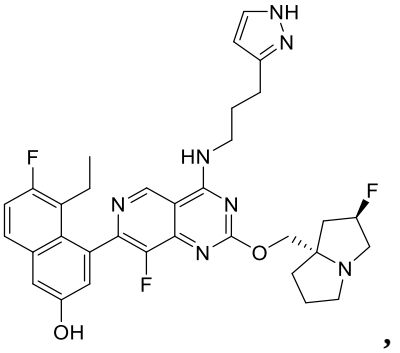
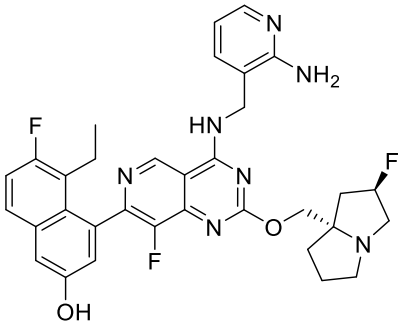
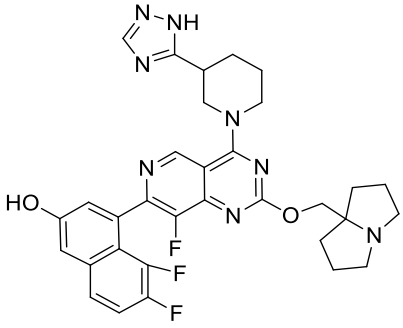
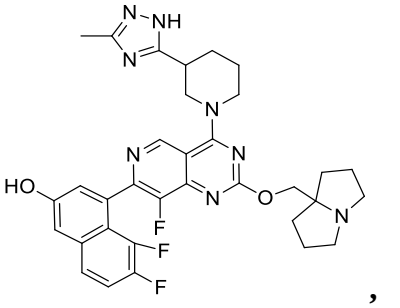
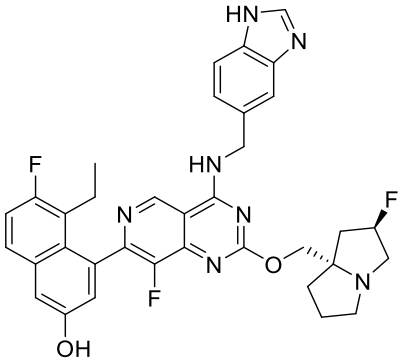
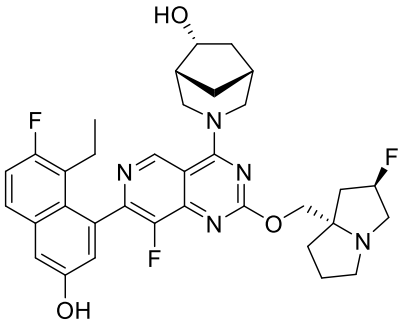
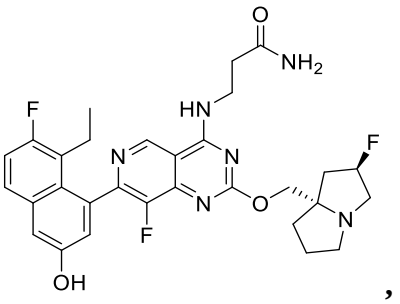
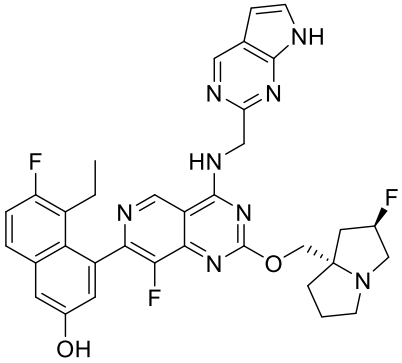
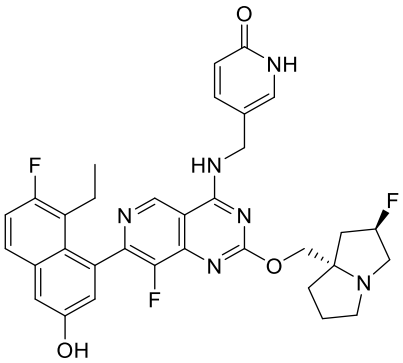

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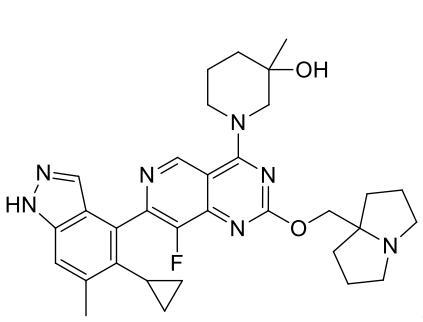
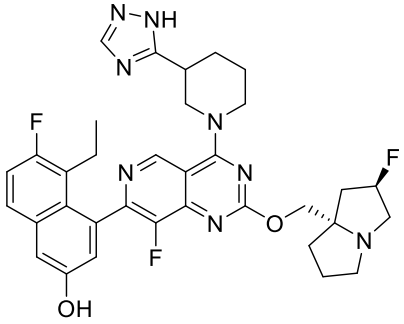
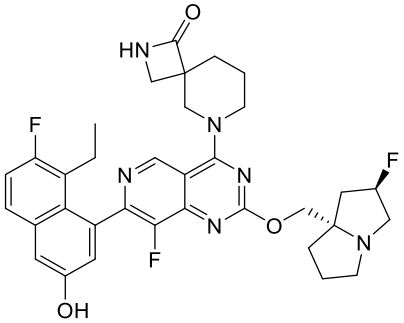
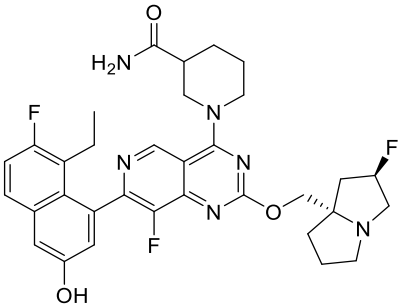
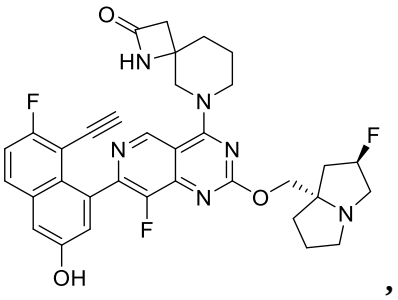
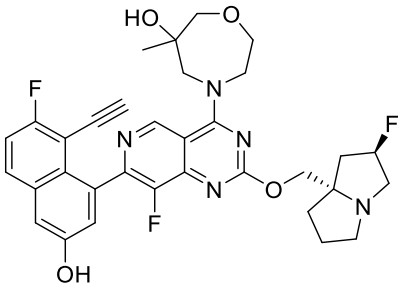
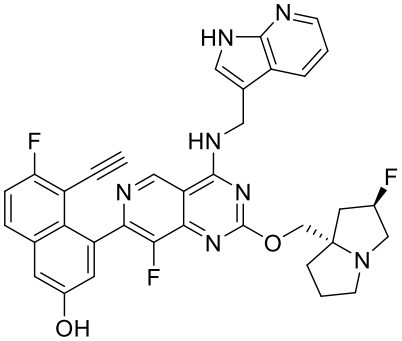
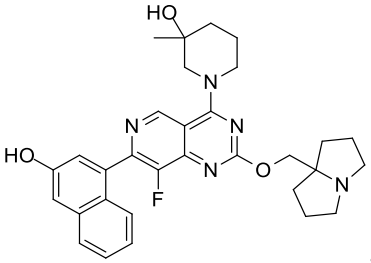
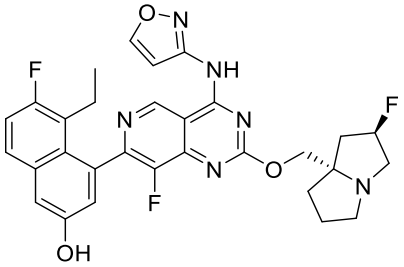
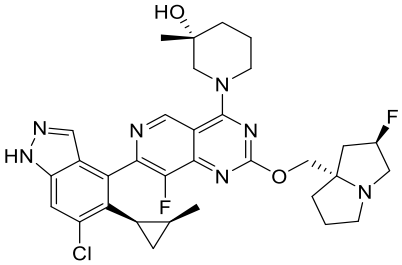
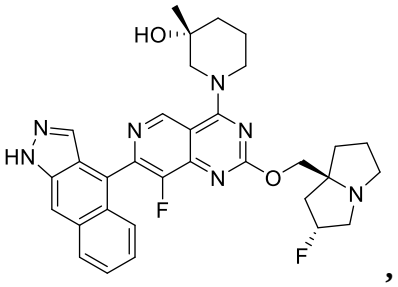
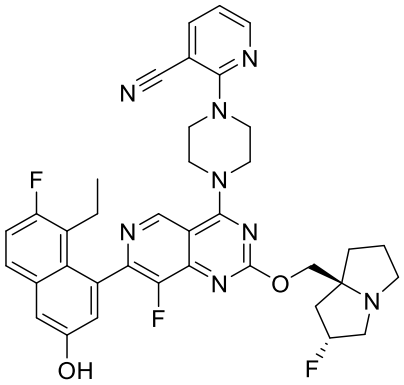
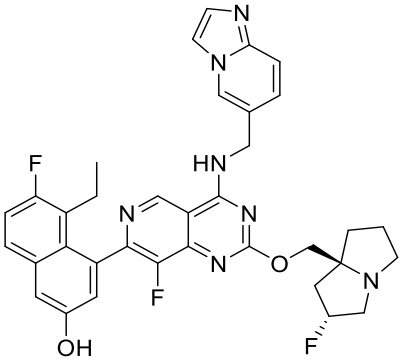
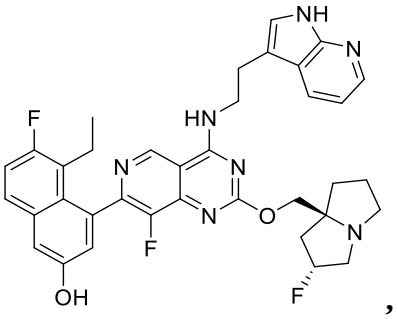

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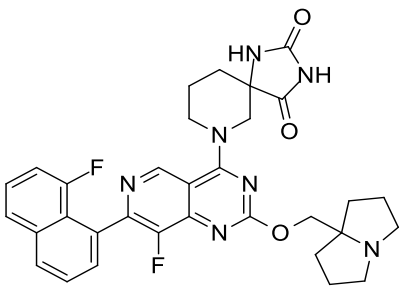
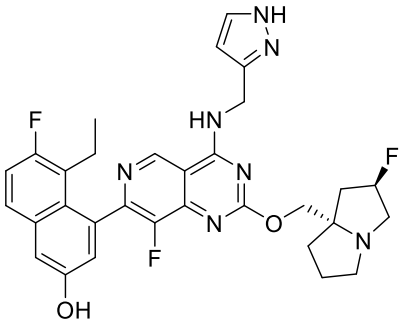
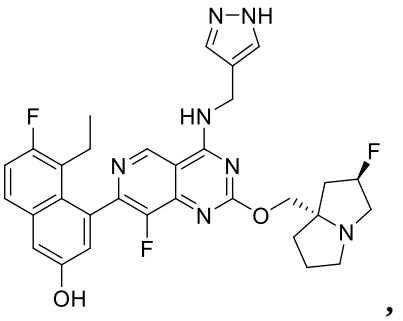
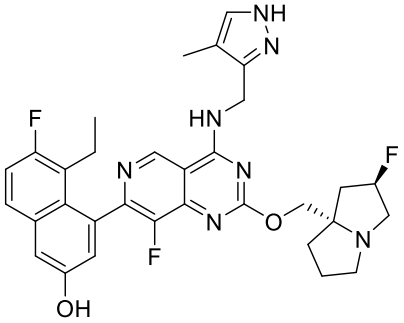
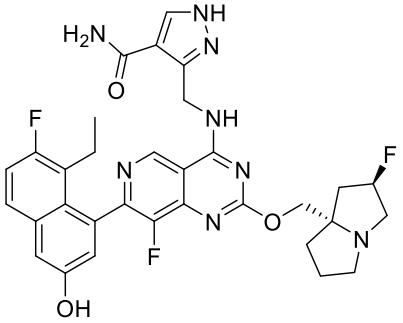
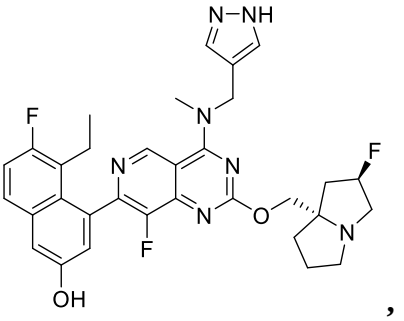
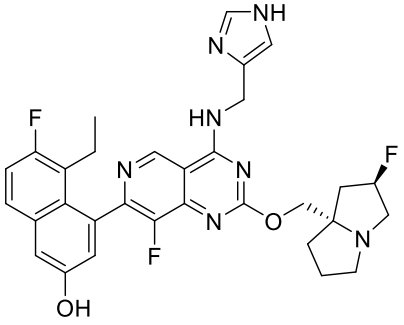
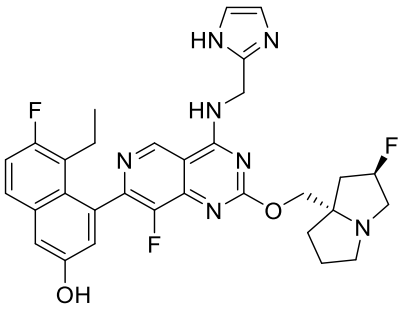
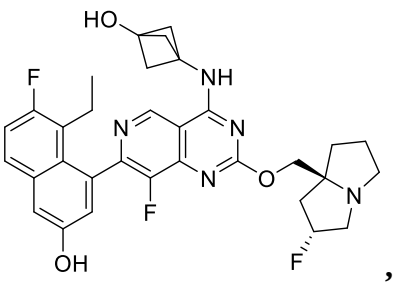
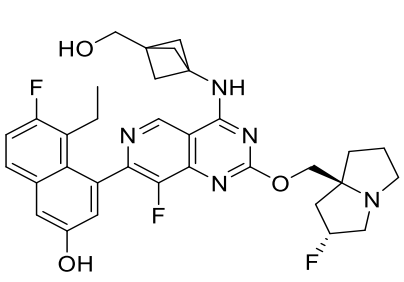
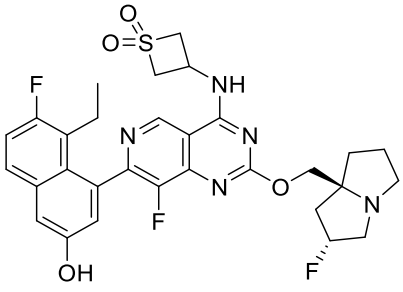
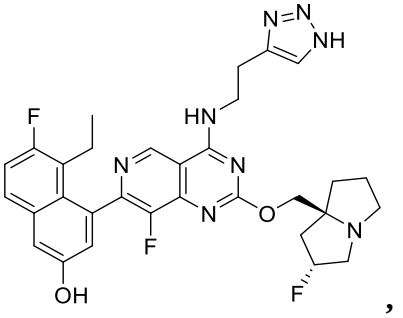
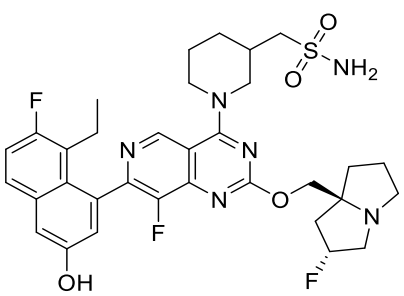
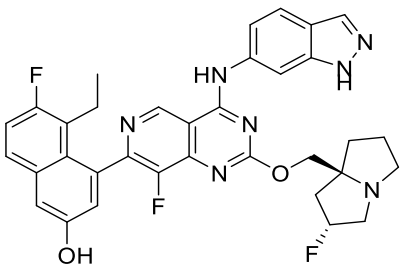
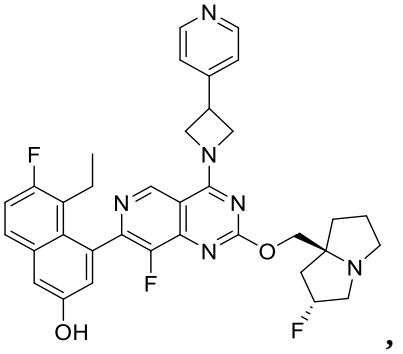

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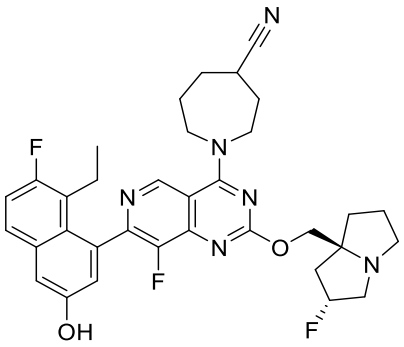
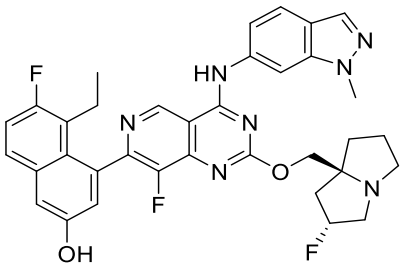
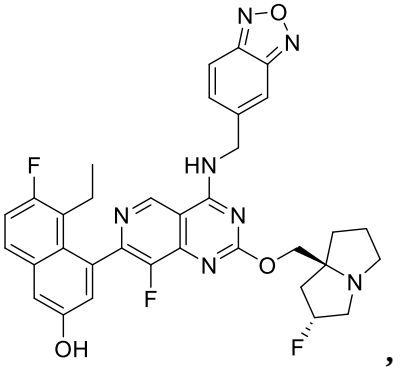
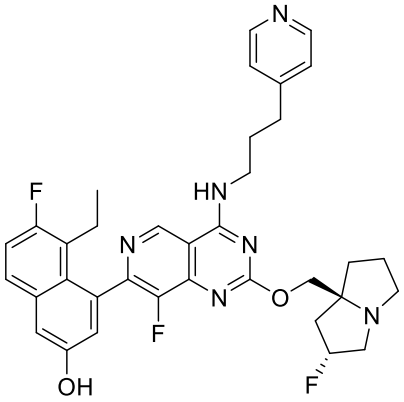
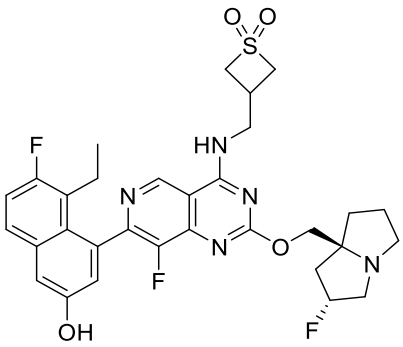
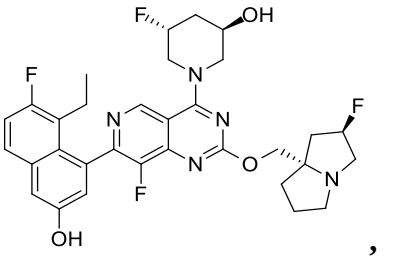
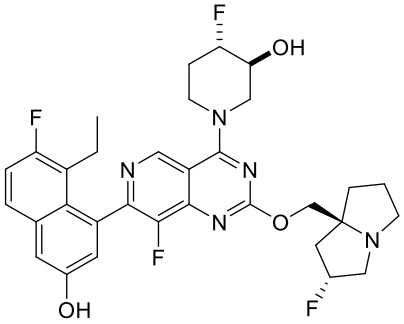
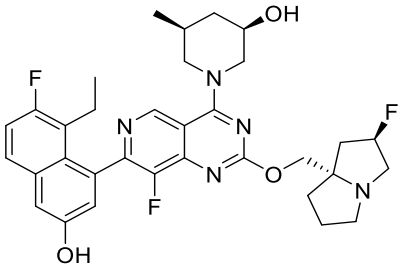
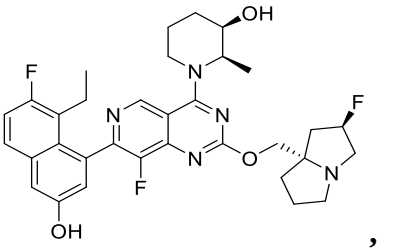
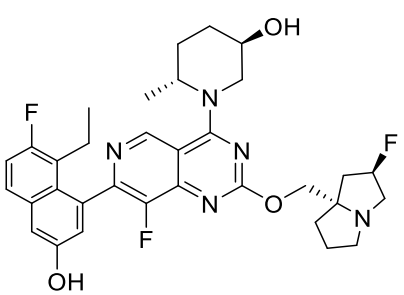
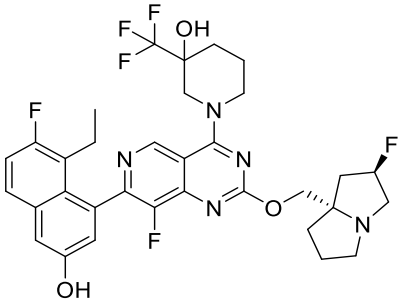
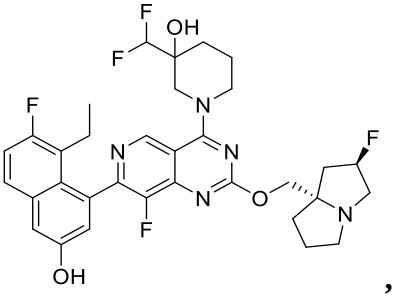
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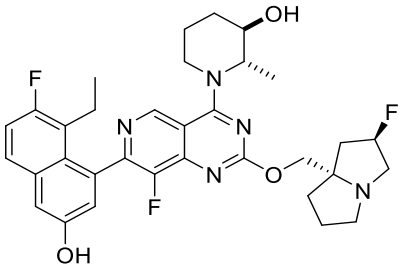
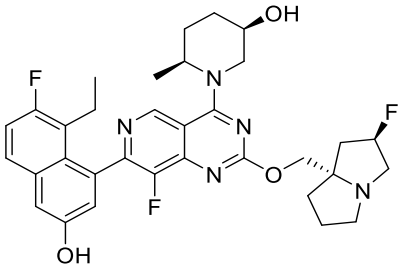
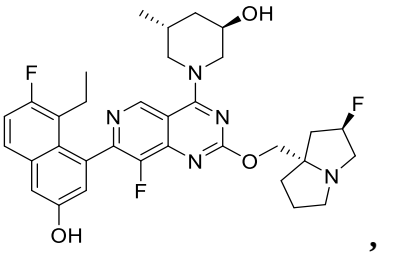
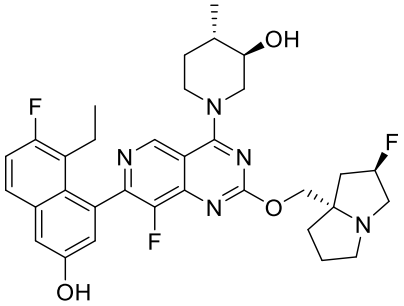
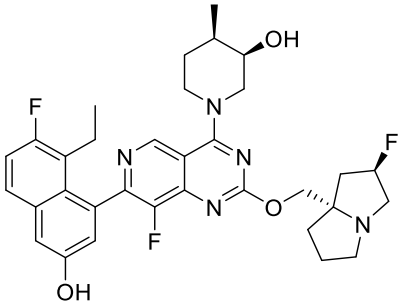
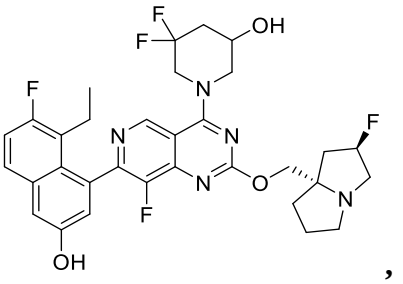
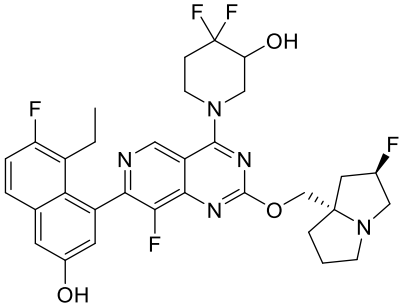
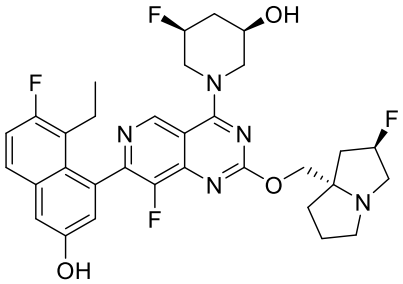
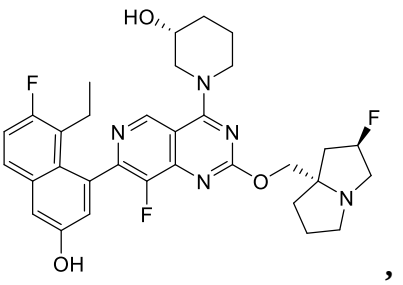
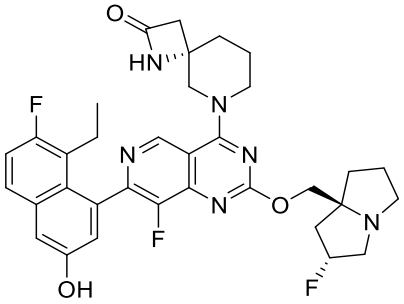
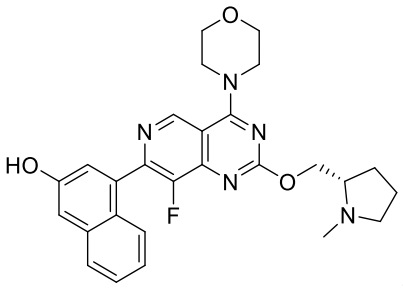
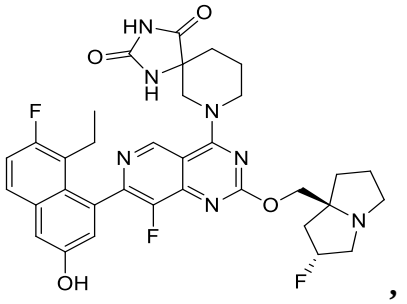
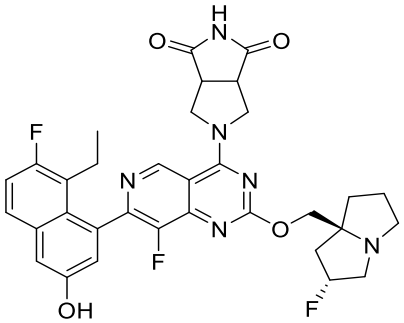
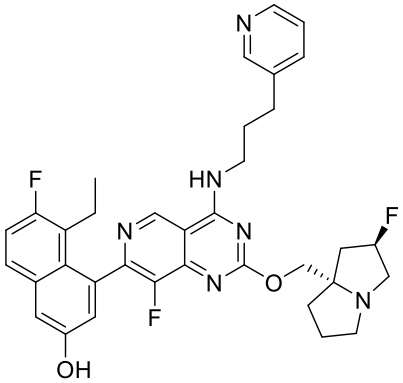
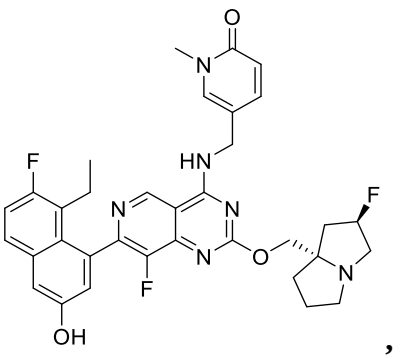
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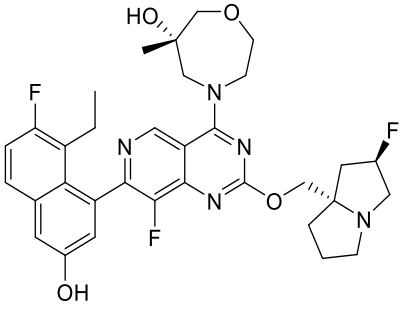
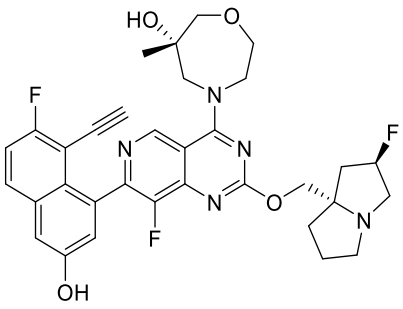
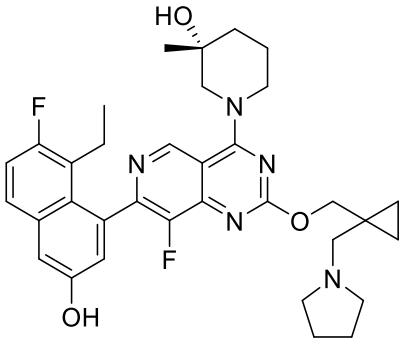
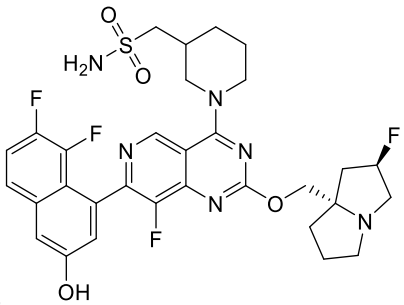
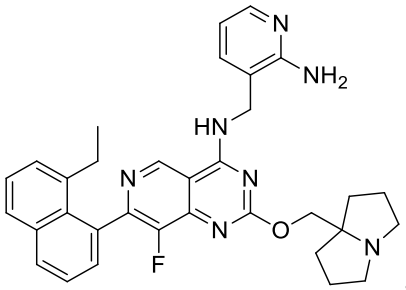
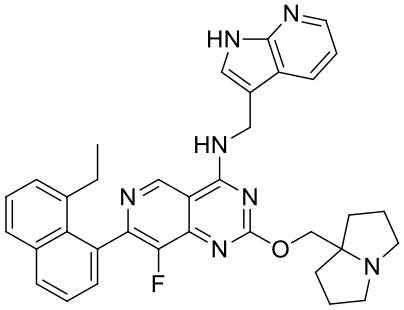
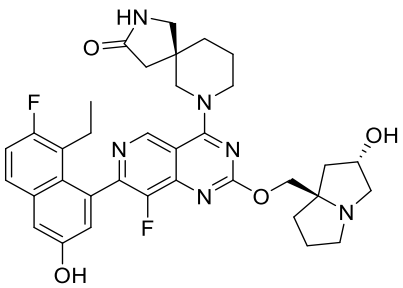
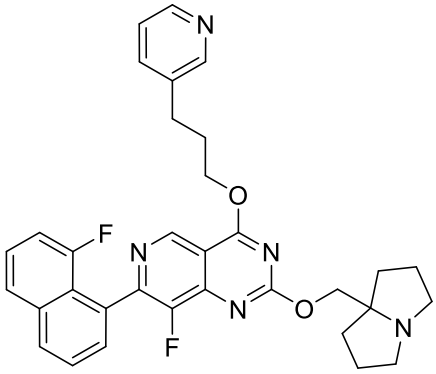
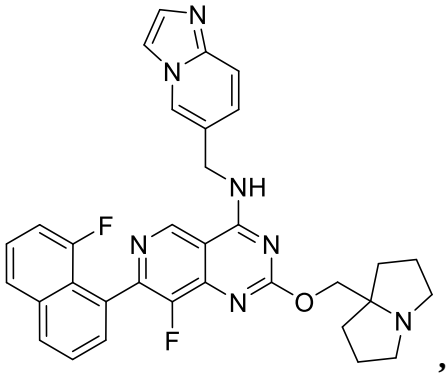
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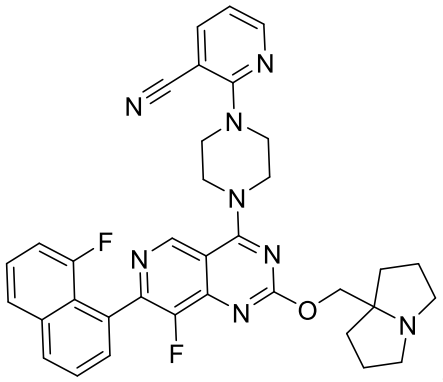
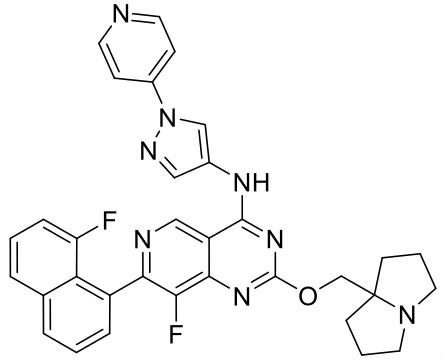
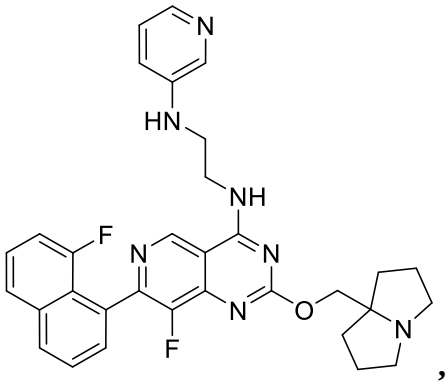
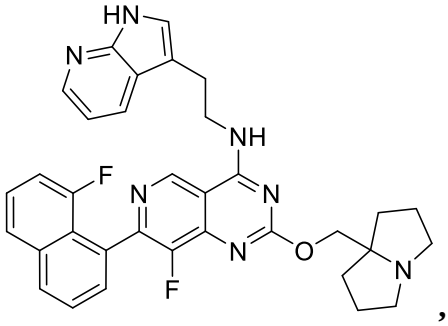
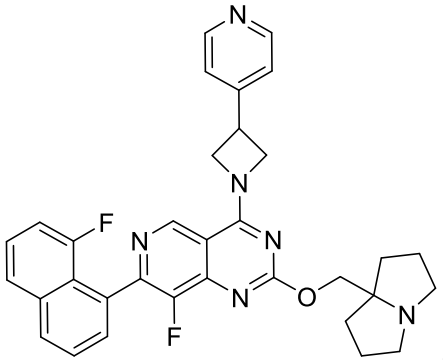
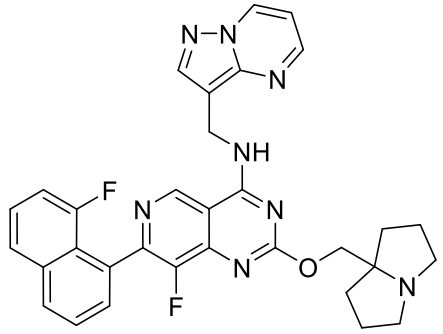
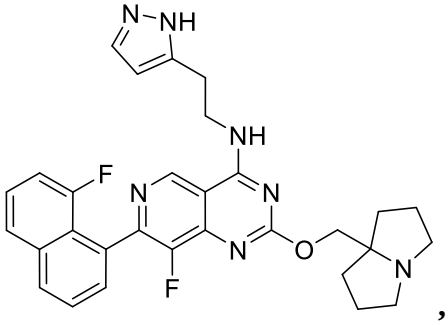
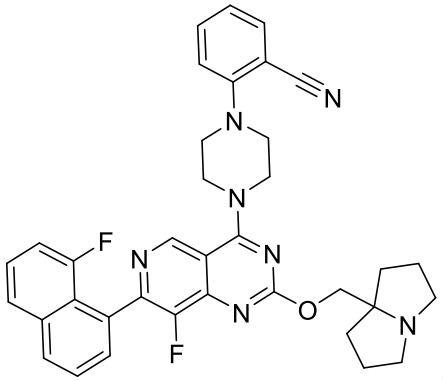

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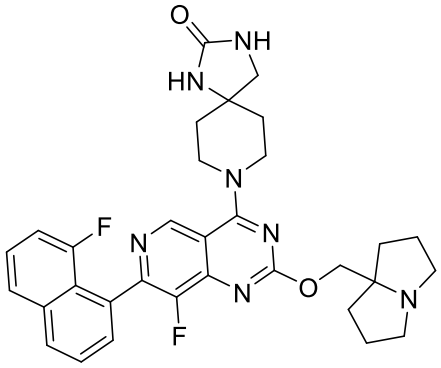
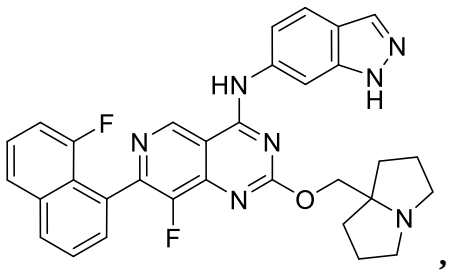
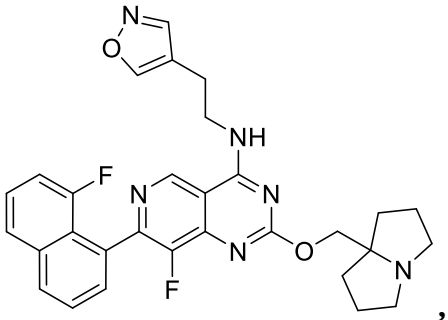
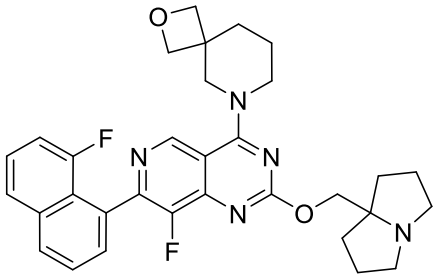
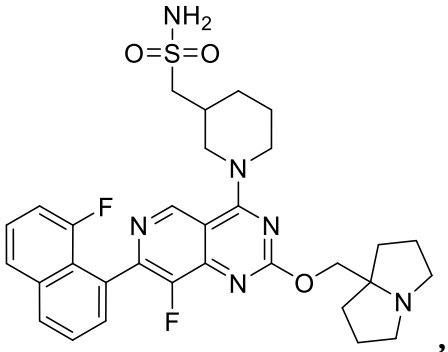
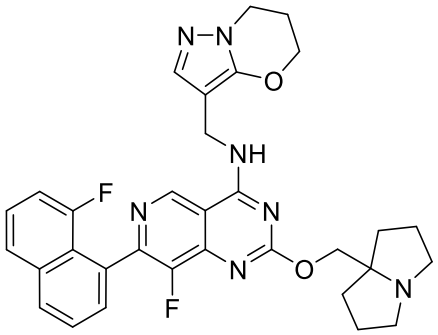
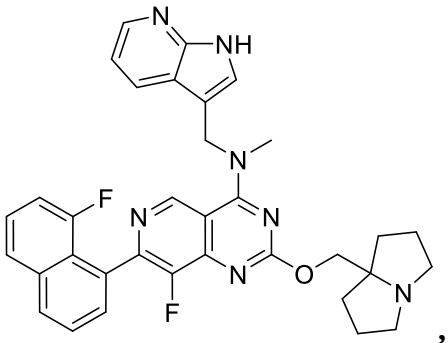
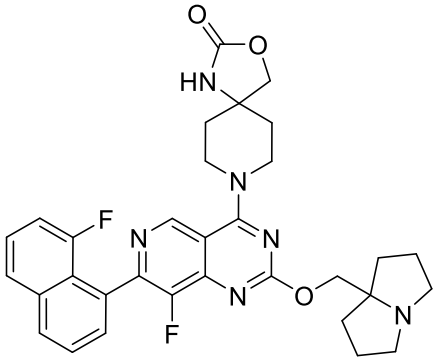

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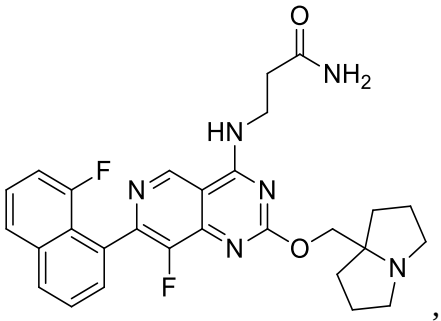
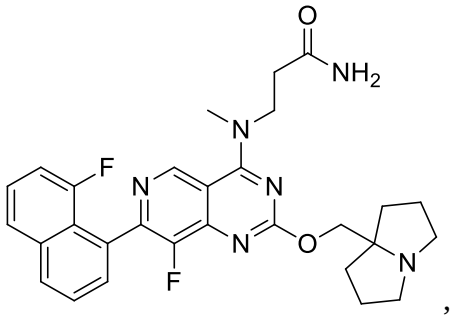
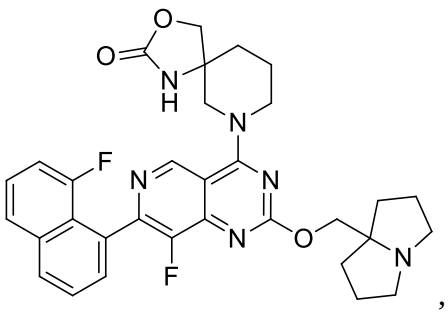
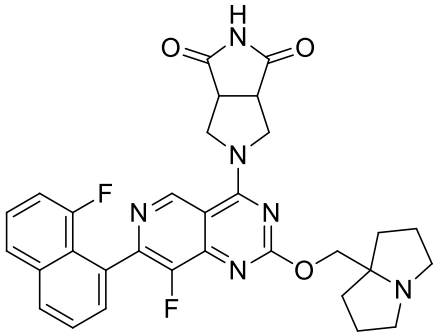
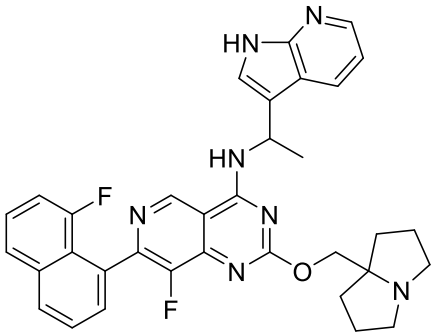
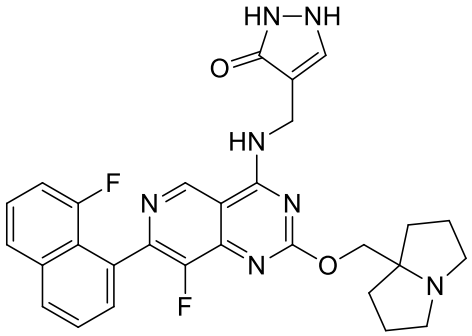
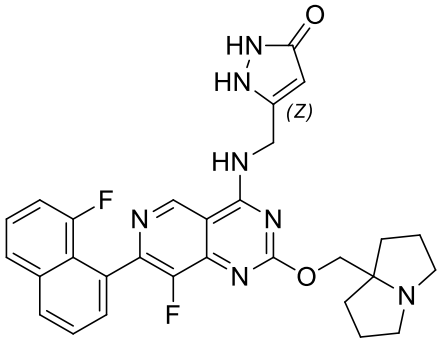
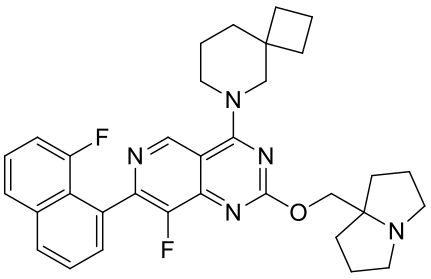
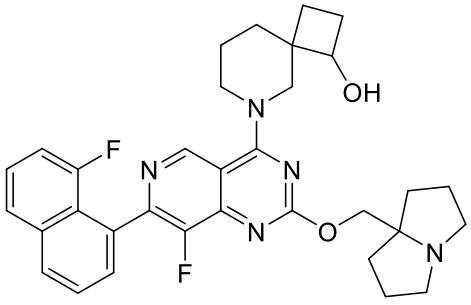
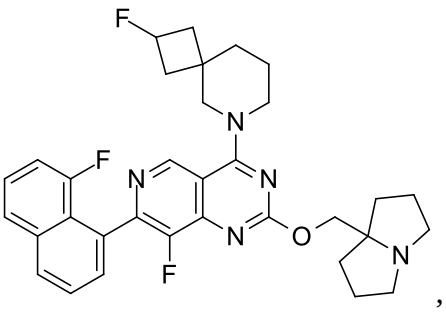

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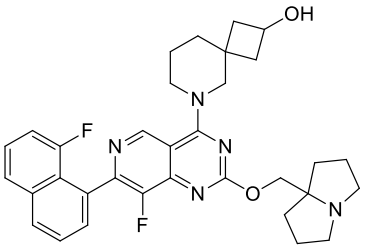
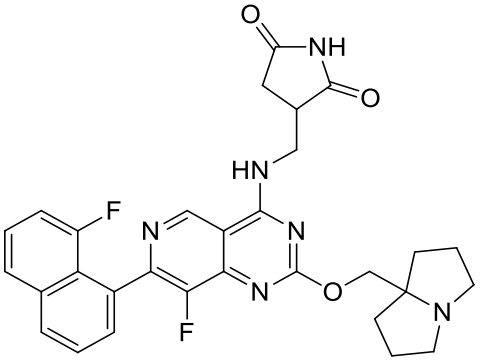
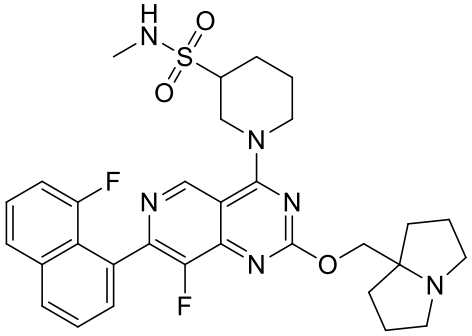
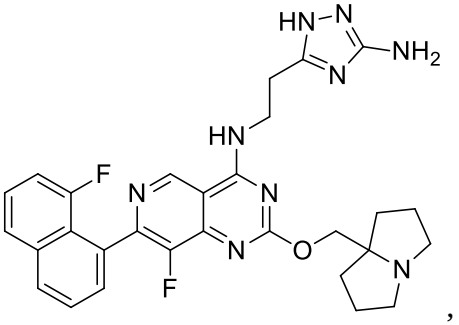
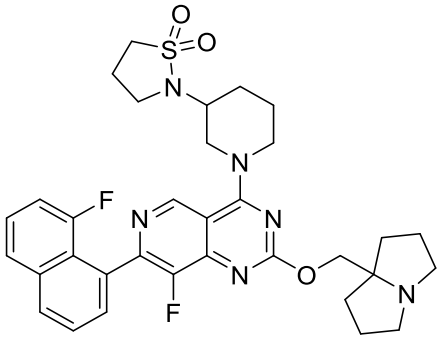
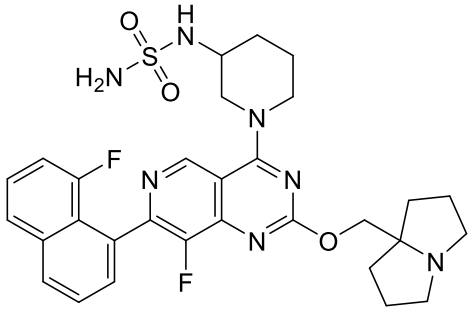
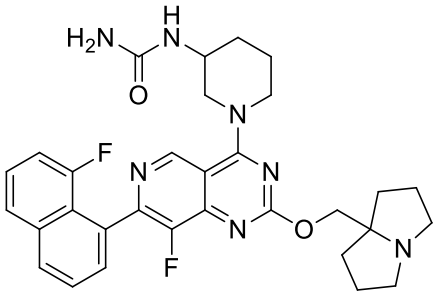
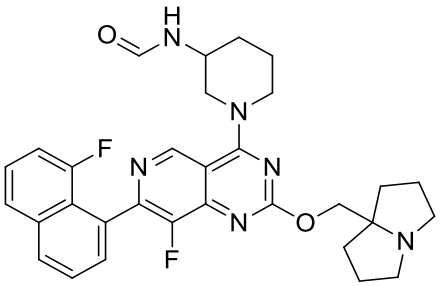

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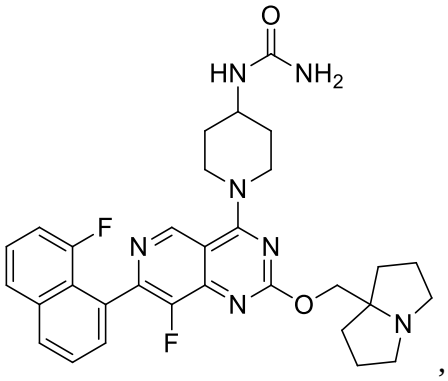
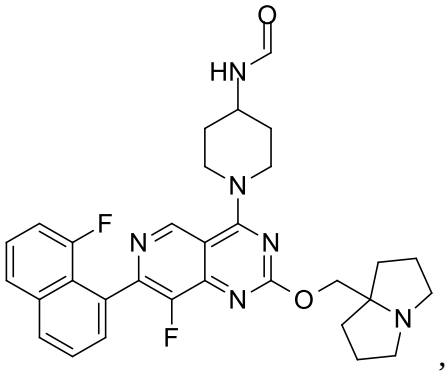
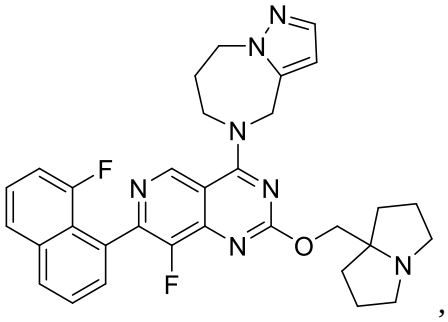
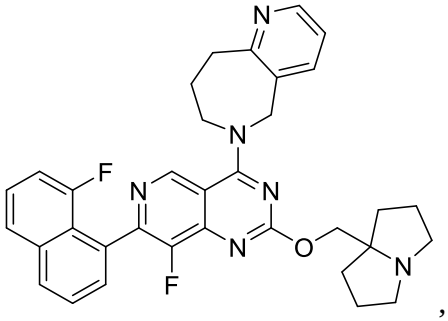
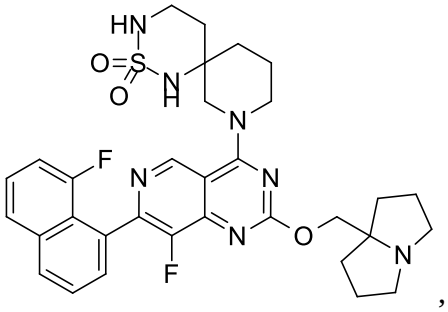
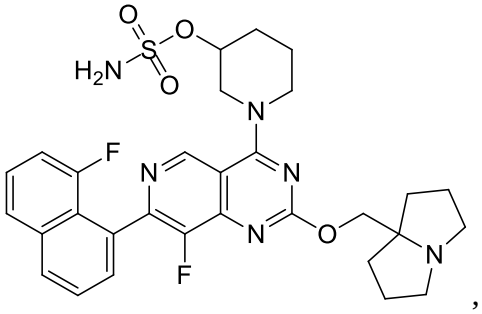
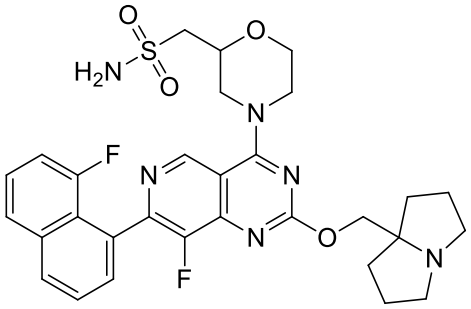
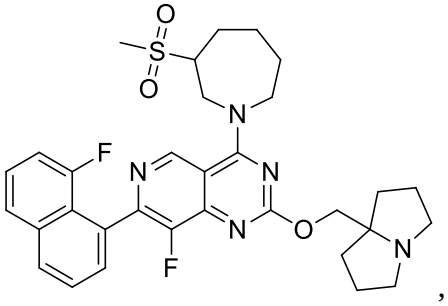
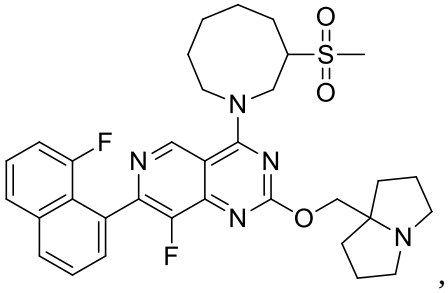
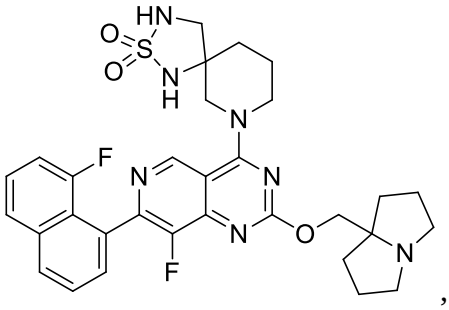

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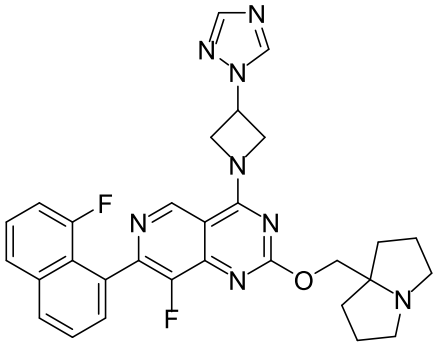
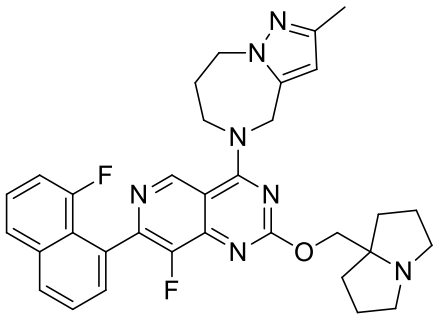
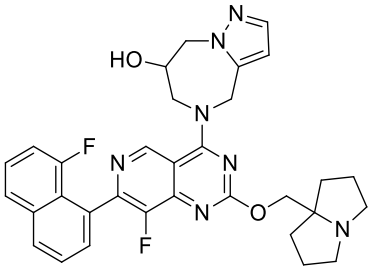
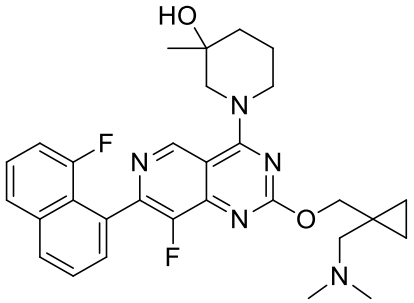
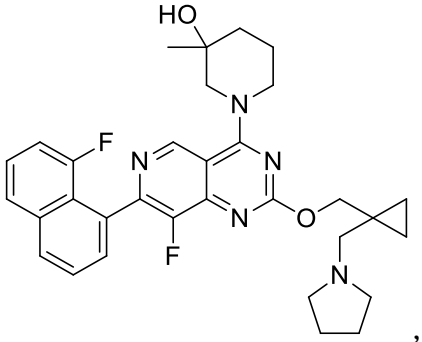
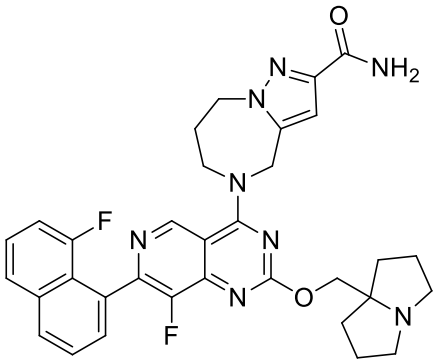
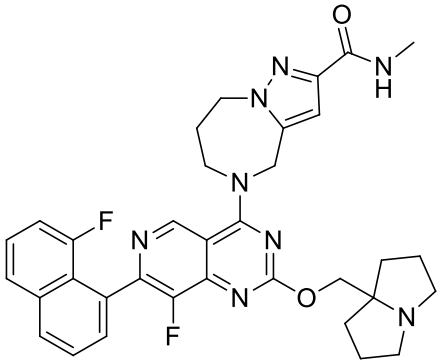
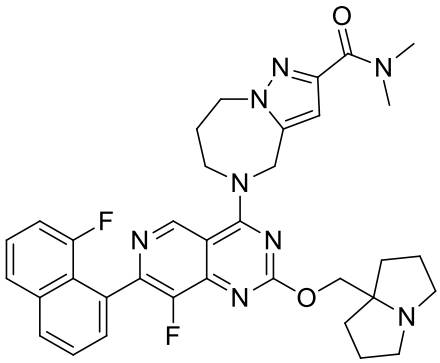
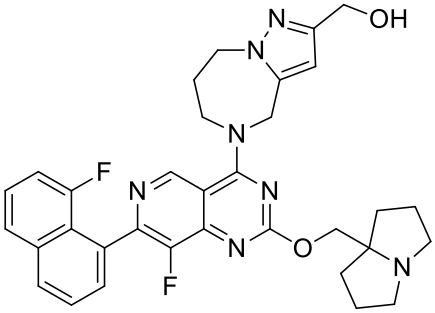

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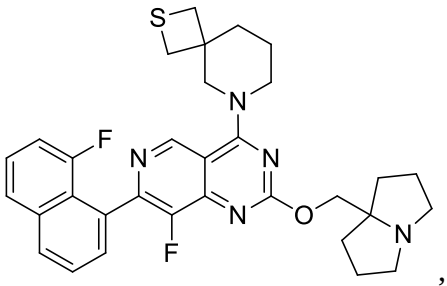
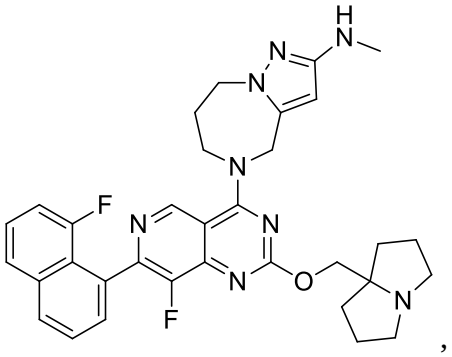
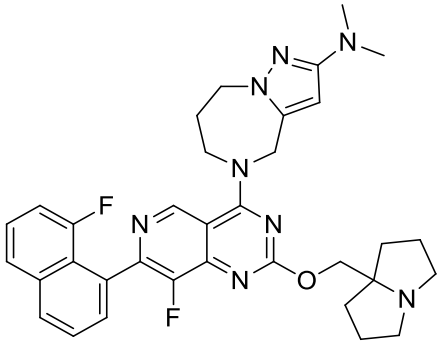
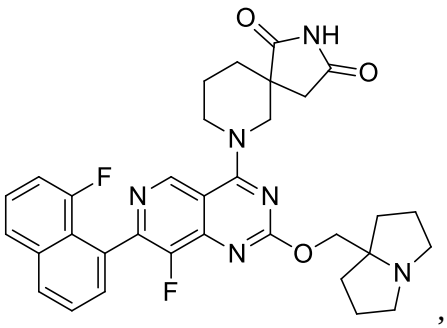
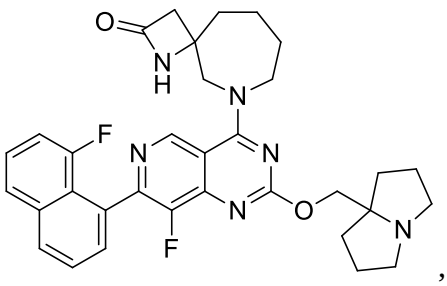
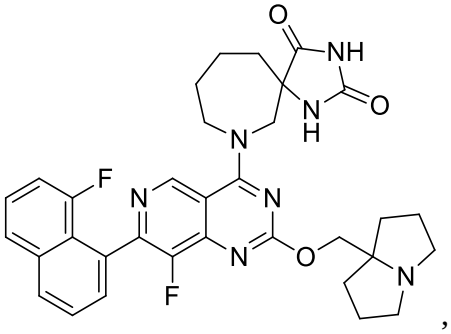
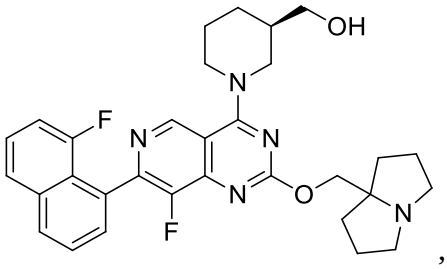
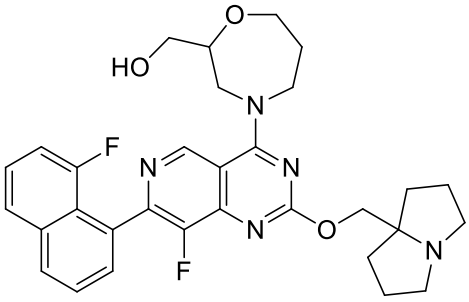
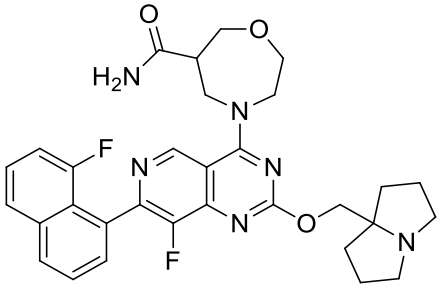
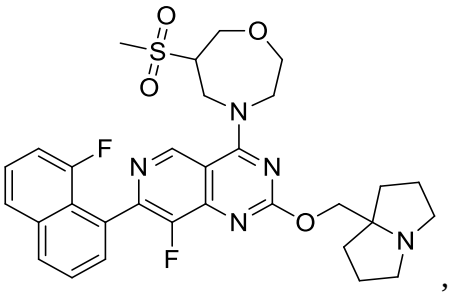

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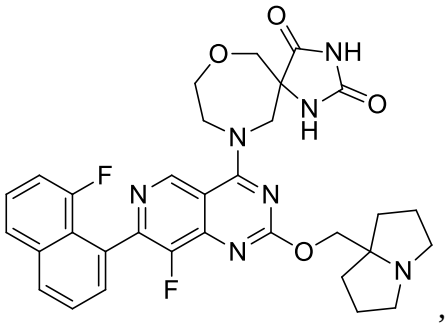
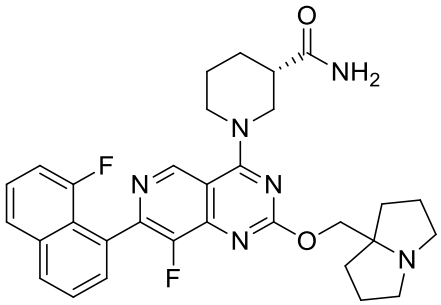
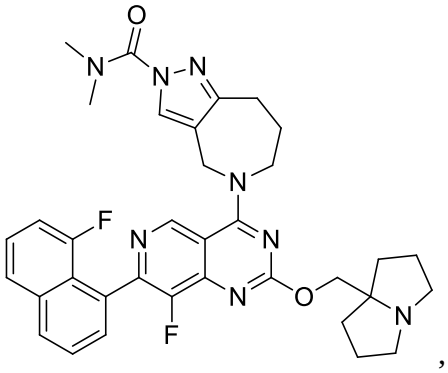
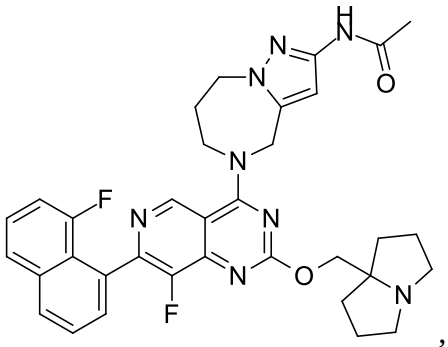
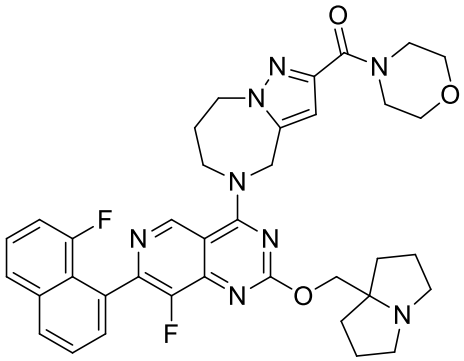
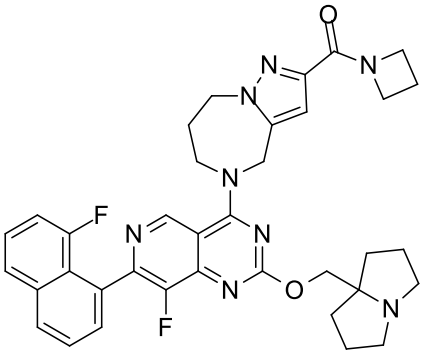
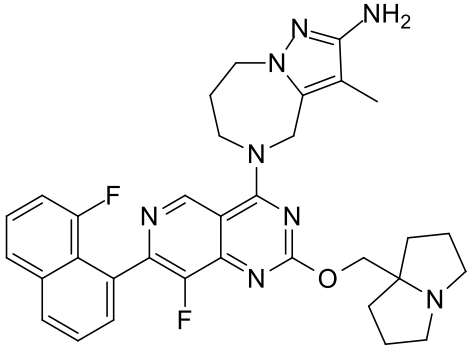
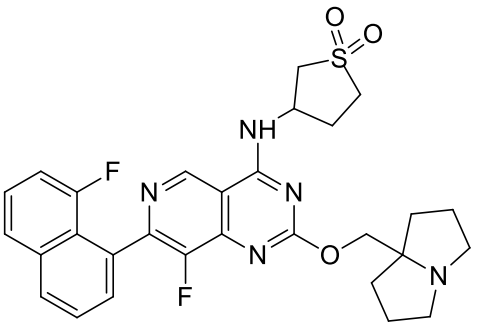

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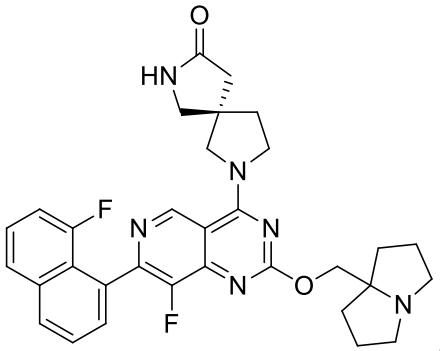
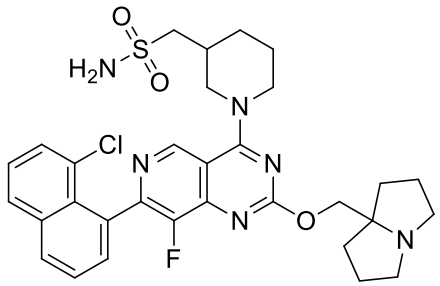
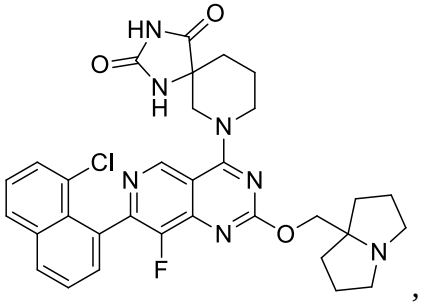
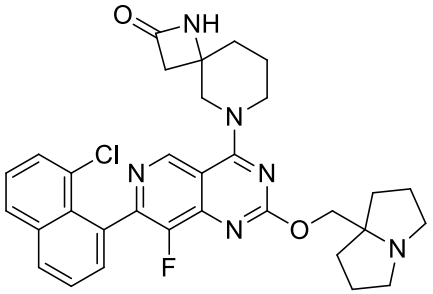
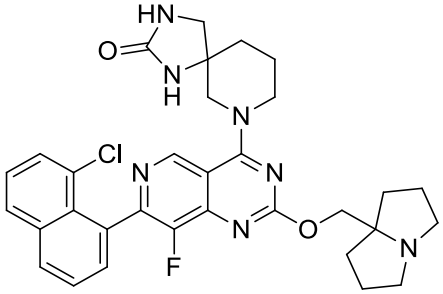
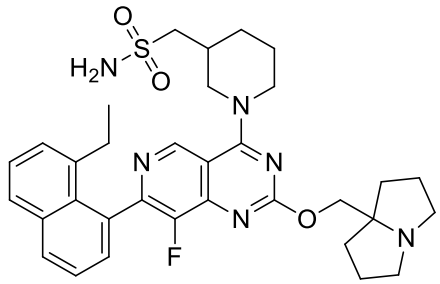
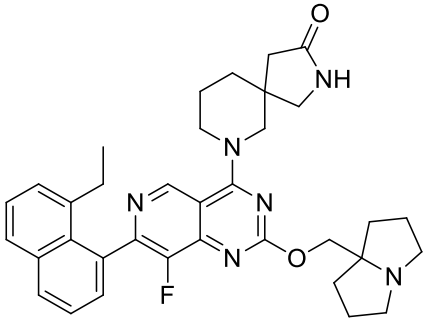
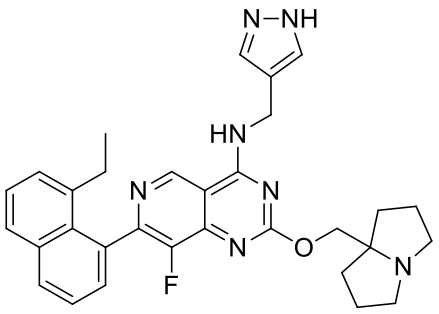
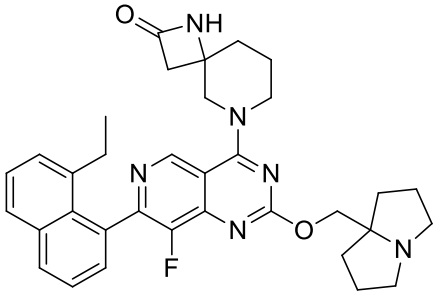
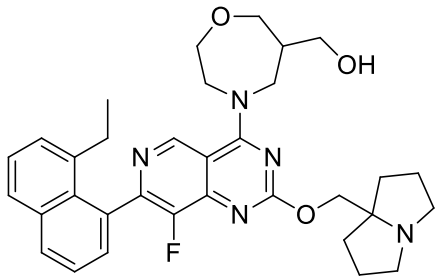

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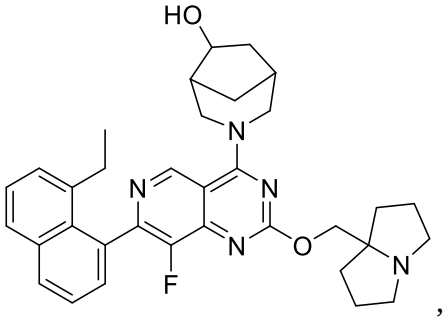
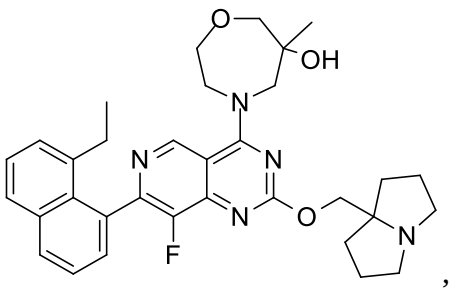
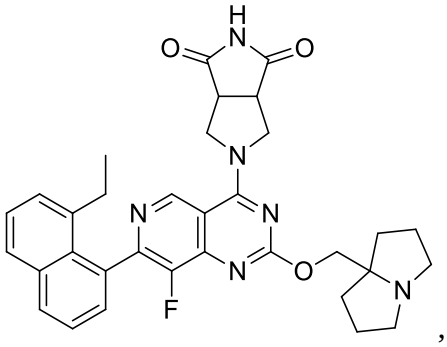
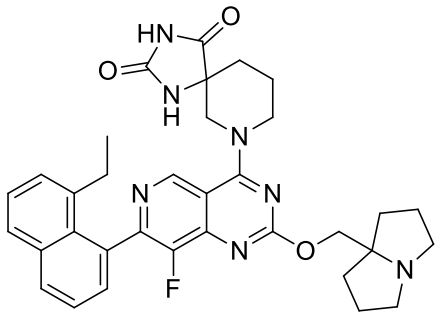
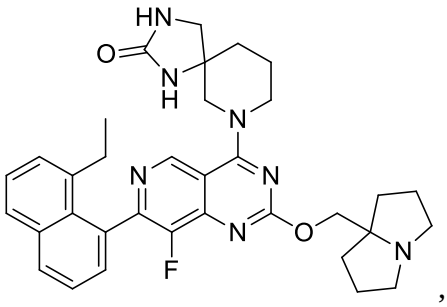
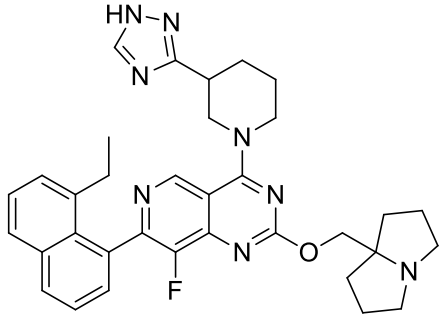
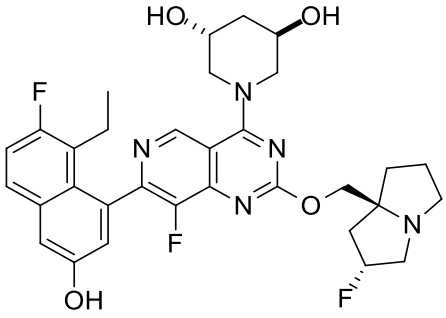
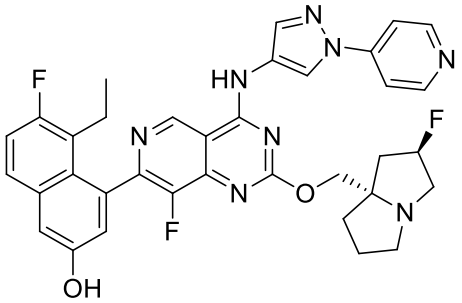

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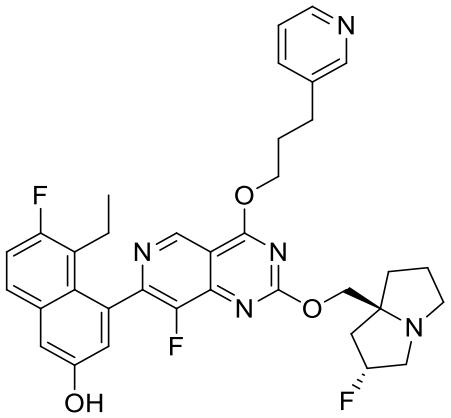
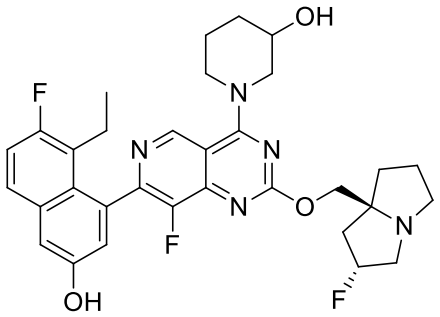
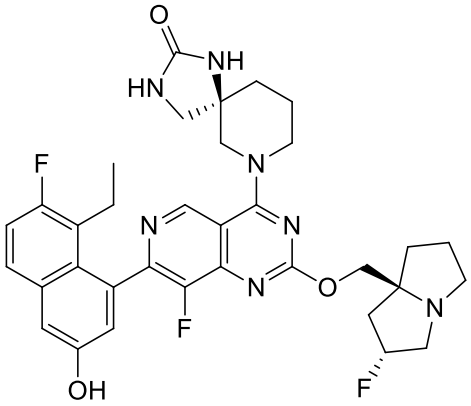
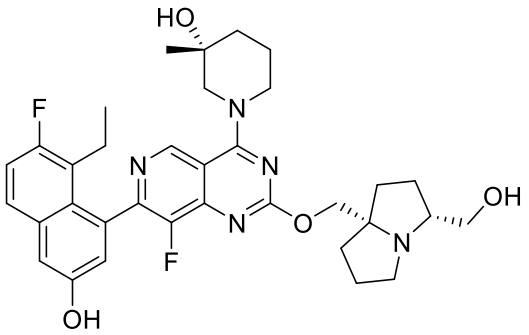
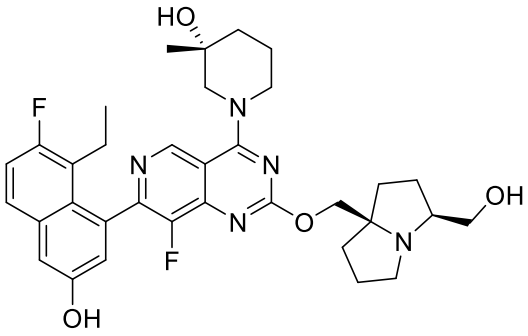
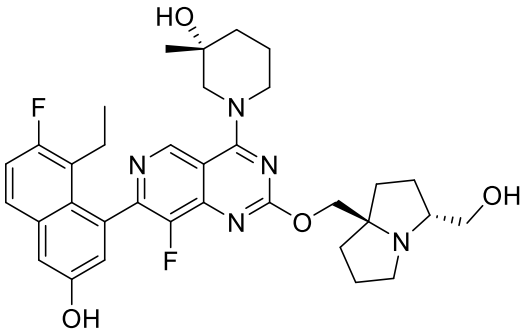
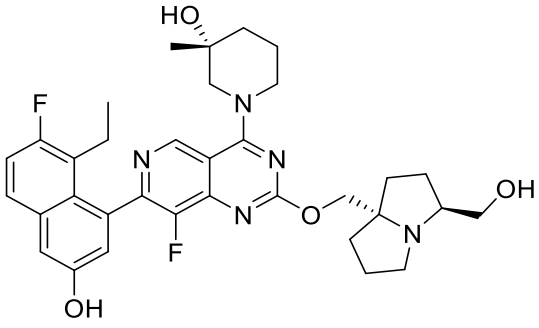
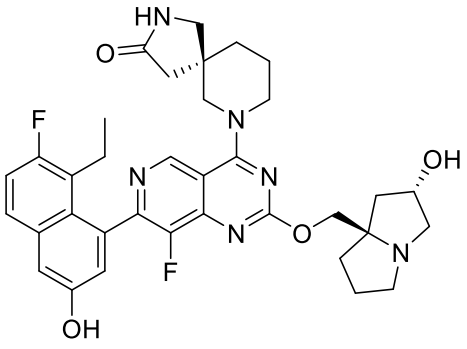

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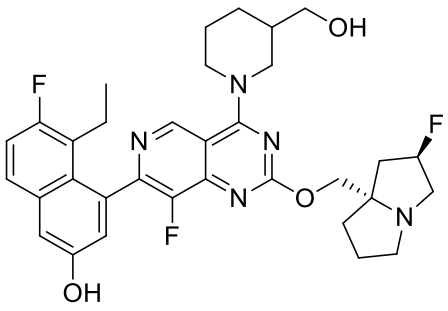
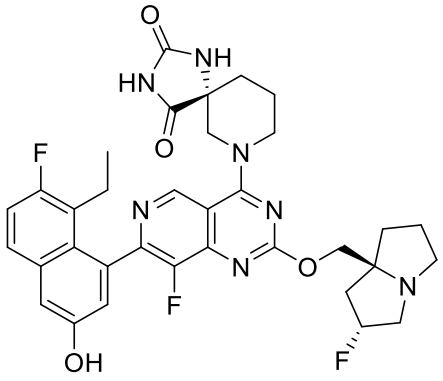
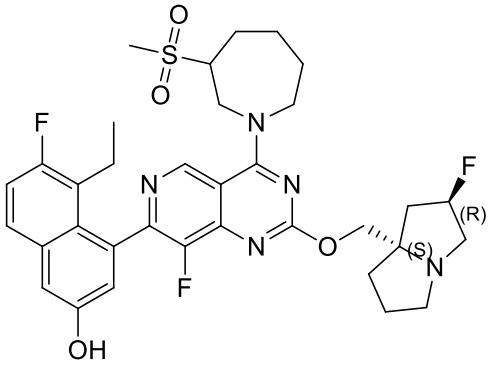
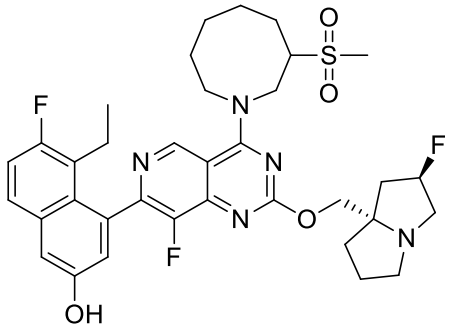
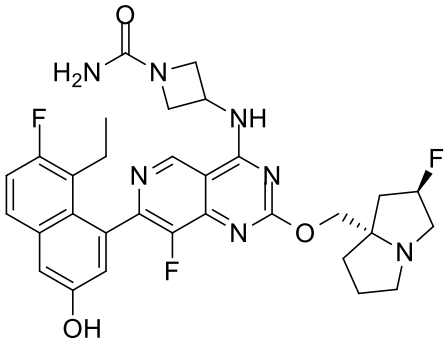
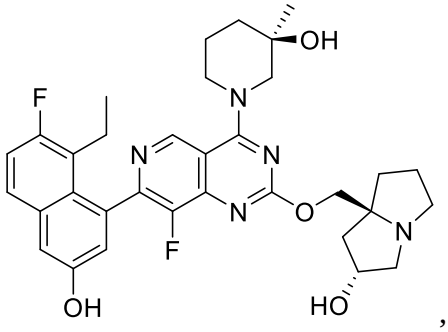
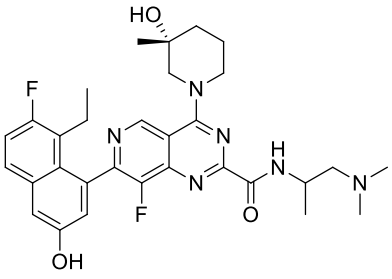
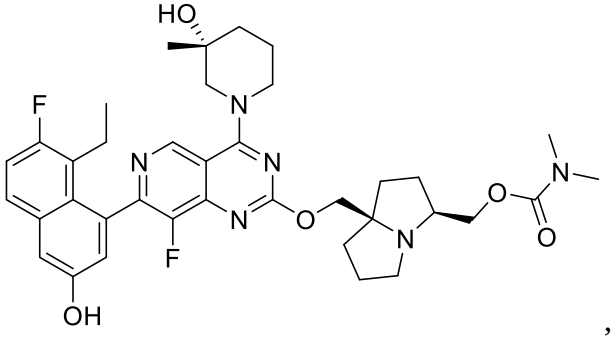

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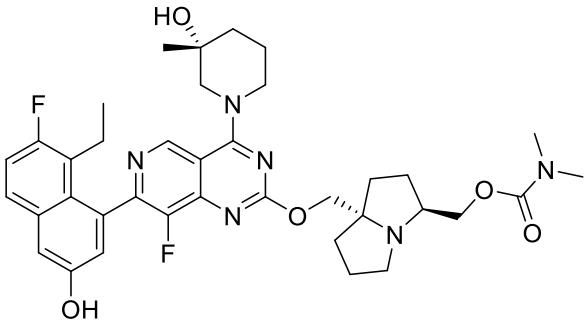
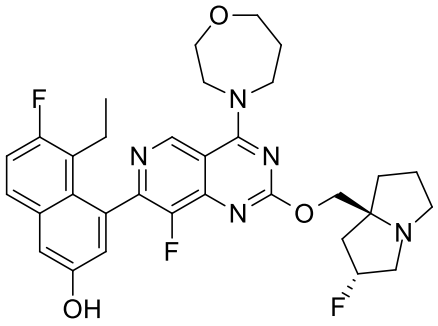
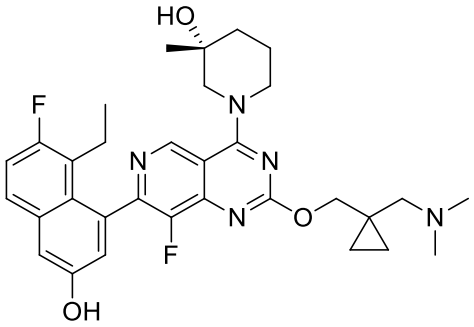
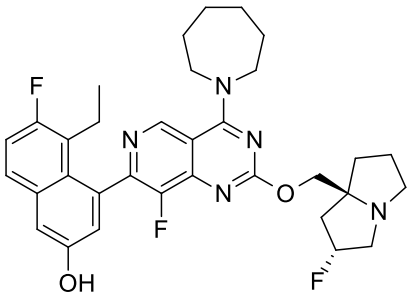
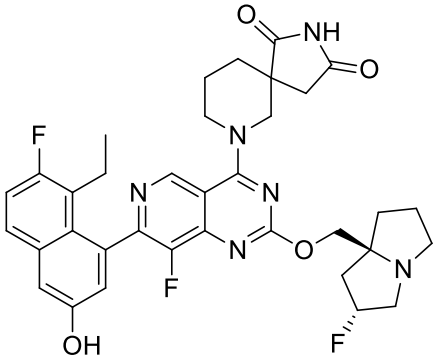
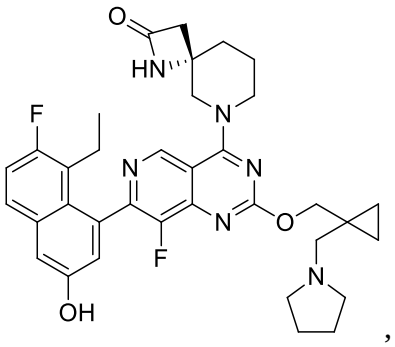
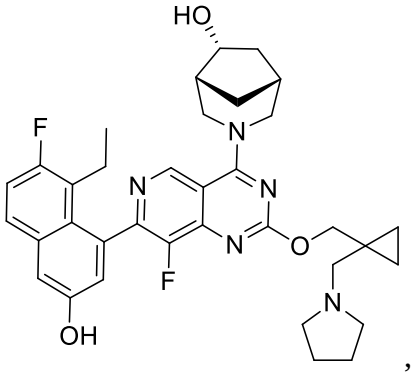
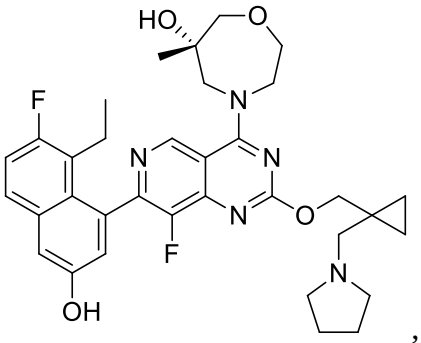

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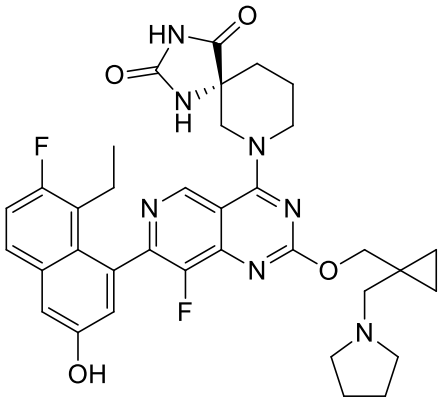
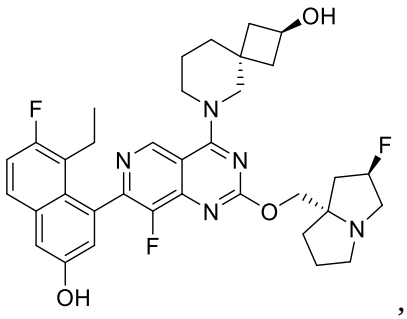
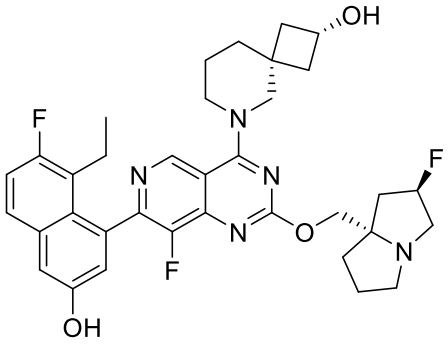
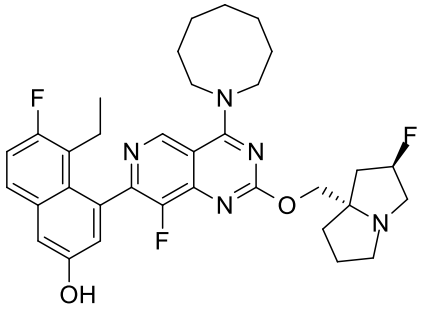
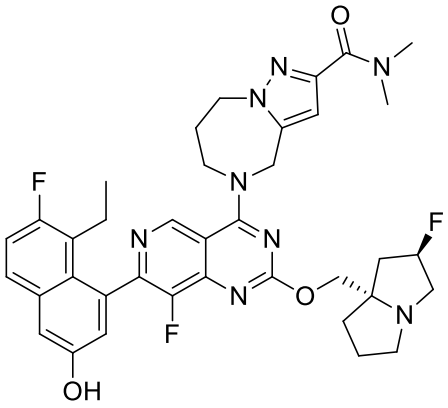
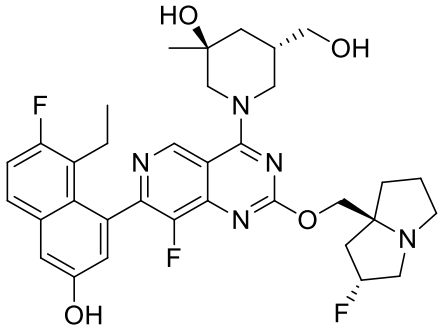
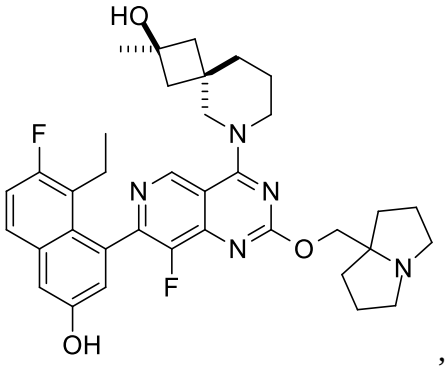
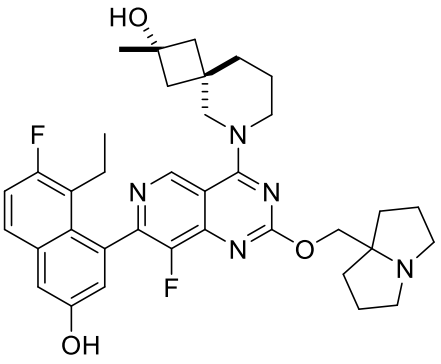

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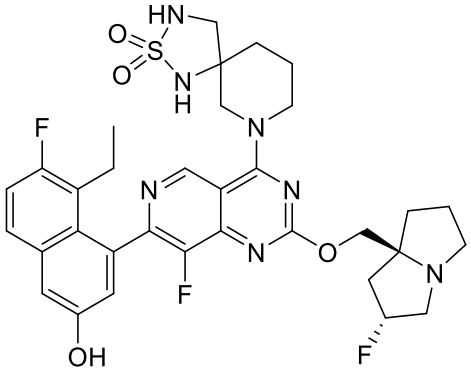
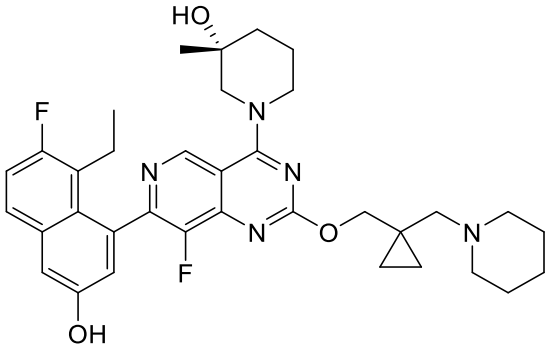
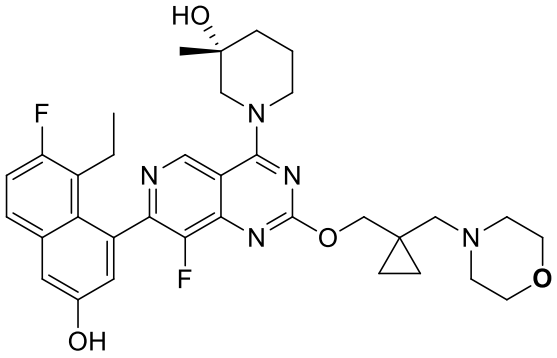
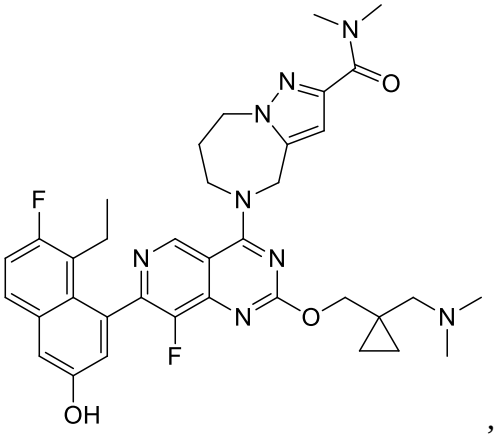
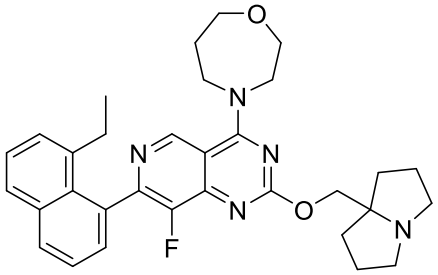
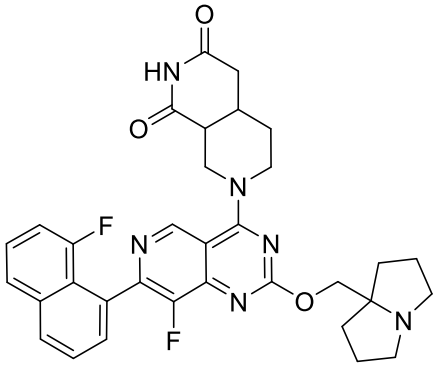
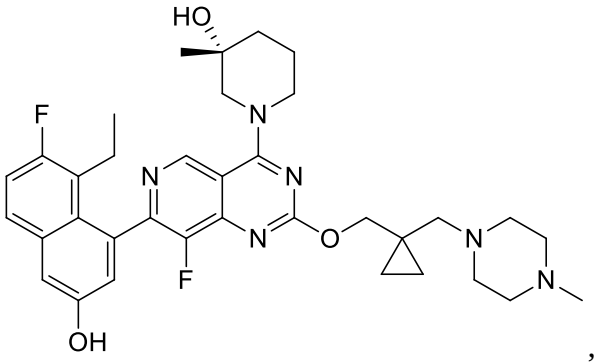
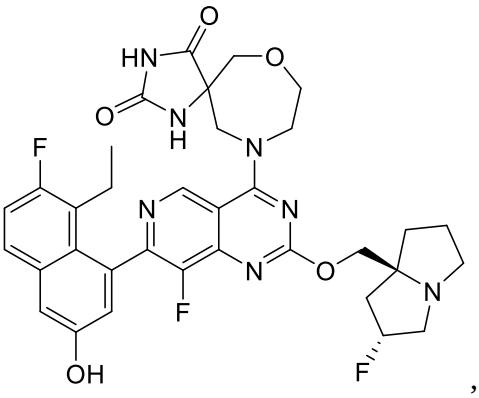

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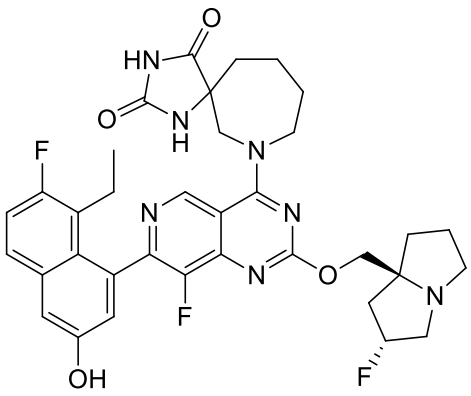
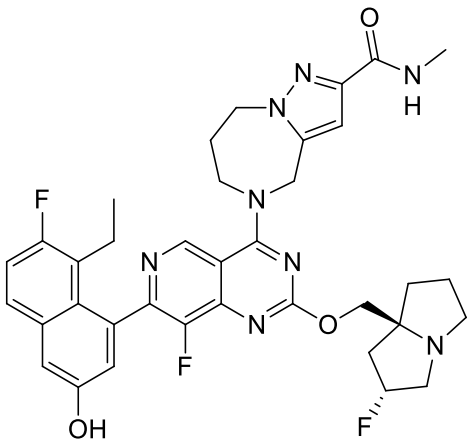
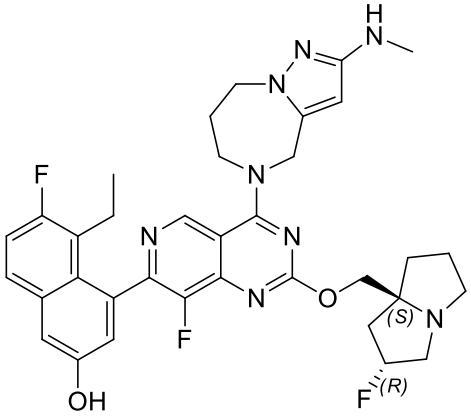
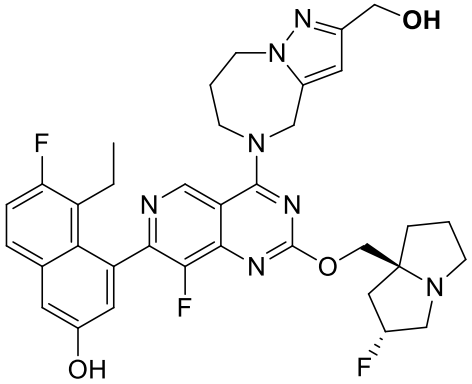
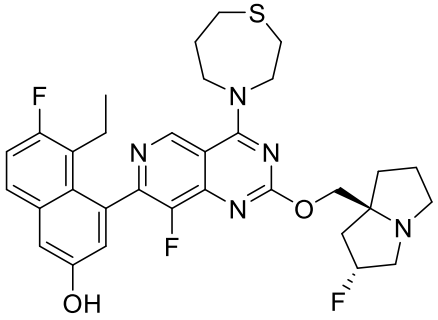
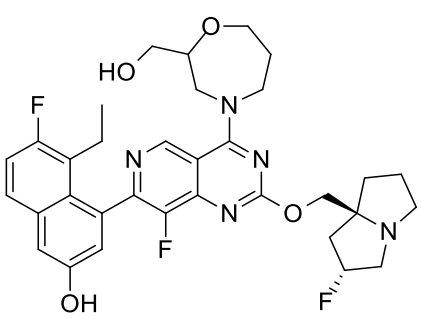
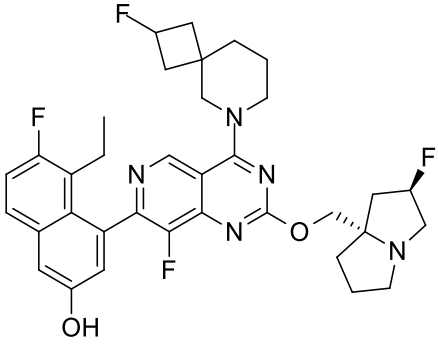
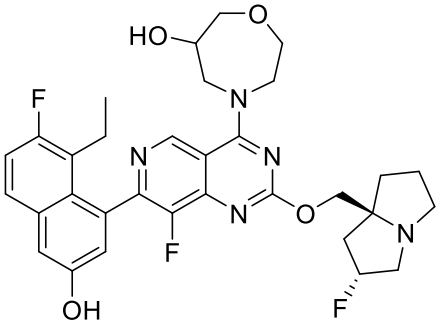

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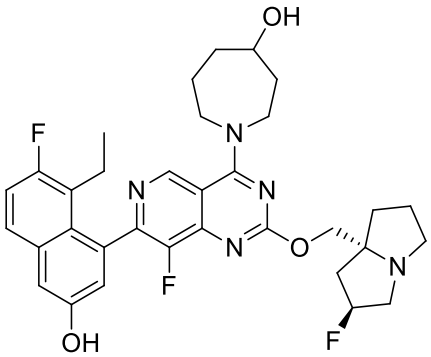
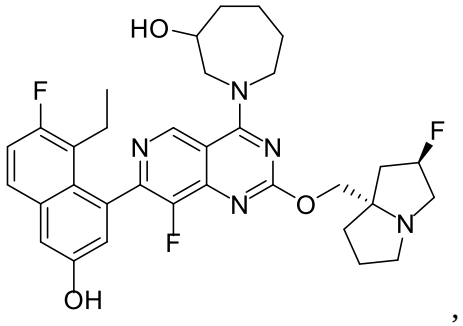
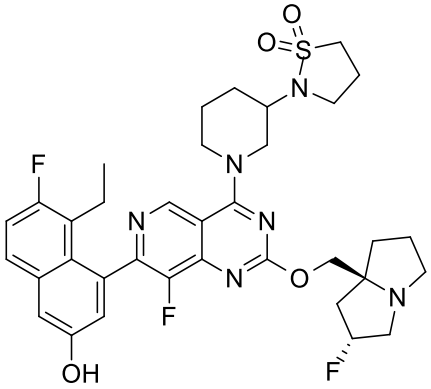
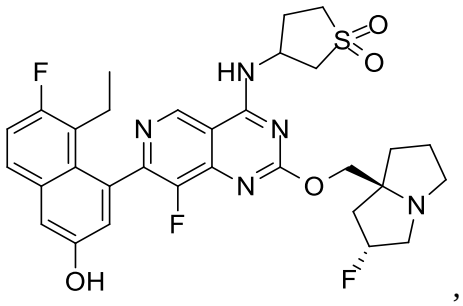
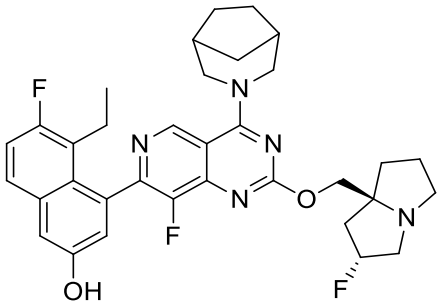
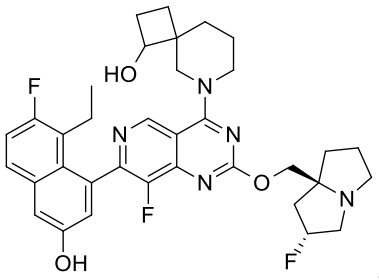
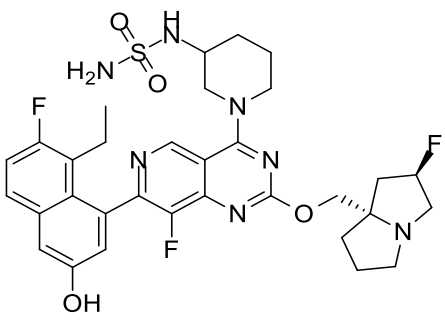
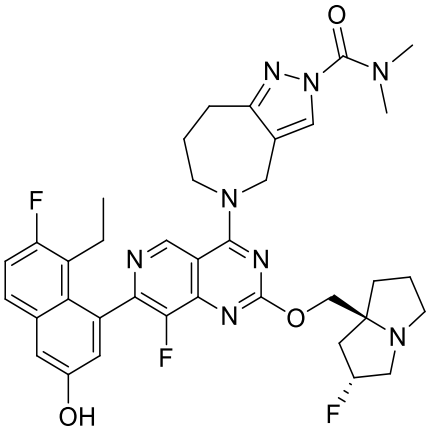

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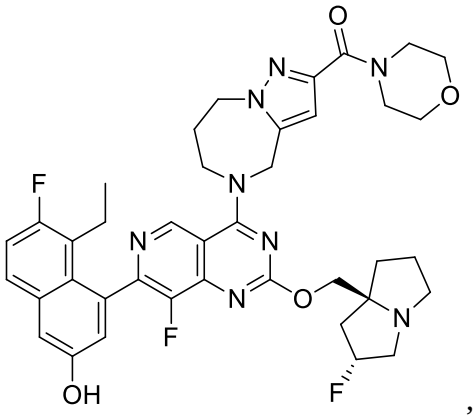
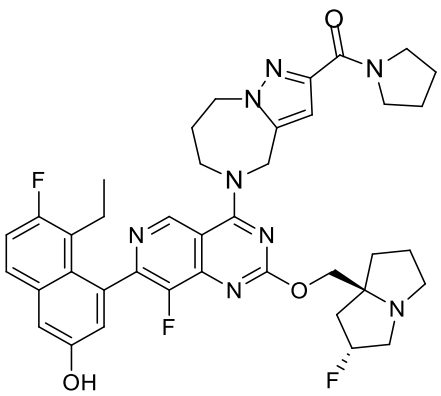
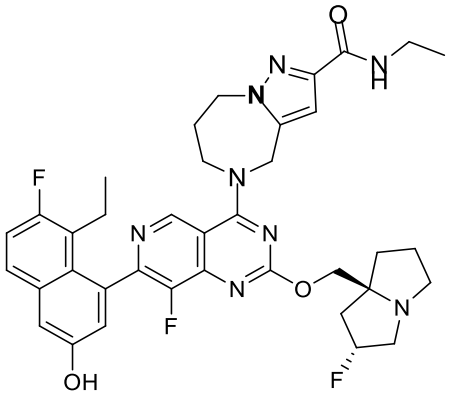
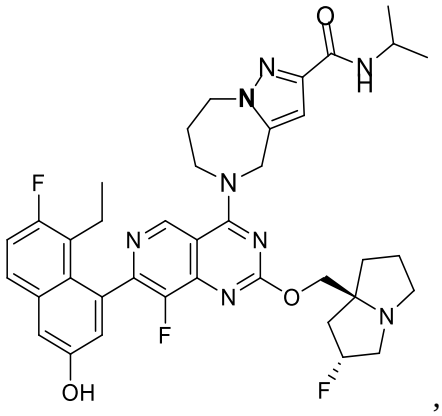
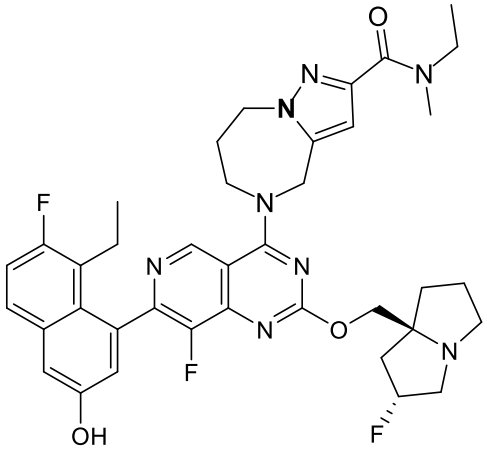
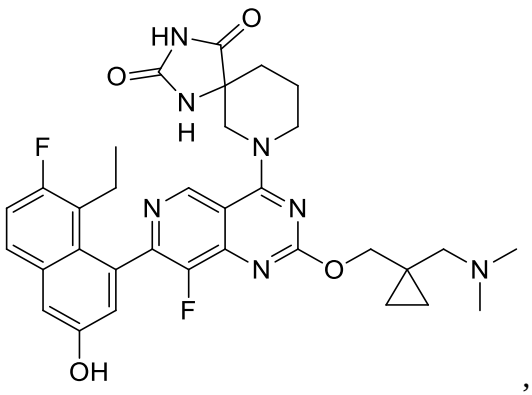
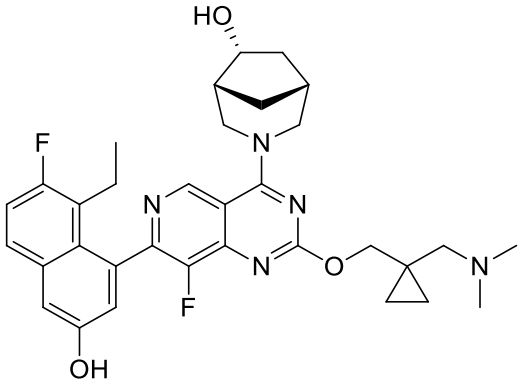
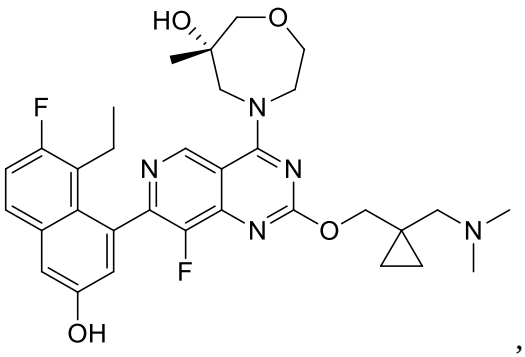

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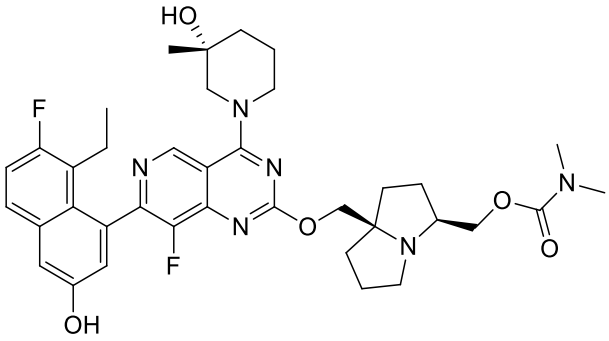
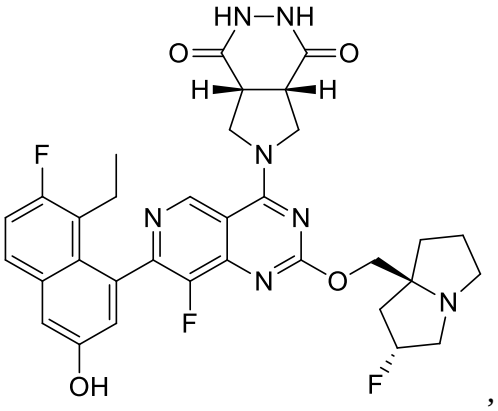
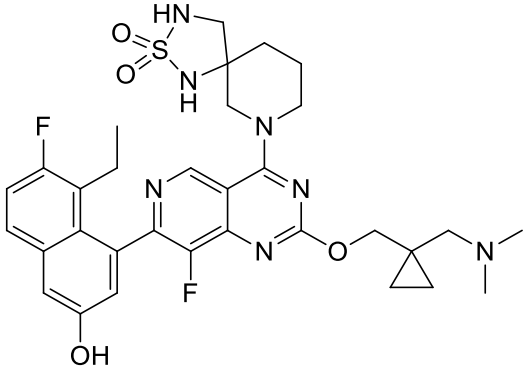
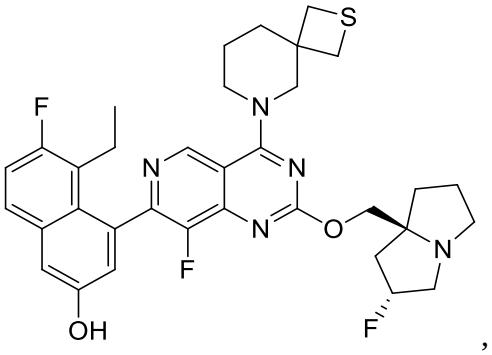
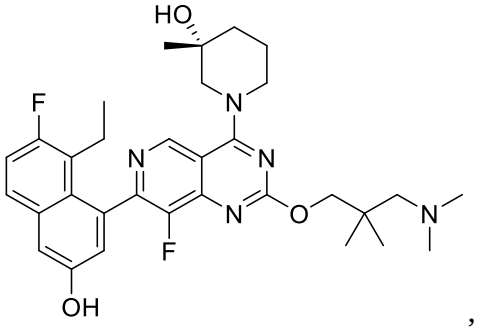
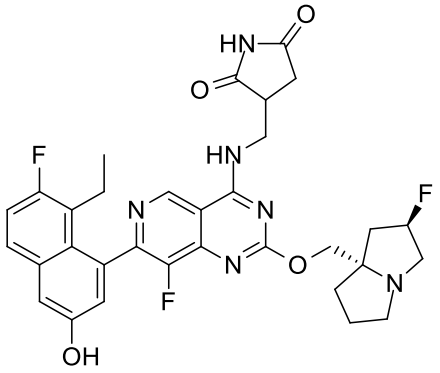
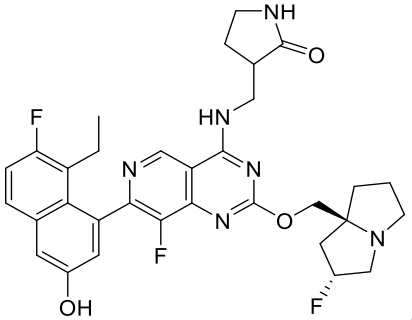
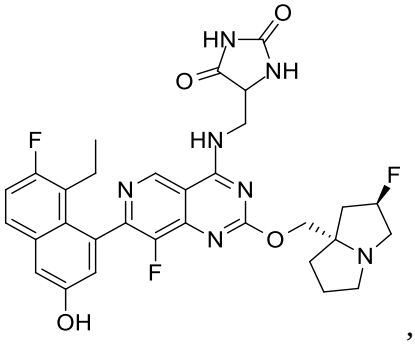









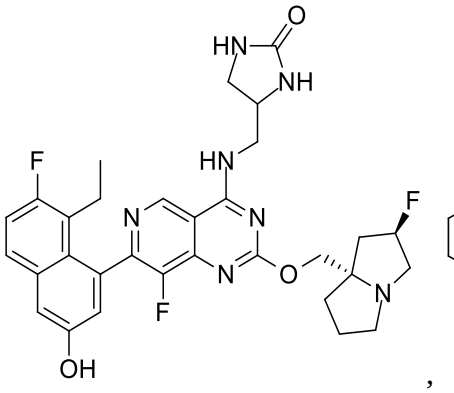
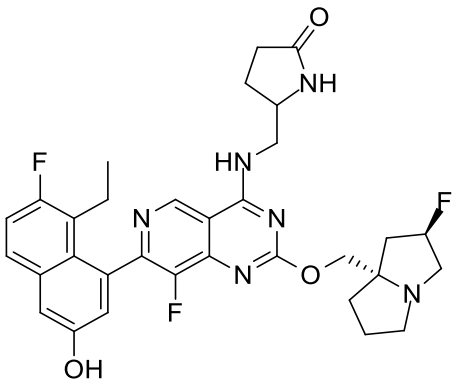
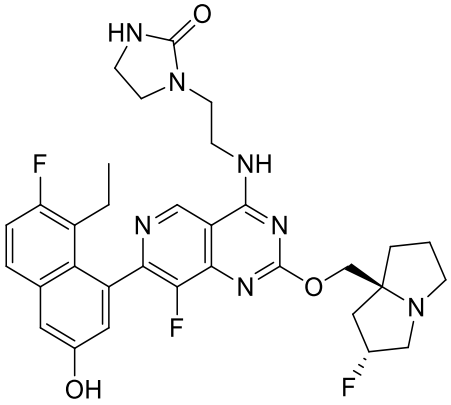
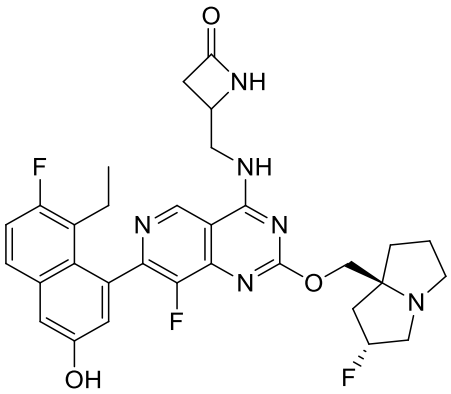
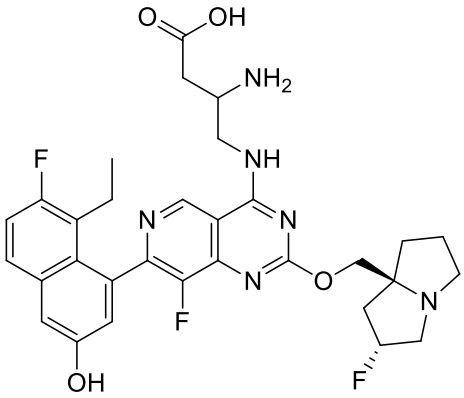
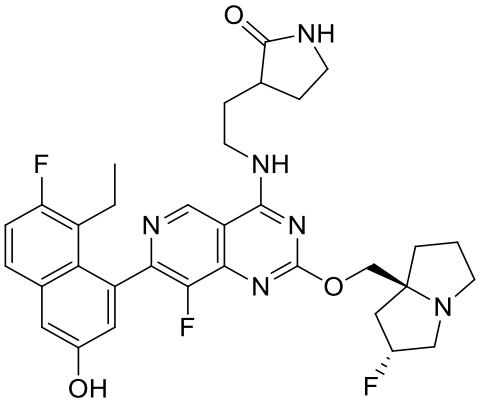
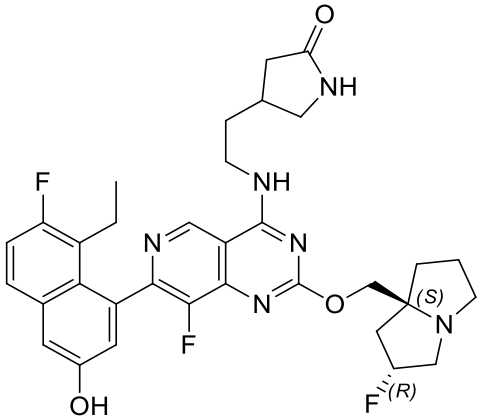
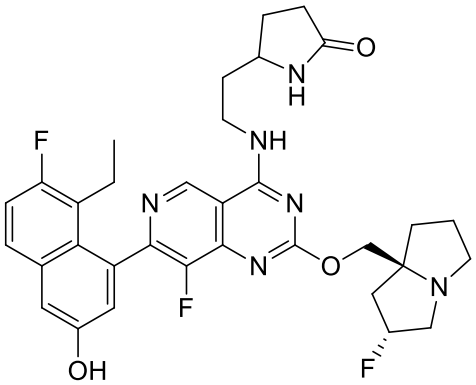

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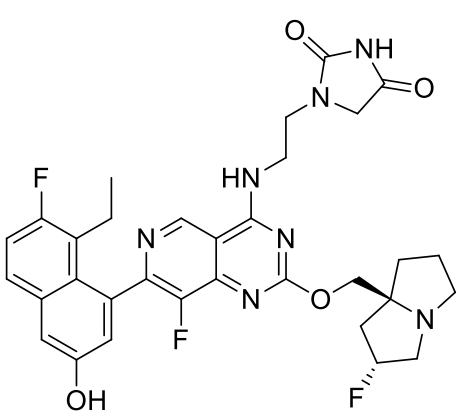
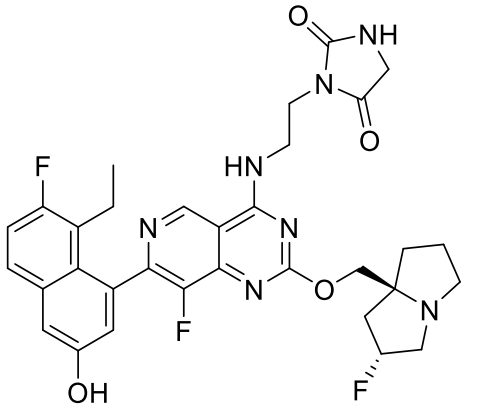
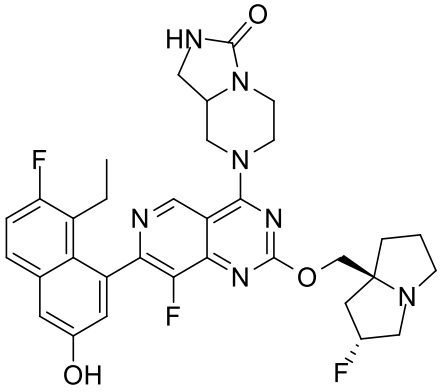
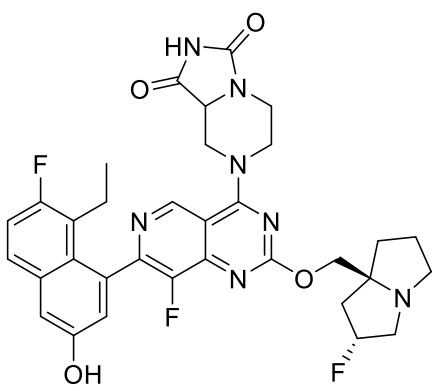
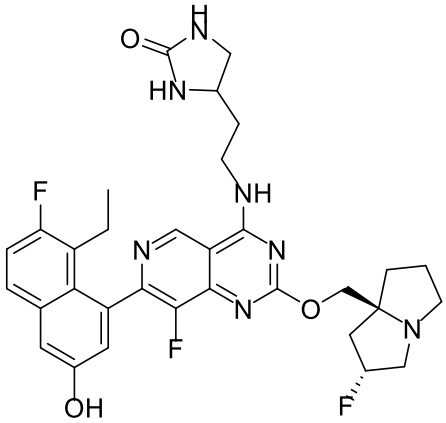
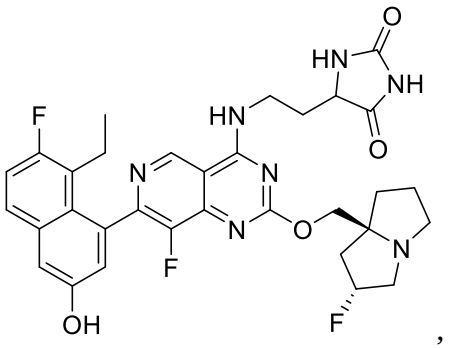
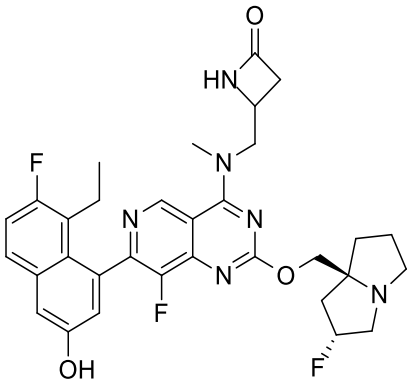
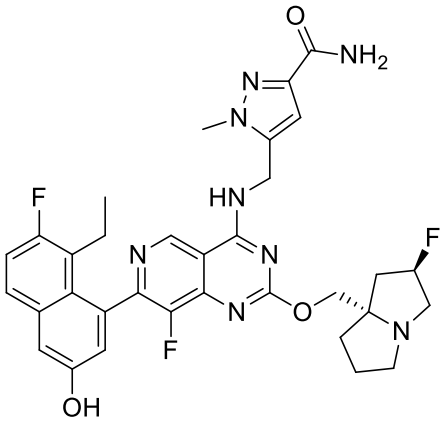

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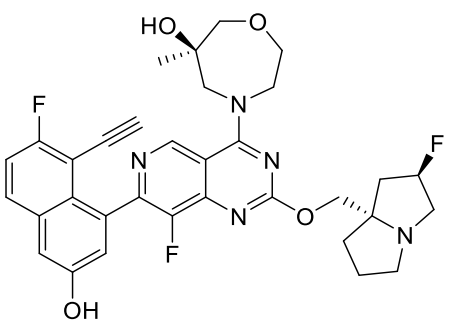
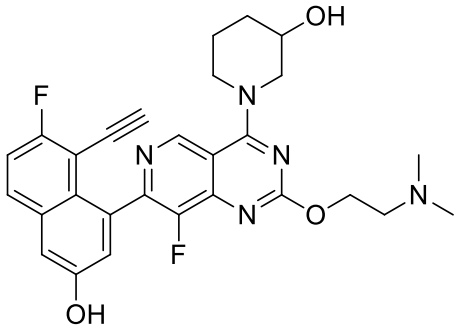
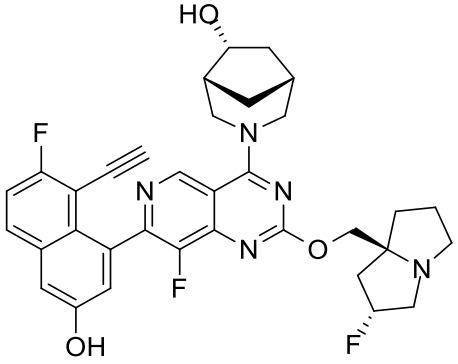
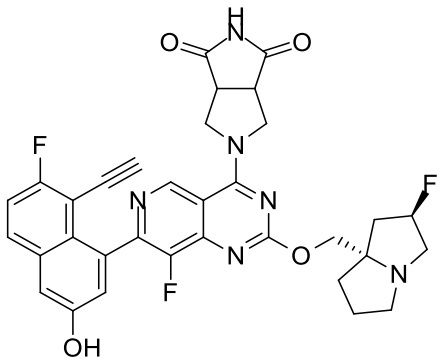
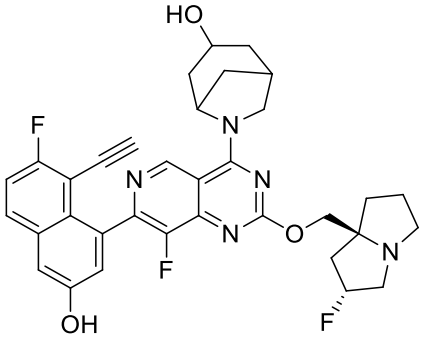
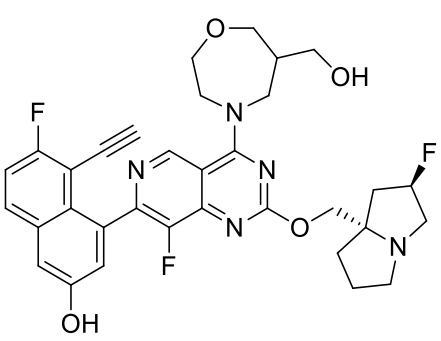
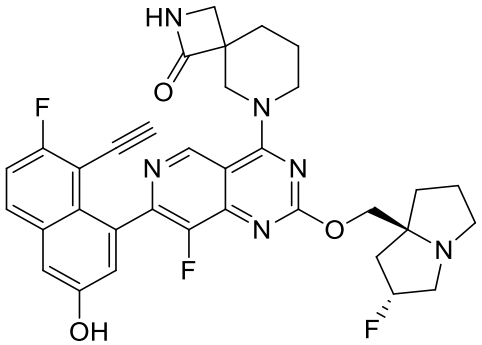
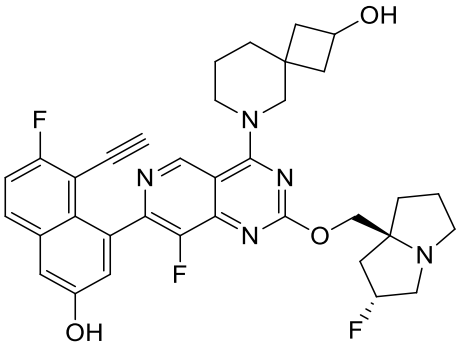









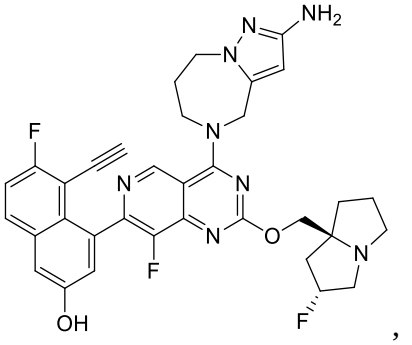
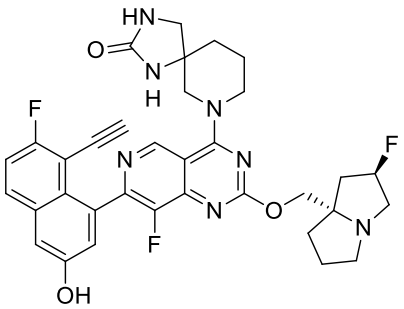
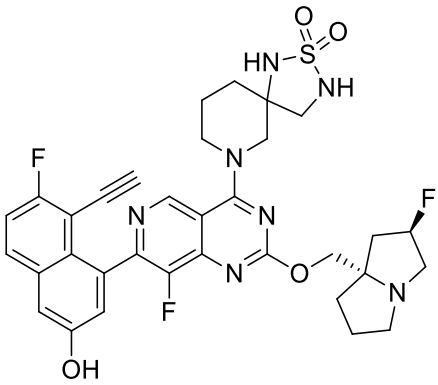
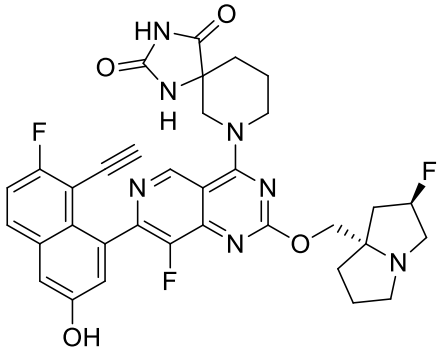
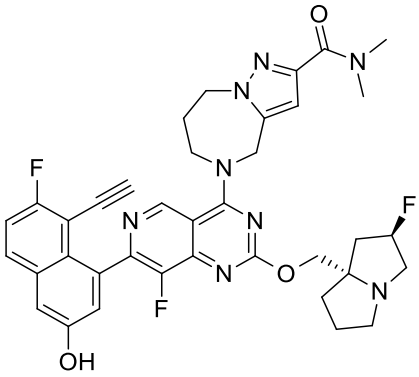
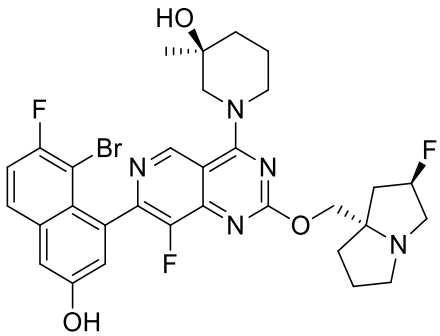
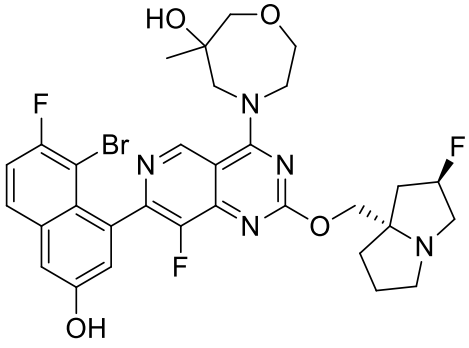
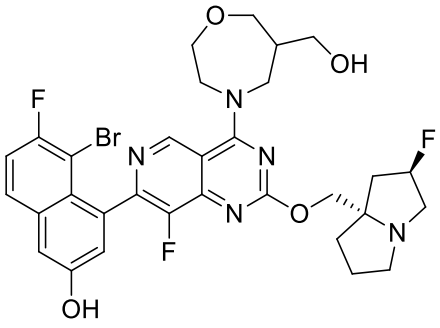

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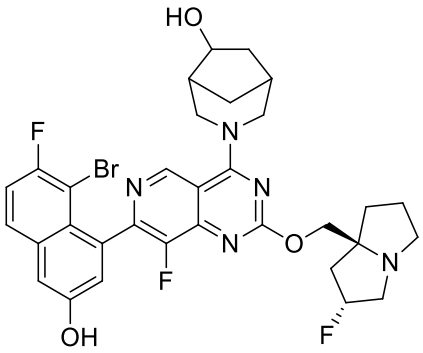
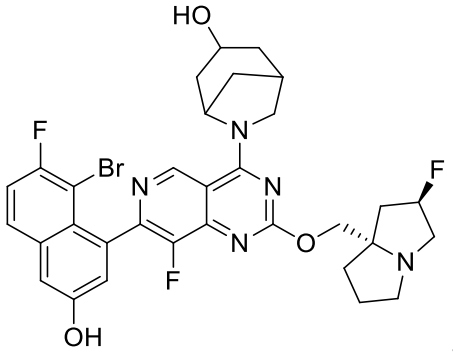
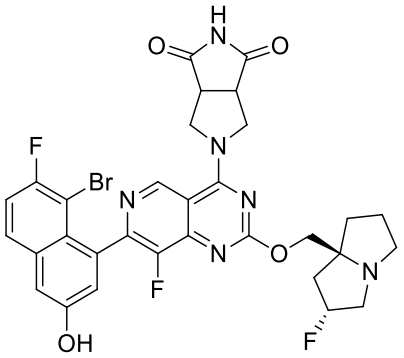
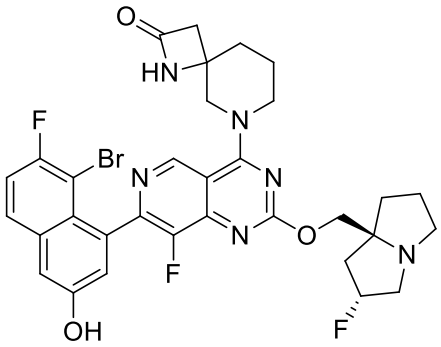
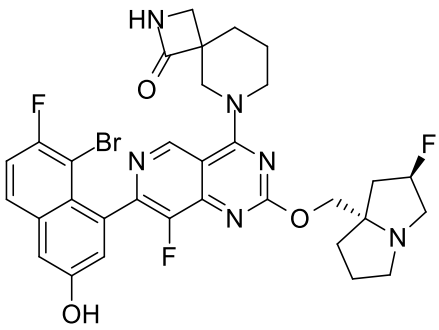
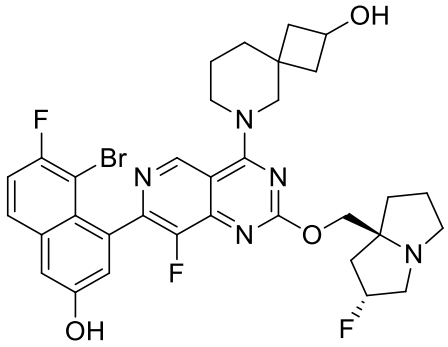
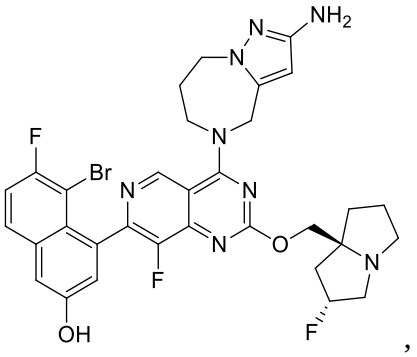
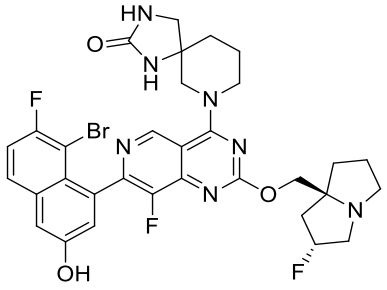

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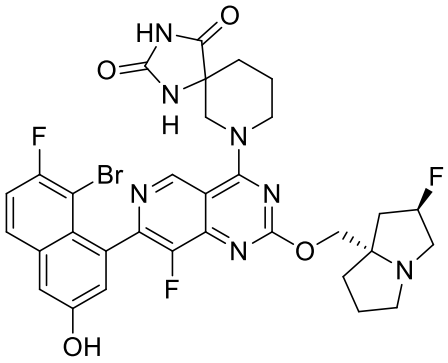
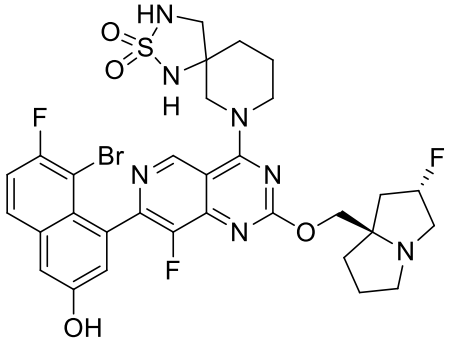
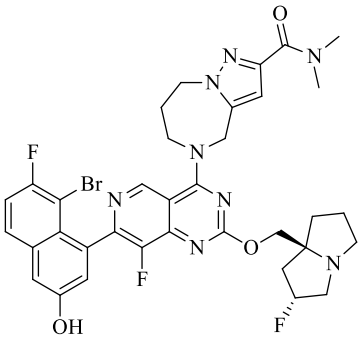
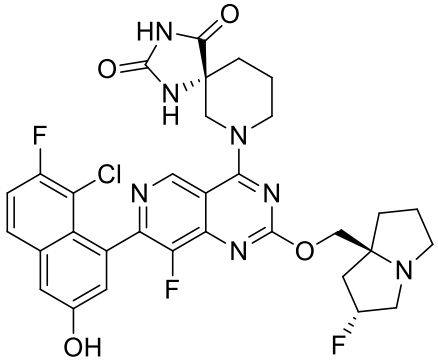
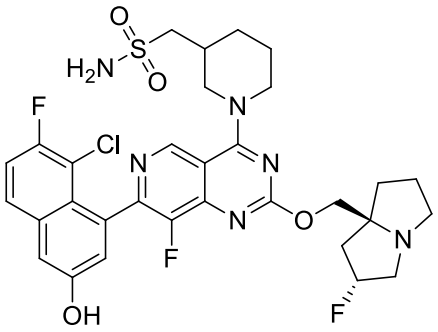
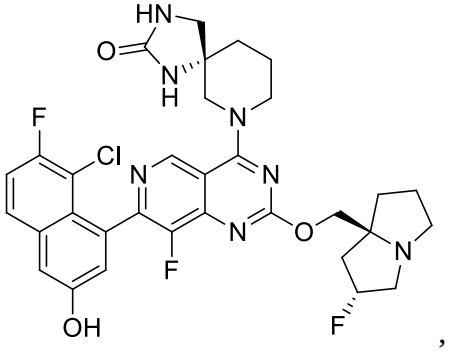
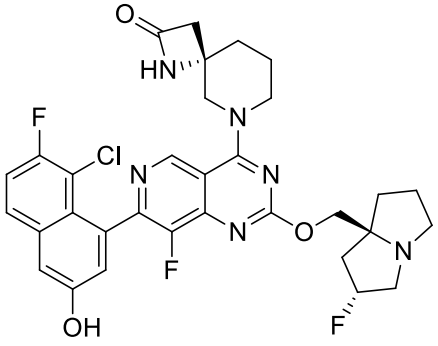
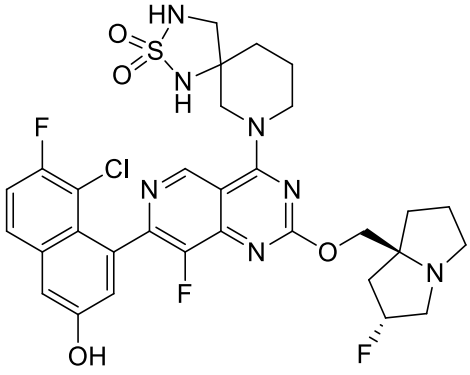

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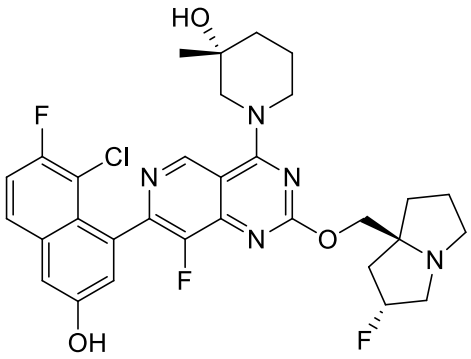
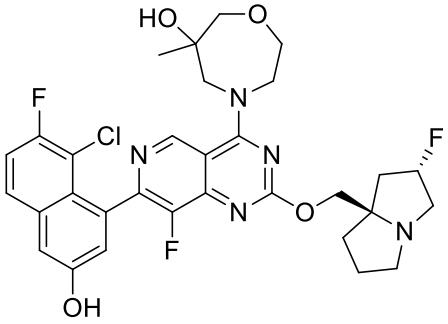
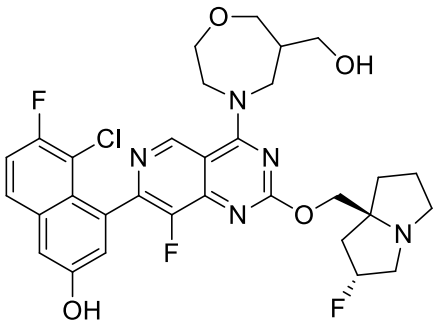
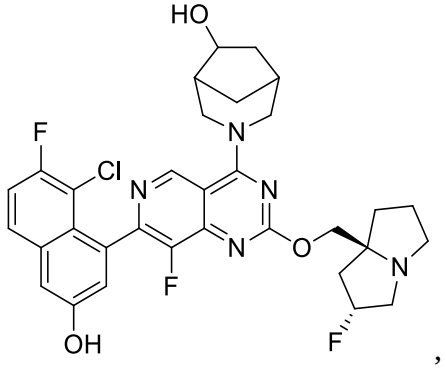
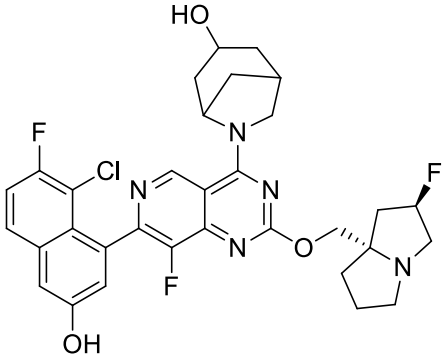
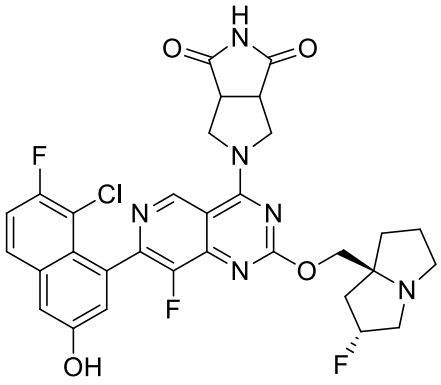
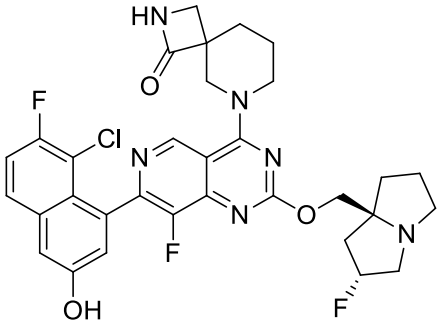
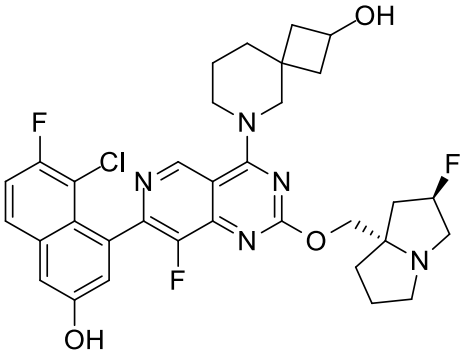

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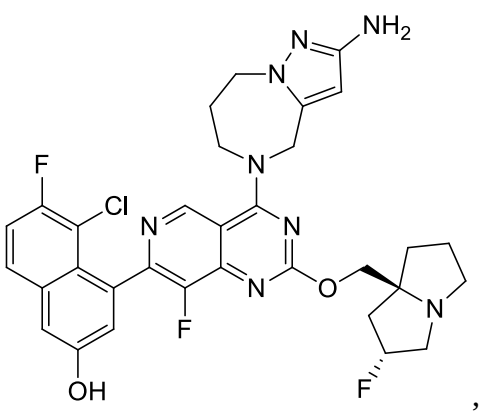
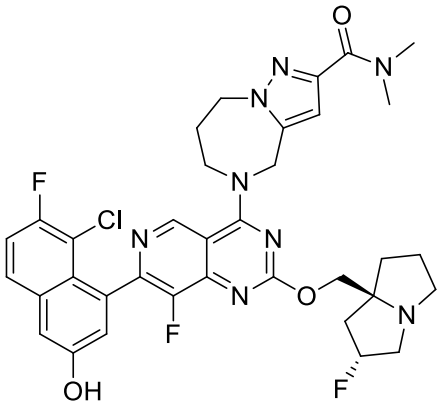
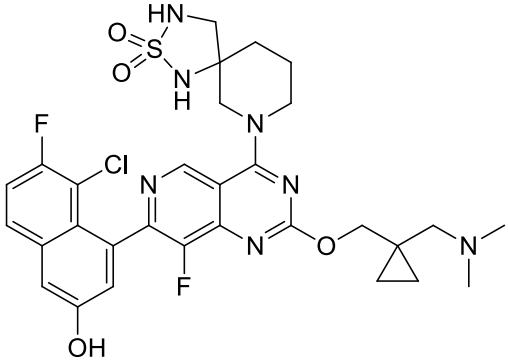
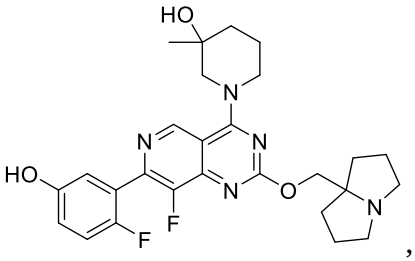
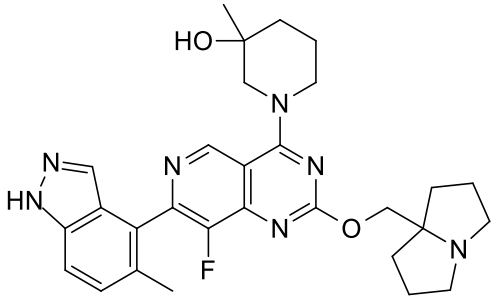
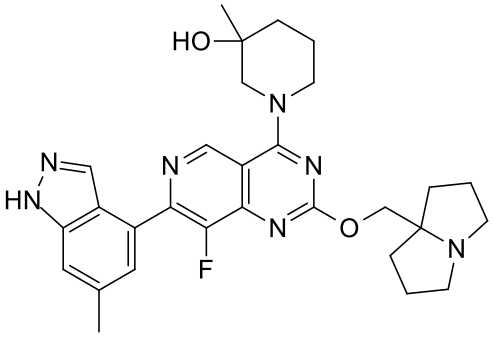
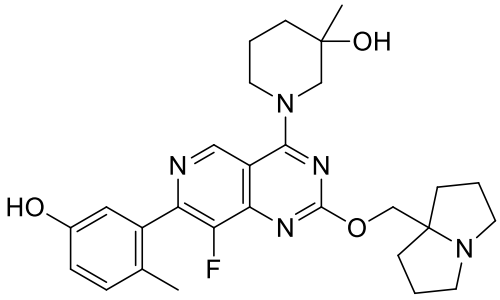
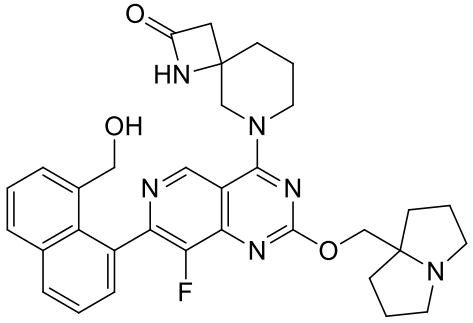









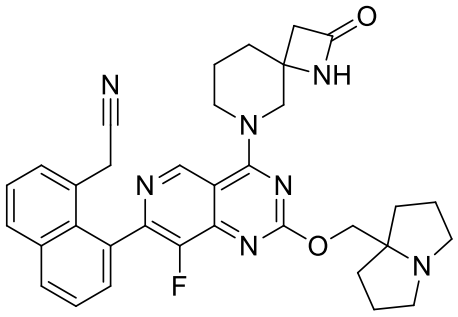
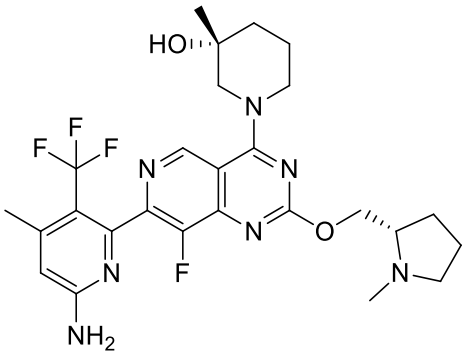
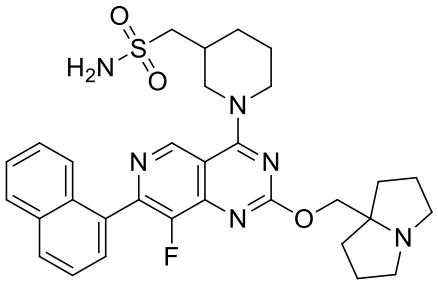
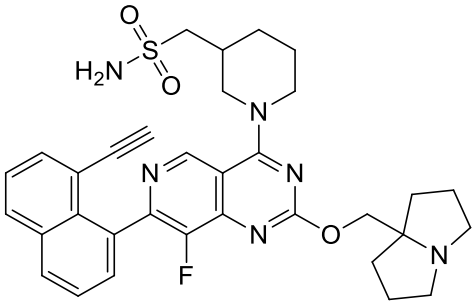
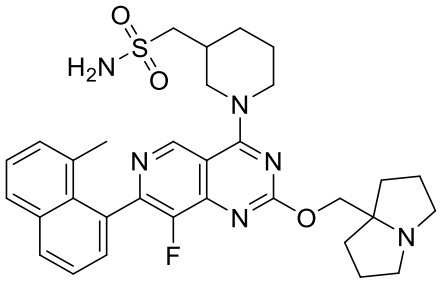
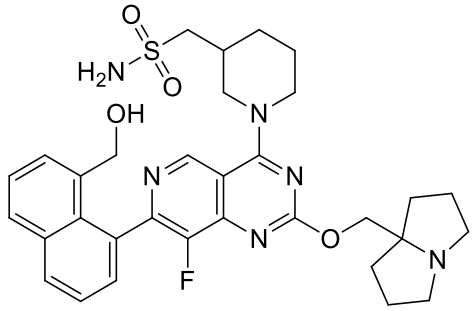
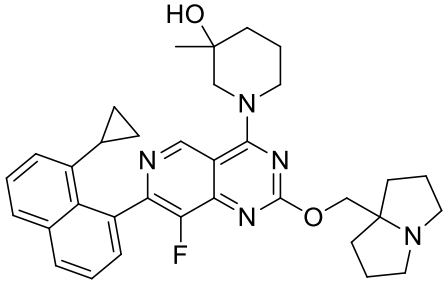
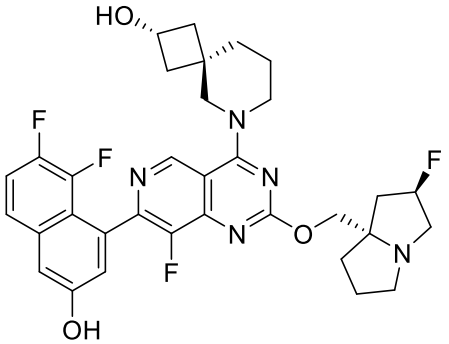

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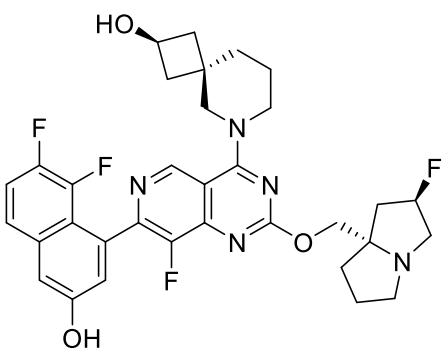
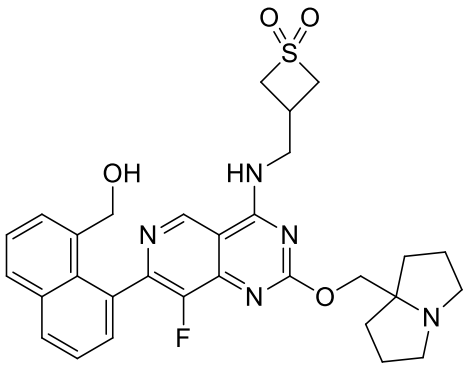
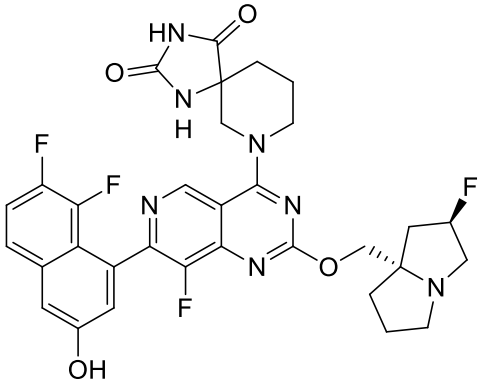
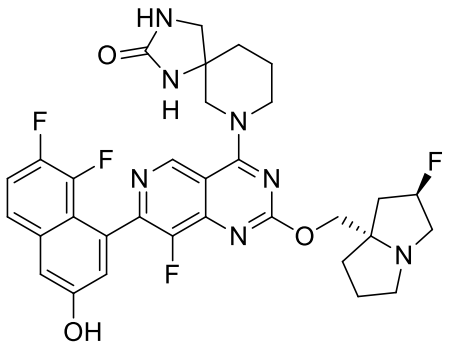
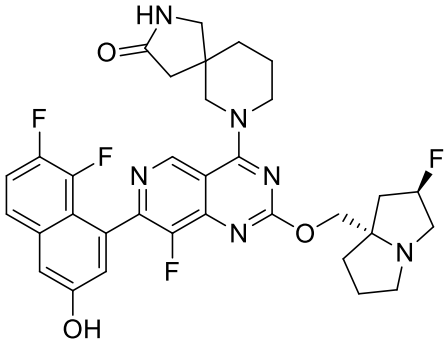
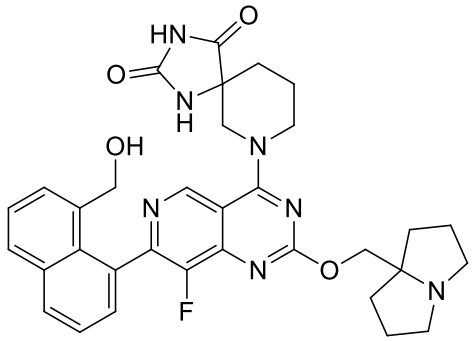
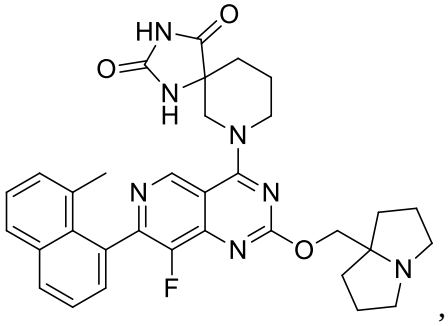
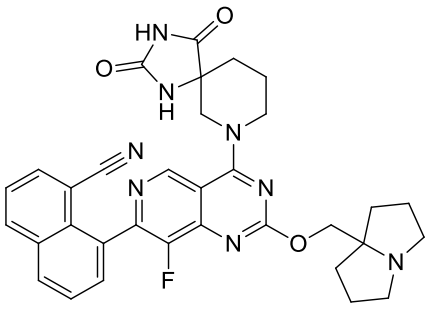

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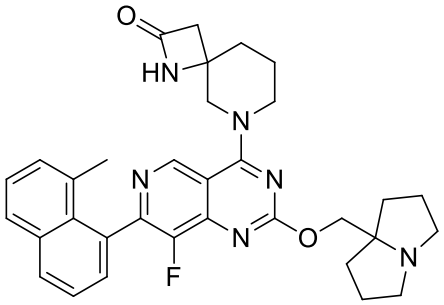
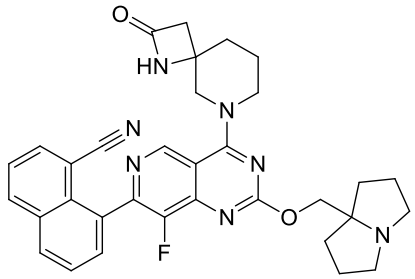
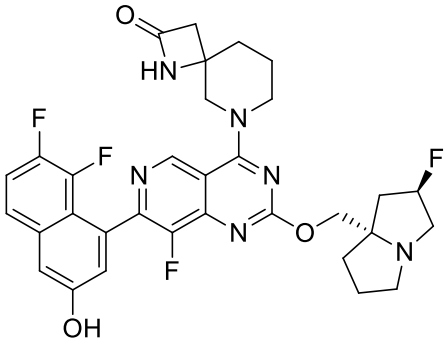
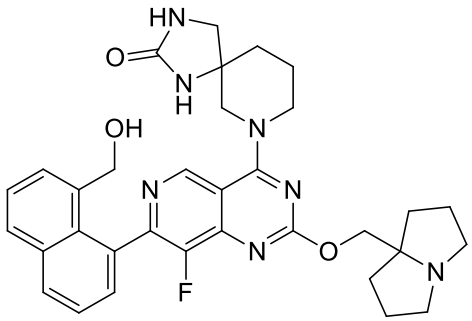
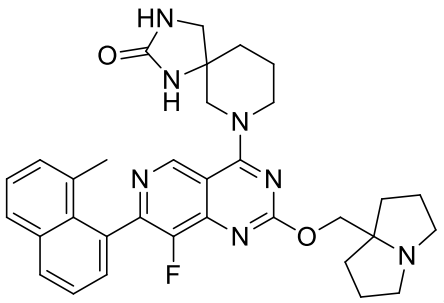
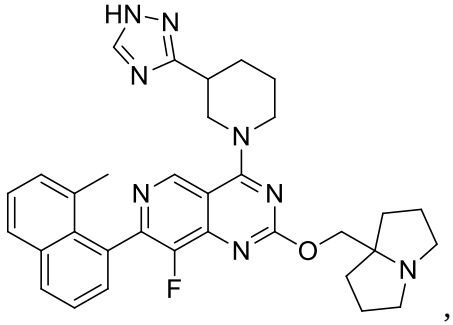
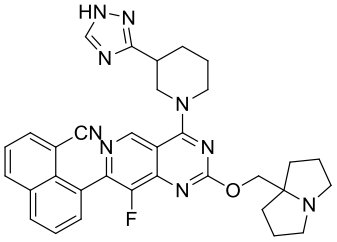
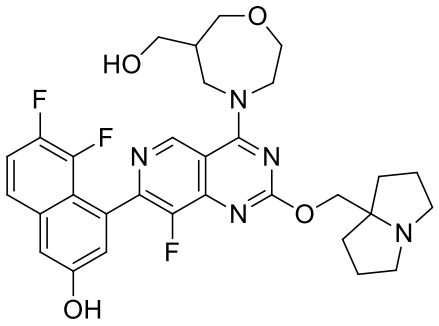
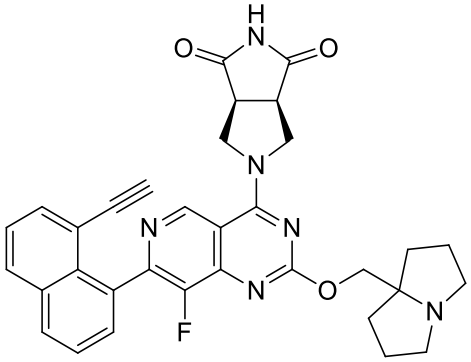
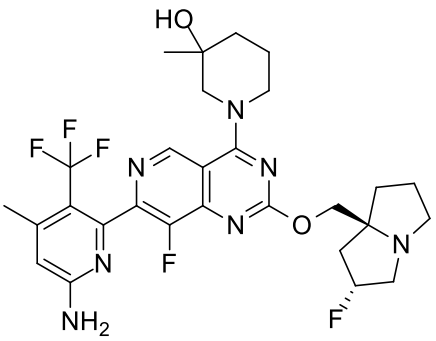









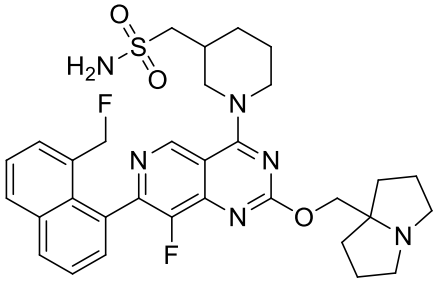
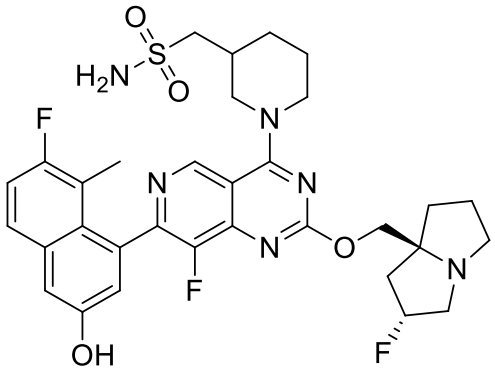
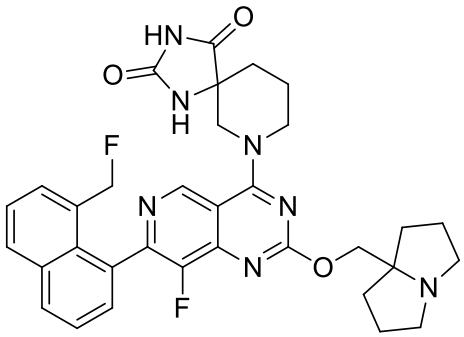
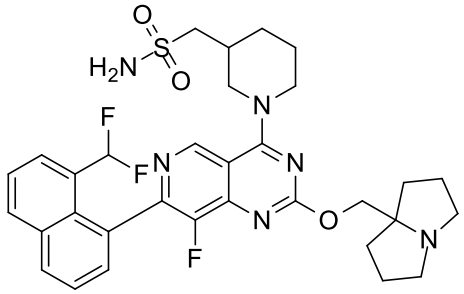
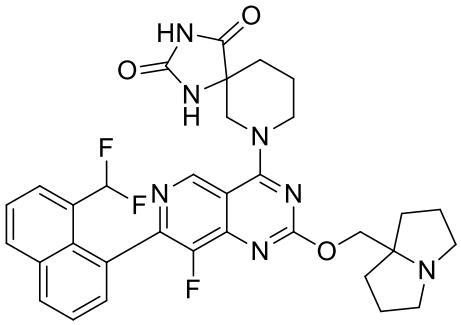
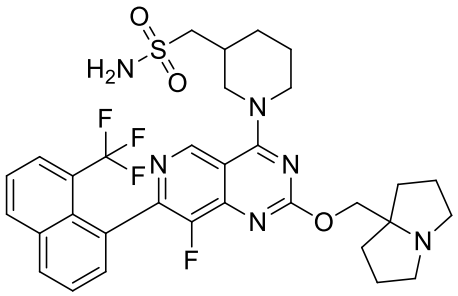
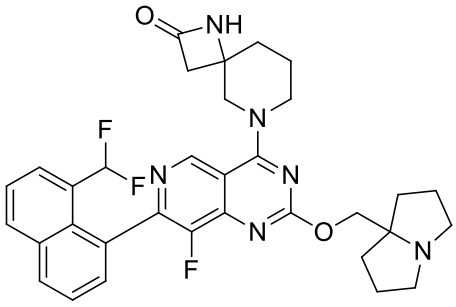
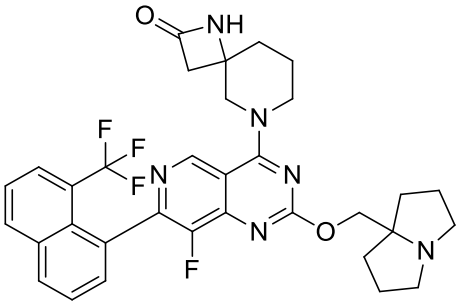
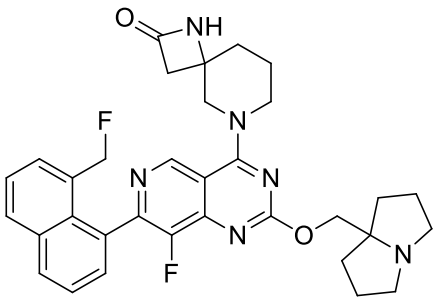
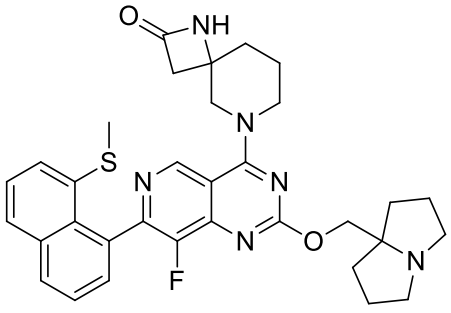

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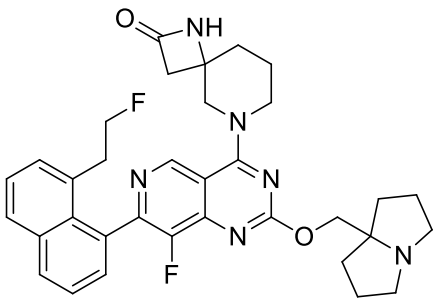
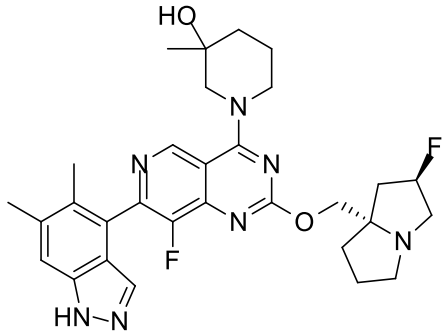
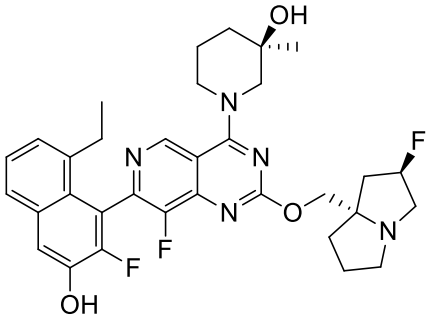
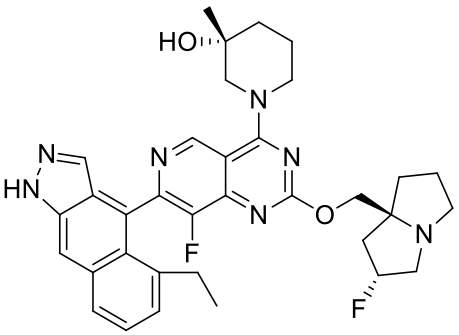
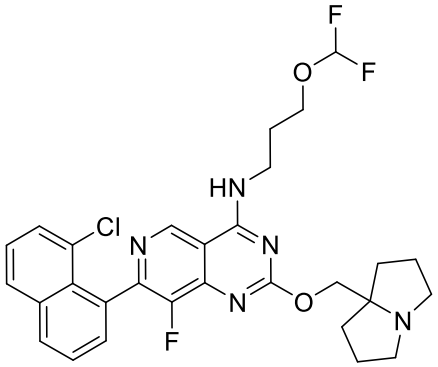
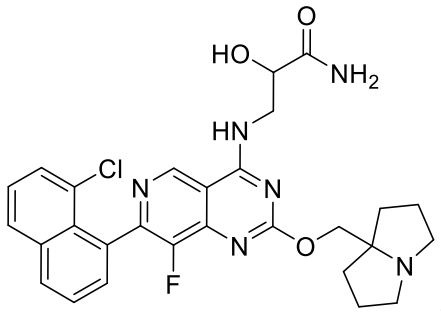
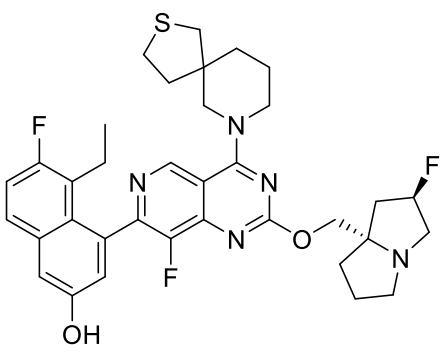
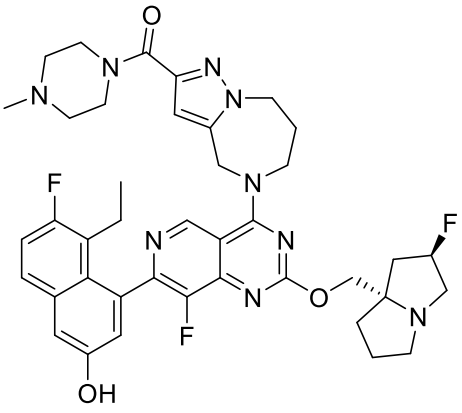

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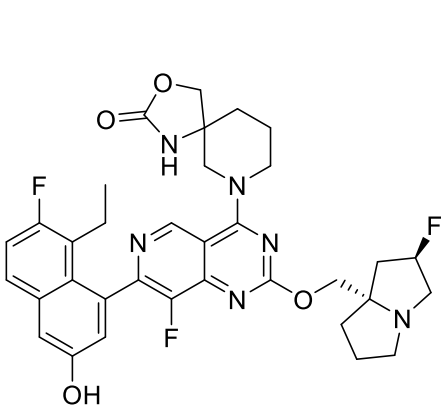
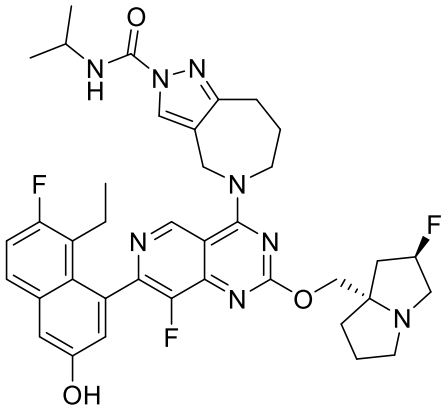
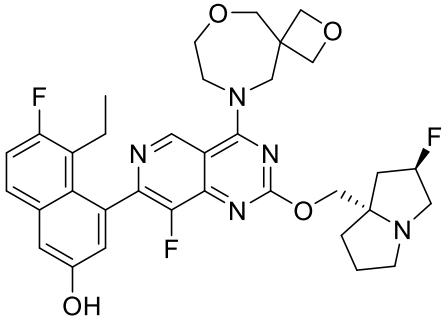
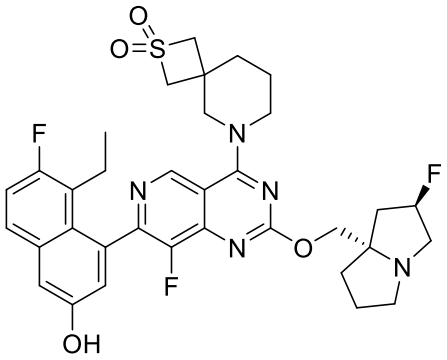
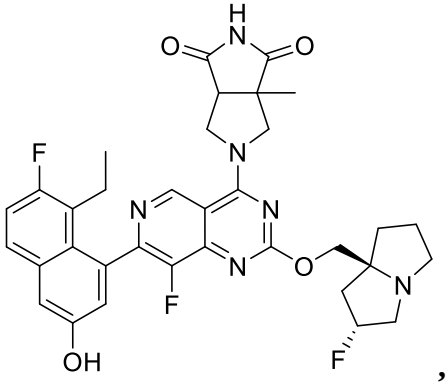
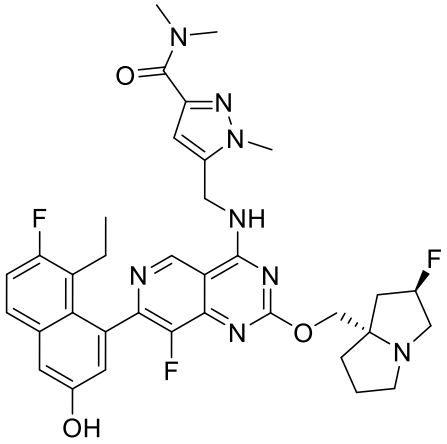
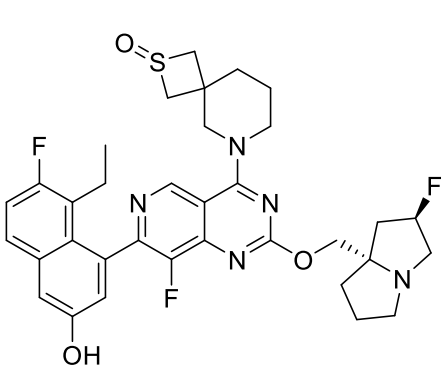
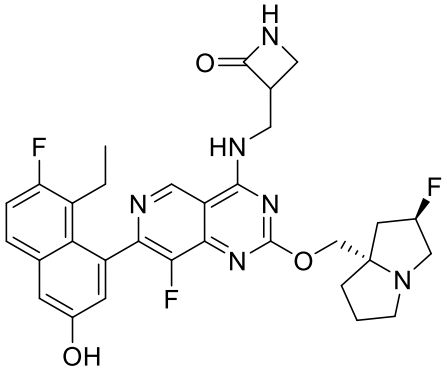
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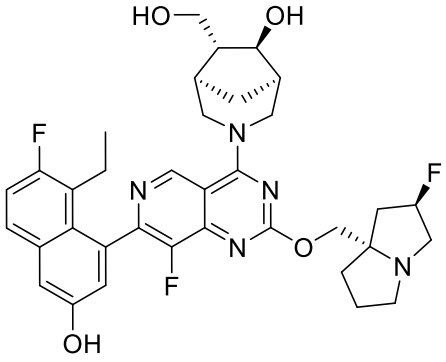
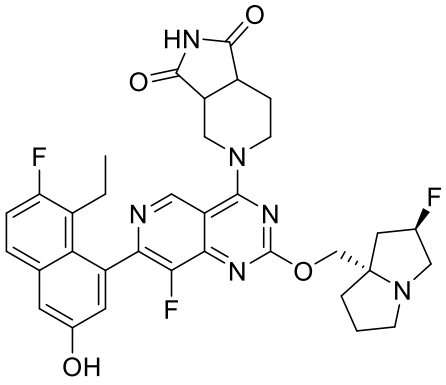
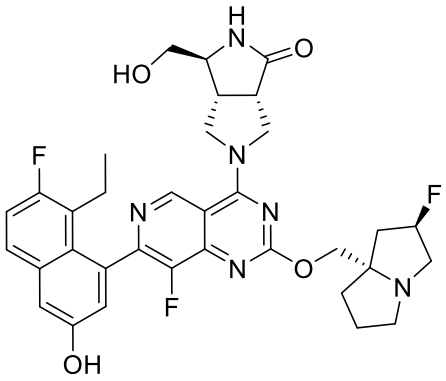
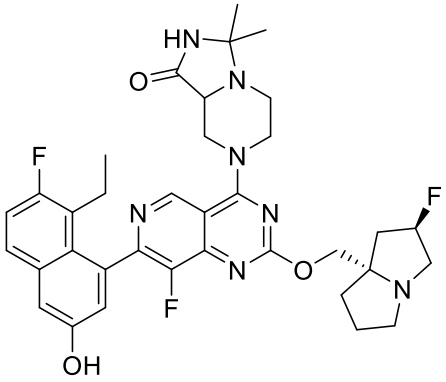
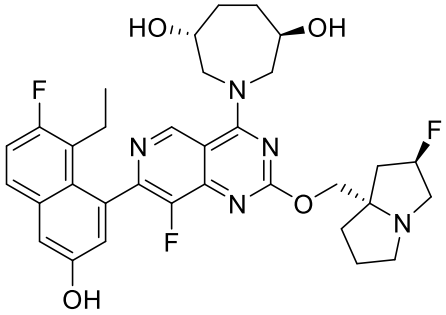
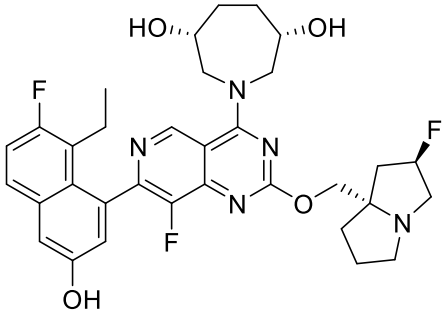
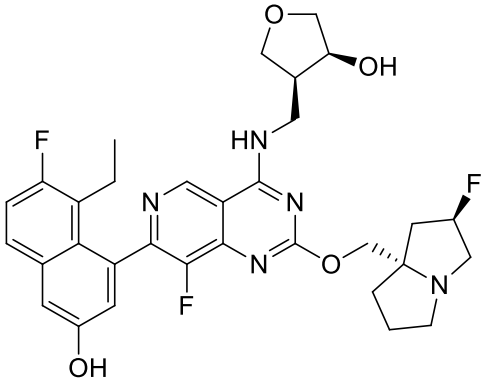
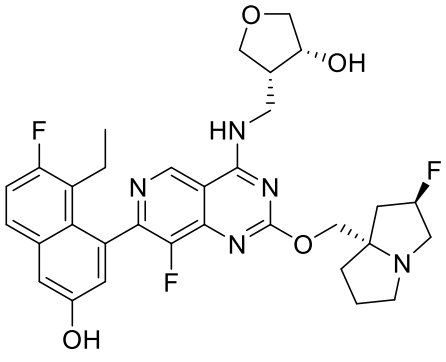









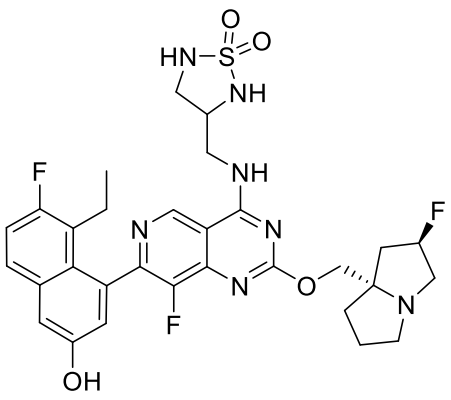
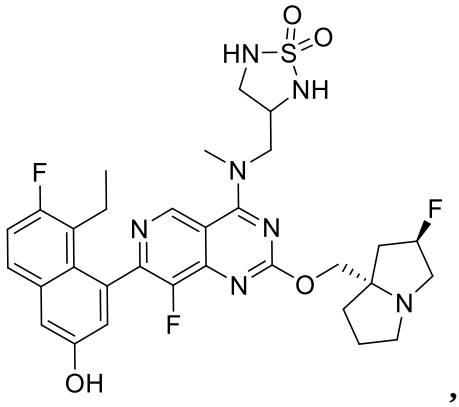
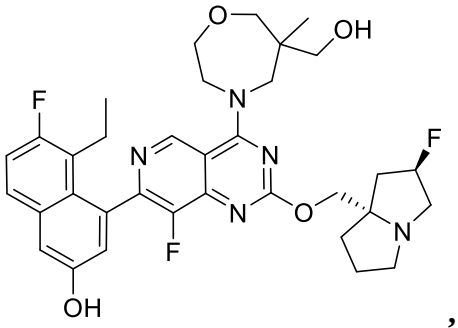
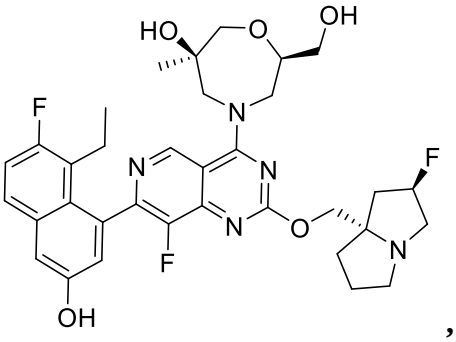
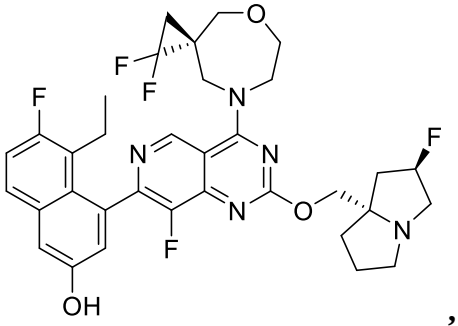
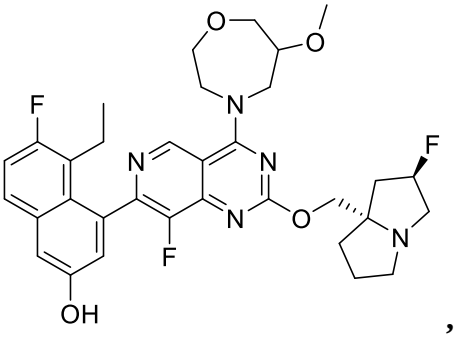
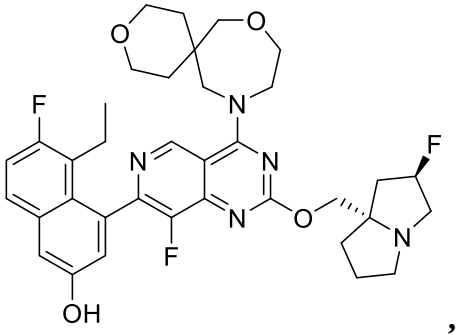
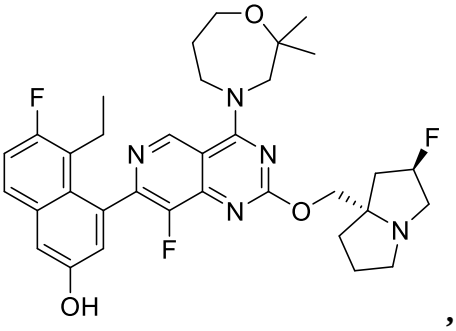

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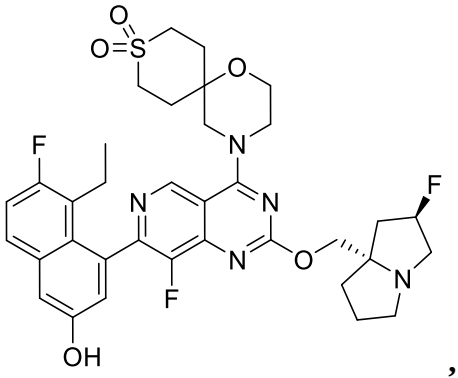
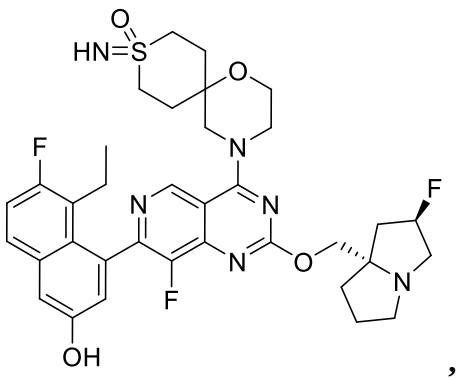
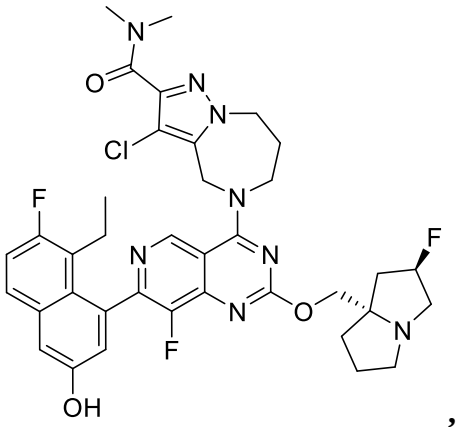
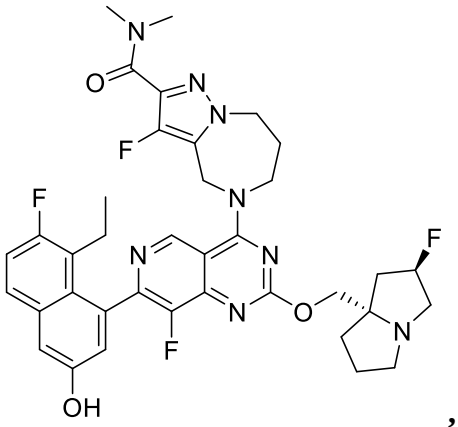
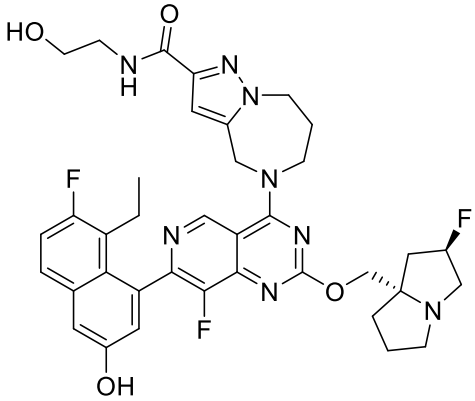
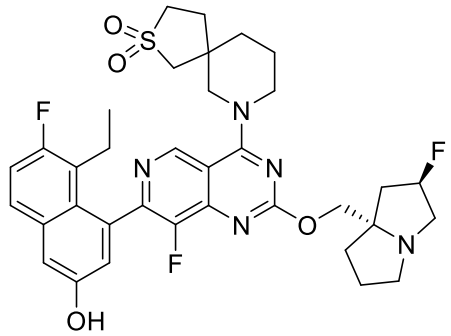
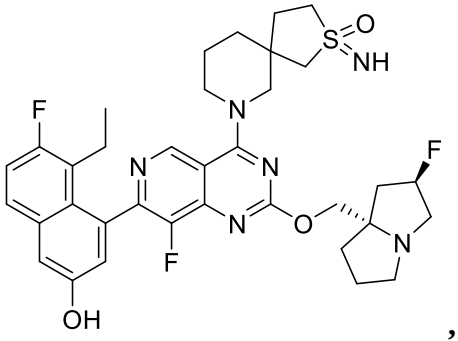
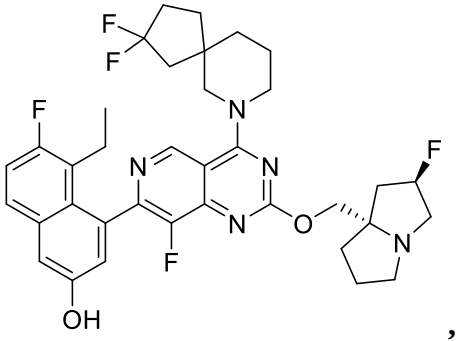

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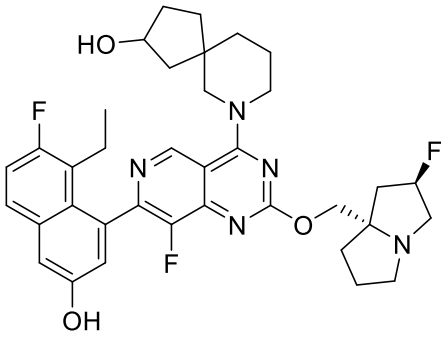
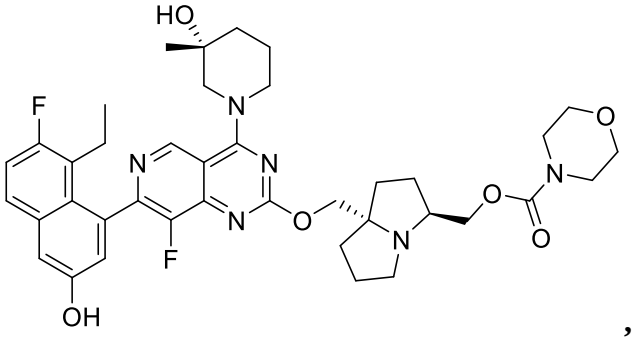
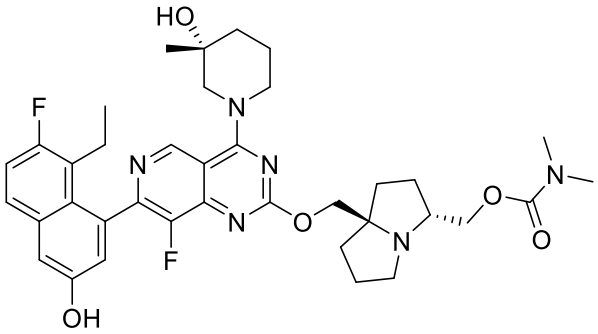
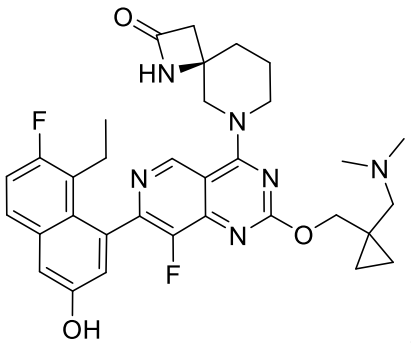
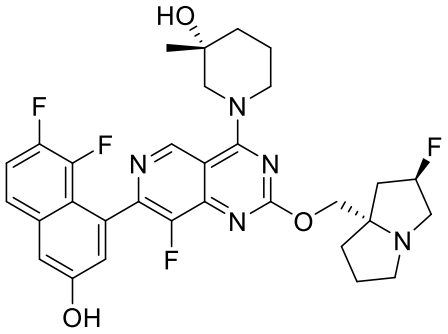
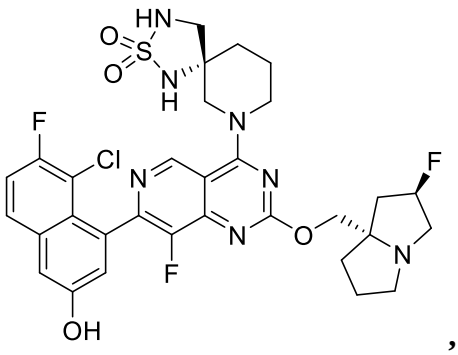
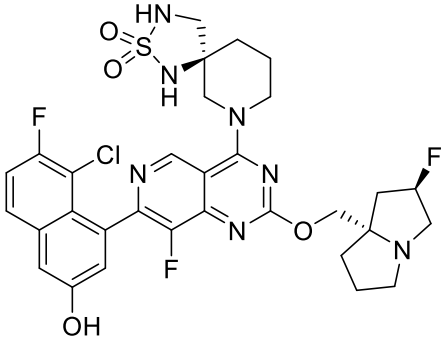
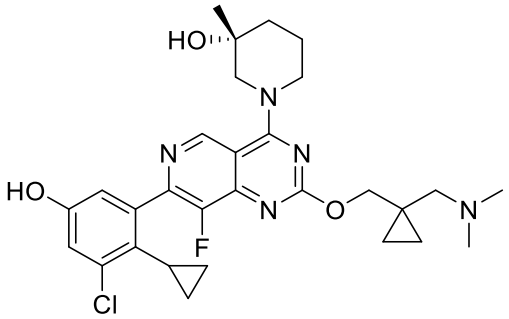

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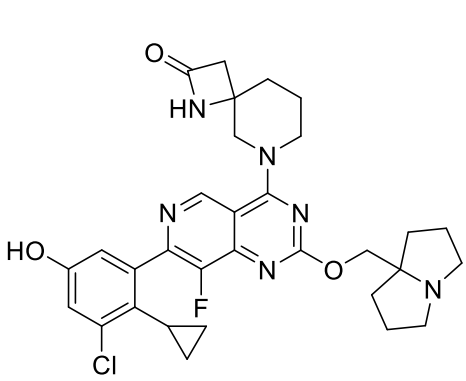
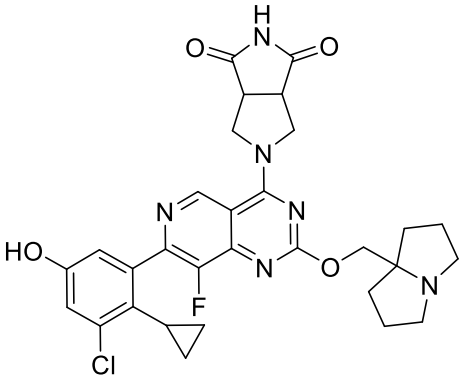
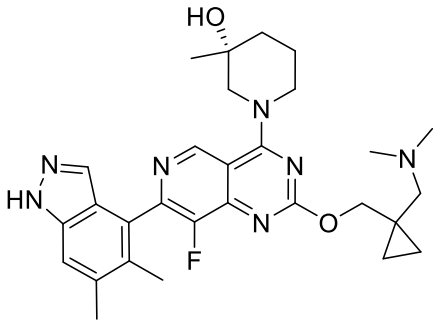
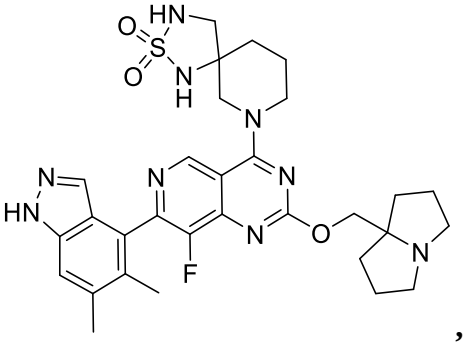
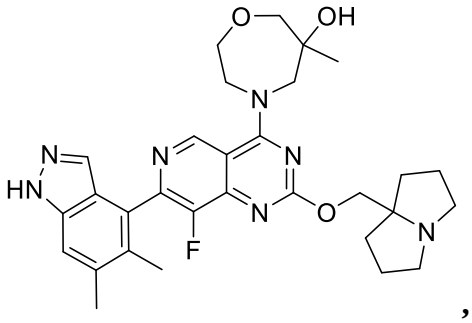
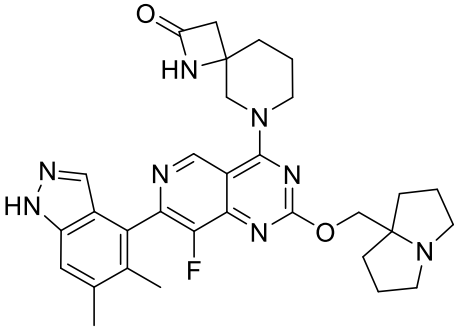

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and pharmaceutically acceptable salts thereof.

62. A pharmaceutical composition, comprising a therapeutically effective amount of a compound of any one of claims 1-53 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

63. A method for inhibiting the wild type KRas, KRas G12A, KRas G12C, KRas G12D, KRas G12R, KRas G12S, KRas G12V, KRas G13D or KRas Q61H activity in a cell, comprising contacting the cell in which inhibition of KRas activity is desired with an effective amount of a compound of according to any one of claims 1-53 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 54.

64. Use of a therapeutically effective amount of a compound according to any one of claims 1-53 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 54 in the manufacture of a medicament for treating cancer in a patient.

65. The use of claim 56, wherein the therapeutically effective amount of the compound is between about 0.01 to 100 mg/kg per day.

66. The use of claim 57, wherein the therapeutically effective amount of the compound is between about 0.1 to 50 mg/kg per day.

67. The use of claim 56, wherein the cancer is selected from the group consisting of Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Biliary tract: gall bladder carcinoma, ampullary carcinoma, cholangiocarcinoma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma,

osteochronfroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial `carcinoma (serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma), granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia (acute and chronic), acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma (malignant lymphoma); Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; and Adrenal glands: neuroblastoma.

68. The use of claim 59, wherein the cancer is a KRas G12A-associated cancer.

69. The use of claim 59, wherein the cancer is a KRas G12C-associated cancer.

70. The use of claim 59, wherein the cancer is a KRas G12D-associated cancer.

71. The use of claim 59, wherein the cancer is a KRas G12R-associated cancer.

72. The use of claim 59, wherein the cancer is a KRas G12S-associated cancer.

73. The use of claim 59, wherein the cancer is a KRas G12V-associated cancer.

74. The use of claim 59, wherein the cancer is a KRas G13D-associated cancer.

75. The use of claim 59, wherein the cancer is a KRas Q61H-associated cancer.

76. The use of claim 59, wherein the cancer is a KRas G12A-associated cancer.

77. The use of claim 59, wherein the cancer is associated with at least one of wild type KRas, KRas G12A, KRas G12C, KRas G12D, KRas G12R, KRas G12S, KRas G12V, KRas G13D or KRas Q61H.

78. The use of any of claims 60-69, wherein the cancer is non-small cell lung cancer, small cell lung cancer, colorectal cancer, rectal cancer or pancreatic cancer.

79. Use of a therapeutically effective amount of a compound according to any one of claims 1-53 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 54 in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the cancer has been determined to be associated with wild type KRas or a KRas G12A, KRas G12C, KRas G12D, KRas G12R, KRas G12S, KRas G12V, KRas G13D or KRas Q61H mutation.

80. The use of any one of claims 55-71, wherein the medicament is to be administered via a route selected from the group consisting of parenteral, intraperitoneal, intradermal, intracardiac, intraventricular, intracranial, intracerebrospinal, intrasynovial, intrathecal administration, intramuscular injection, intravitreous injection, intravenous injection, intra-arterial injection, oral, buccal, sublingual, transdermal, topical, intratracheal, intrarectal, subcutaneous, and topical administration.

81. The use of claim 72, wherein the administration route is oral.

82. The use of claim 72, wherein the administration is intravenous injection.

83. The use of claim 72, wherein the administration route is intramuscular injection.

84. The use of claim 72, wherein the administration route utilizes a delivery device.

85. The use of claim 72, wherein administration is done in a hospital setting.