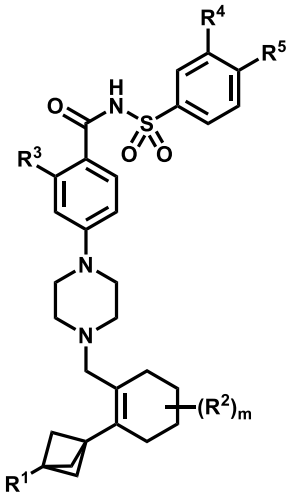
Claims

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof, having the structure:



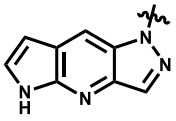
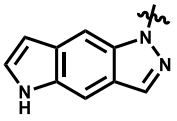
(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 haloalkyl, a substituted or unsubstituted C_3-C_6 cycloalkyl, a substituted or unsubstituted C_1-C_6 alkoxy, an unsubstituted mono-C_1-C_6 alkylamine and an unsubstituted di-C_1-C_6 alkylamine;

each R^2 is independently selected from the group consisting of halogen, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 haloalkyl and a substituted or unsubstituted C_3-C_6 cycloalkyl; or

when m is 2 or 3, each R^2 is independently selected from the group consisting of halogen, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 haloalkyl and a substituted or unsubstituted C_3-C_6 cycloalkyl, or two R^2 groups taken together with the atom(s) to which they are attached form a substituted or unsubstituted C_3-C_6 cycloalkyl or a substituted or unsubstituted 3 to 6 membered heterocyclyl;

R^3 is selected from the group consisting of X-R^{3A},  and ;

R^{3A} is a substituted or unsubstituted 5 to 10 membered heteroaryl;

R^4 is selected from the group consisting of NO_2, $S(O)R^6$, SO_2R^6, halogen, cyano and an unsubstituted C_1-C_6 haloalkyl;

R^5 is $–X^1$-$(Alk^1)_n$-R^7;

Alk^1 is selected from an unsubstituted C_1-C_4 alkylene and a C_1-C_4 alkylene substituted with 1, 2 or 3 substituents independently selected from fluoro, chloro, an unsubstituted C_1-C_3 alkyl and an unsubstituted C_1-C_3 haloalkyl;

R^6 is selected from the group consisting of a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 haloalkyl and a substituted or unsubstituted C_3-C_6 cycloalkyl;

R^7 is selected from a substituted or unsubstituted C_3-C_{10} cycloalkyl and a substituted or unsubstituted 3 to 10 membered heterocyclyl;

m is 0, 1, 2 or 3;

n is selected from 0 and 1;

X^1 is –NH-; and

X is selected from the group consisting of –O–, –S– and –NH–.

2. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is -CH_2F or –CF_3.

3. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is -CHF_2.

4. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is not -CH_2F, -CHF_2 or -CF_3.

5. The compound of any one of Claims 1-4, or a pharmaceutically acceptable salt thereof, wherein m is 1.

6. The compound of any one of Claims 1-4, or a pharmaceutically acceptable salt thereof, wherein m is 2.

7. The compound of any one of Claims 1-4, or a pharmaceutically acceptable salt thereof, wherein m is 3.

8. The compound of any one of Claims 1-7, or a pharmaceutically acceptable salt thereof, wherein one R^2 is an unsubstituted C_1-C_6 alkyl and any other R^2, if present, is independently selected from the group consisting of halogen, a substituted or unsubstituted C_1-C_6 alkyl, a substituted or unsubstituted C_1-C_6 haloalkyl and a substituted or unsubstituted C_3-C_6 cycloalkyl.

9. The compound of any one of Claims 1-8, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently an unsubstituted C_1-C_6 alkyl.

10. The compound of any one of Claims 1-4, 8 or 9, or a pharmaceutically acceptable salt thereof, wherein m is 2; and each R^2 is an unsubstituted methyl.

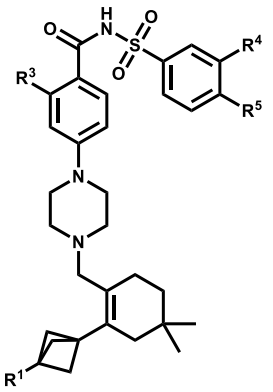
11. The compound of any one of Claims 1-4, or a pharmaceutically acceptable salt thereof, wherein m is 0.

12. The compound of any one of Claims 1-4 or 6, or a pharmaceutically acceptable salt thereof, wherein two R^2 groups taken together with the atom(s) to which they are attached form a substituted or unsubstituted C_3-C_6 cycloalkyl.

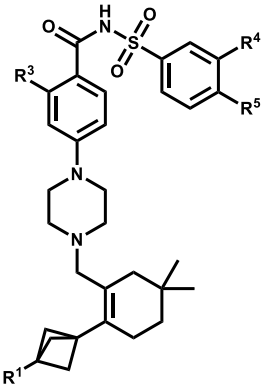
13. The compound of any one of Claims 1-4, 6-7 or 12, or a pharmaceutically acceptable salt thereof, wherein two R^2 groups taken together with the atom to which they are attached form an unsubstituted cyclopropyl.

14. The compound of any one of Claims 1-4 or 6-7, or a pharmaceutically acceptable salt thereof, wherein two R^2 groups taken together with the atom(s) to which they are attached form a substituted or unsubstituted 3 to 6 membered heterocyclyl.

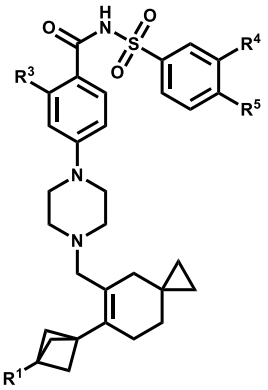
15. The compound of any one of Claims 1-4, that is also a compound of Formula (Ia), Formula (Ib), Formula (Ic) or Formula (Id):



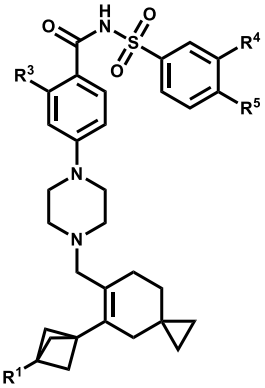
(Ia)



(Ib)



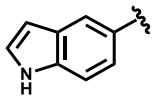
(Ic)

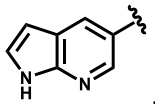


(Id)

or pharmaceutically acceptable salts of any of the foregoing.

16. The compound of any one of Claims 1-15, wherein R^3 is X-R^{3A}.

17. The compound of any one of Claims 1-16, wherein R^{3A} is .

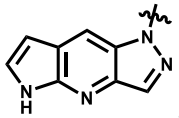
18. The compound of any one of Claims 1-16, wherein R^{3A} is .

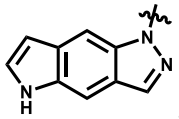
19. The compound of any one of Claims 1-16, wherein R^{3A} is a substituted 5 to 10 membered heteroaryl.

20. The compound of any one of Claims 1-19, wherein X is –O–.

21. The compound of any one of Claims 1-19, wherein X is –S–.

22. The compound of any one of Claims 1-19, wherein X is –NH–.

23. The compound of any one of Claims 1-15, wherein R^3 is .

24. The compound of any one of Claims 1-15, wherein R^3 is .

25. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is NO_2.

26. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is cyano.

27. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is halogen.

28. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is an unsubstituted C_1-C_6 haloalkyl.

29. The compound of any one of Claims 1-24 or 28, or a pharmaceutically acceptable salt thereof, wherein R^4 is $–CF_3$.

30. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is $S(O)R^6$.

31. The compound of any one of Claims 1-24, or a pharmaceutically acceptable salt thereof, wherein R^4 is SO_2R^6.

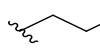
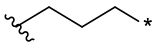
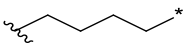
32. The compound of any one of Claims 1-24 or 30-31, or a pharmaceutically acceptable salt thereof, wherein R^6 is a substituted or unsubstituted C_1-C_6 alkyl.

33. The compound of any one of Claims 1-24 or 30-31, or a pharmaceutically acceptable salt thereof, wherein R^6 is a substituted or unsubstituted C_3-C_6 cycloalkyl.

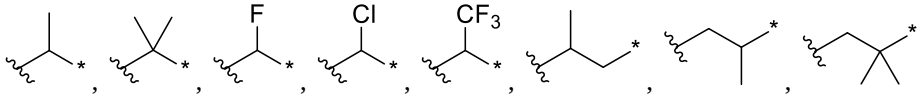
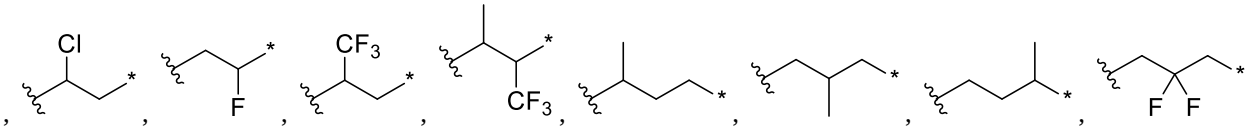
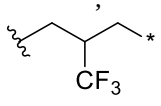
34. The compound of any one of Claims 1-24 or 30-31, or a pharmaceutically acceptable salt thereof, wherein R^6 is a substituted or unsubstituted C_1-C_6 haloalkyl.

35. The compound of any one of Claims 30-31 or 34, or a pharmaceutically acceptable salt thereof, wherein R^6 is $–CF_3$.

36. The compound of any one of Claims 1-35, or a pharmaceutically acceptable salt thereof, wherein Alk^1 is unsubstituted $–(CH_2)_{1\text{-}4}–*$ for which "*" represents the point of attachment to R^7.

37. The compound of any one of Claims 1-35, or a pharmaceutically acceptable salt thereof, wherein Alk^1 is selected from , ,  and .

38. The compound of any one of Claims 1-35, or a pharmaceutically acceptable salt thereof, wherein Alk^1 is a substituted  for which "*" represents the point of attachment to R^7.

39. The compound of any one of Claims 1-35 or 38, or a pharmaceutically acceptable salt thereof, wherein Alk^1 is selected from: ,  and .

40. The compound of any one of Claims 1-39, or a pharmaceutically acceptable salt thereof, wherein n is 1.

41. The compound of any one of Claims 1-35, or a pharmaceutically acceptable salt thereof, wherein n is 0.

42. The compound of any one of Claims 1-41, or a pharmaceutically acceptable salt thereof, wherein R^7 is a substituted or unsubstituted C_3-C_{10} cycloalkyl.

43. The compound of any one of Claims 1-42, or a pharmaceutically acceptable salt thereof, wherein R^7 is a substituted or unsubstituted C_6-C_{10} spirocycloalkyl.

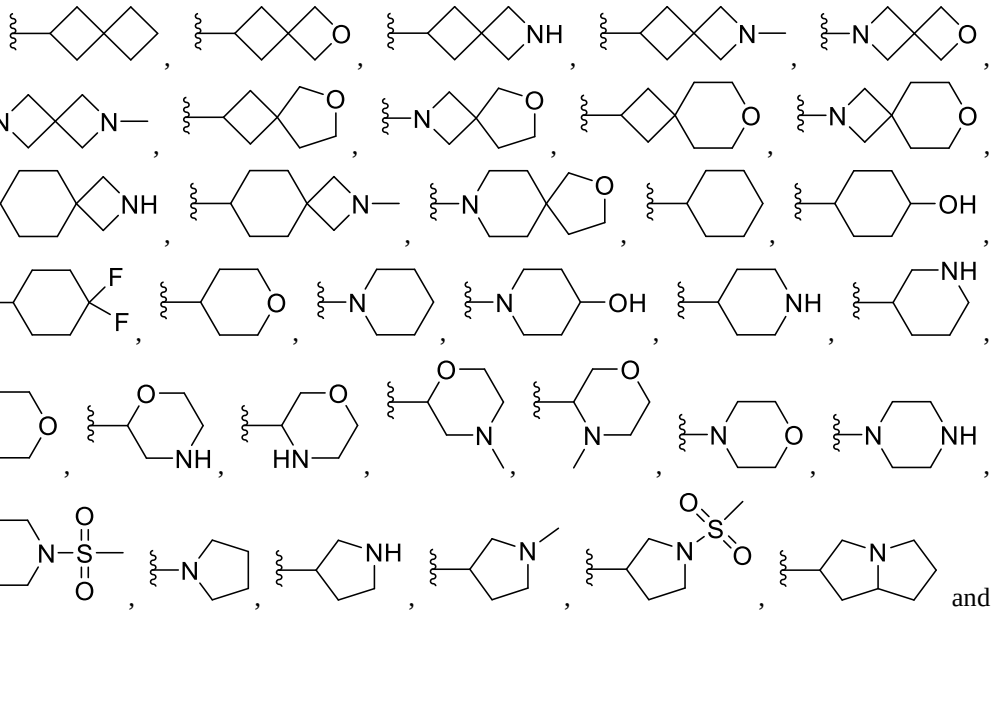
44. The compound of any one of Claims 1-41, or a pharmaceutically acceptable salt thereof, wherein R^7 is a substituted or unsubstituted 3 to 10 membered heterocyclyl.

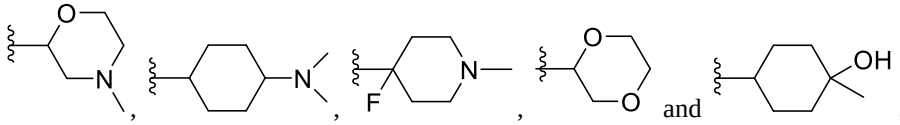
45. The compound of any one of Claims 1-41 or 44, or a pharmaceutically acceptable salt thereof, wherein R^7 is a substituted or unsubstituted 6 to 10 membered spiro heterocyclyl.

46. The compound of any one of Claims 1-45, or a pharmaceutically acceptable salt thereof, wherein R^7 is unsubstituted.

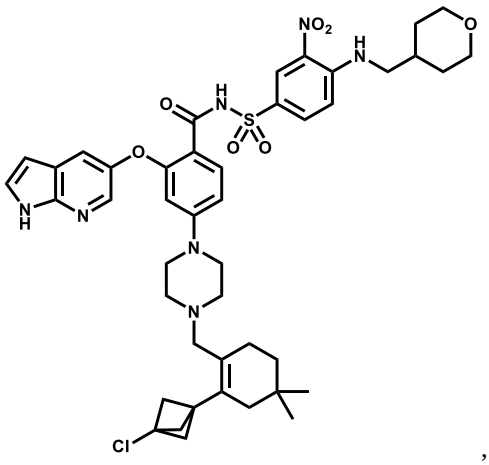
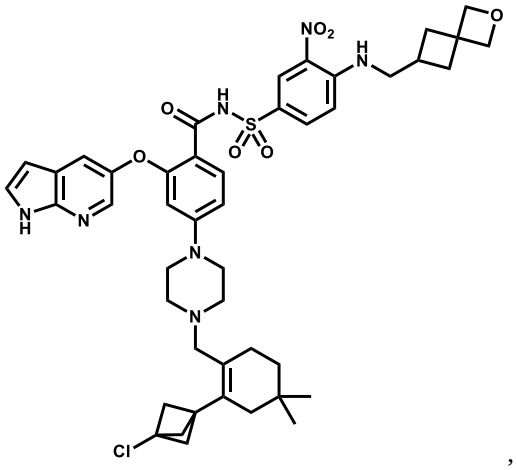
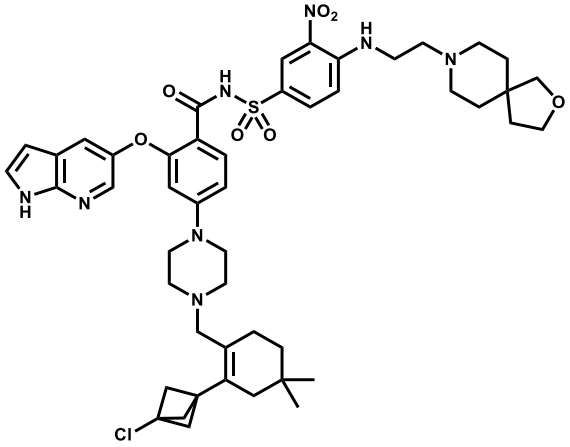
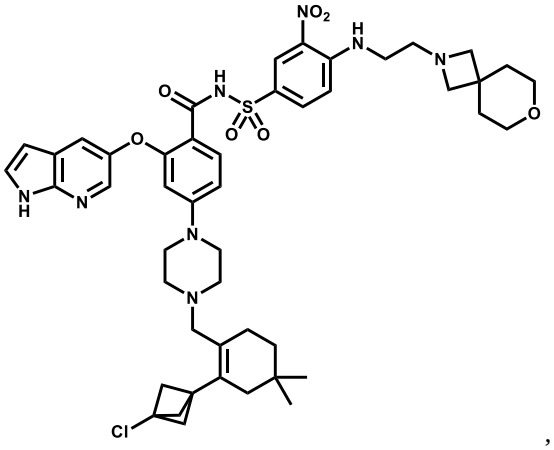
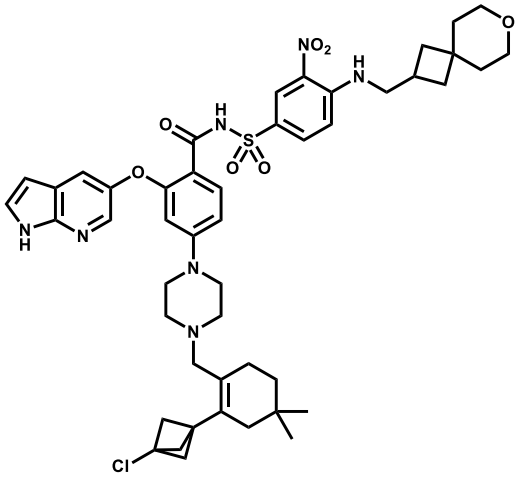
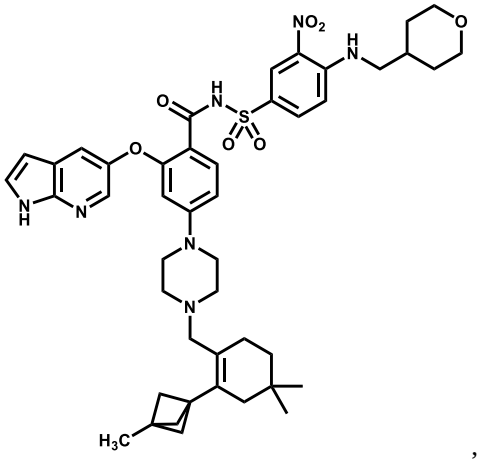
47. The compound of any one of Claims 1-45, or a pharmaceutically acceptable salt thereof, wherein R^7 is substituted.

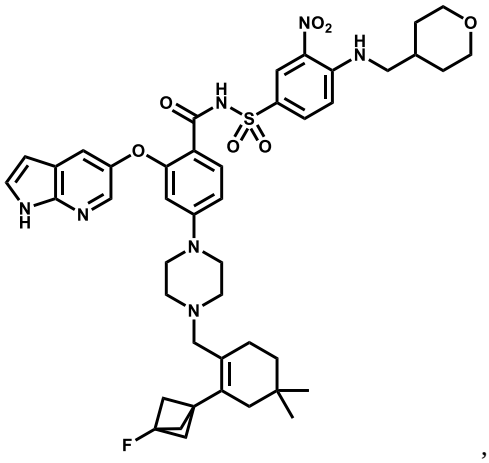
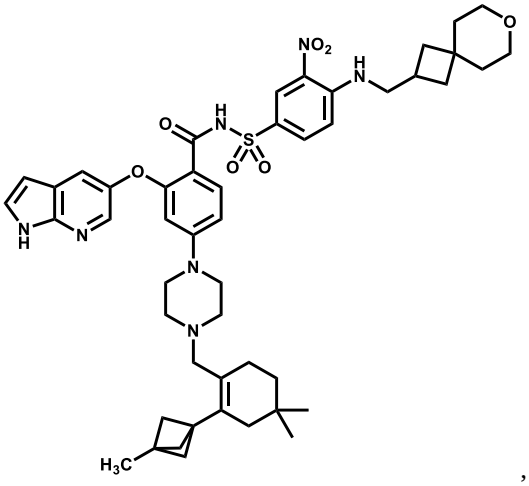
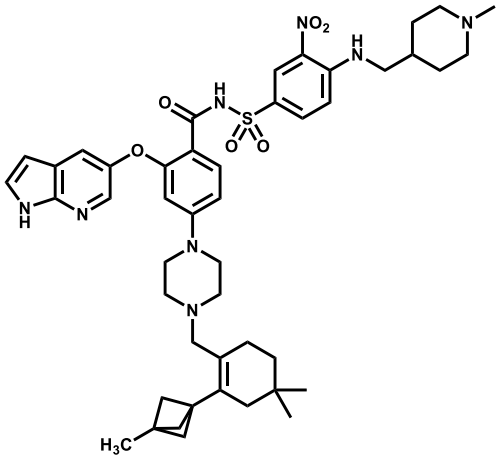
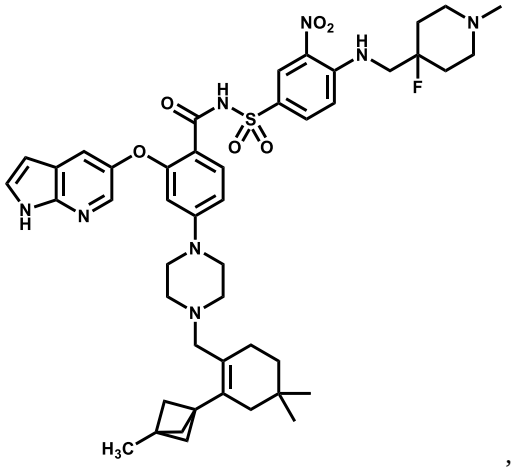
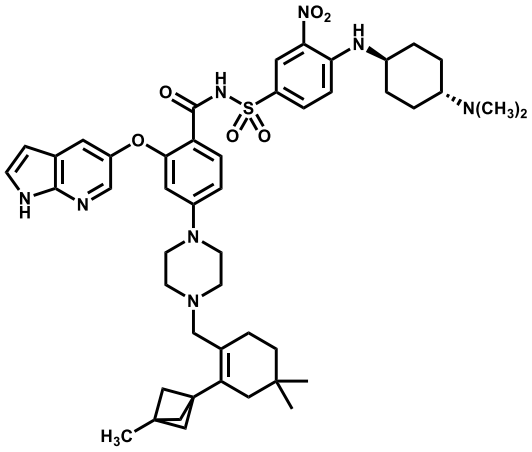
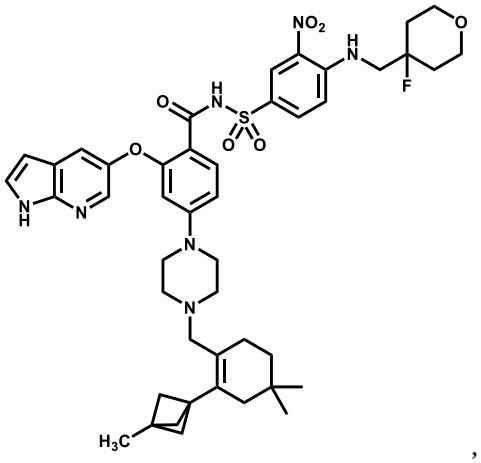
48. The compound of any one of Claims 1-45 or 47, or a pharmaceutically acceptable salt thereof, wherein R^7 is substituted with 1 or 2 substituents independently selected from an unsubstituted C_1-C_6 alkyl, an unsubstituted C_1-C_6 alkoxy, fluoro, chloro, hydroxy and -SO_2-(unsubstituted C_1-C_6 alkyl).

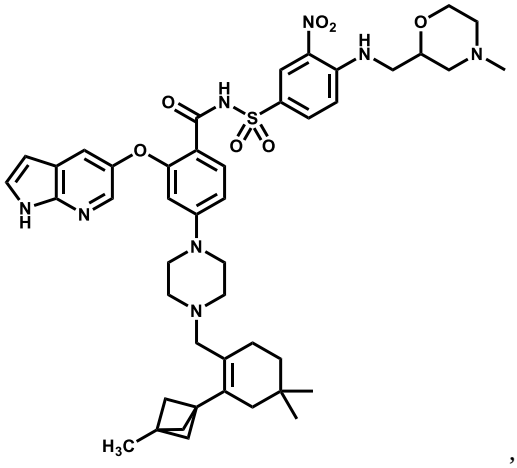
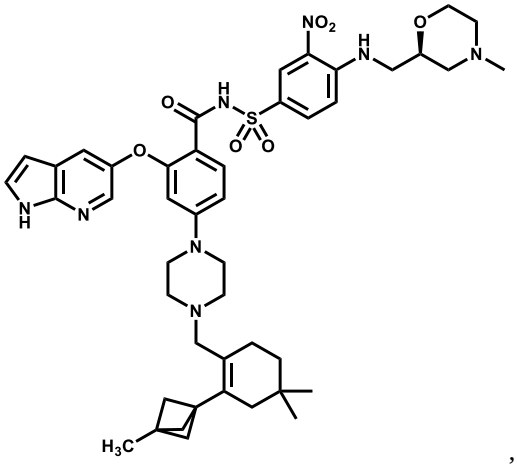
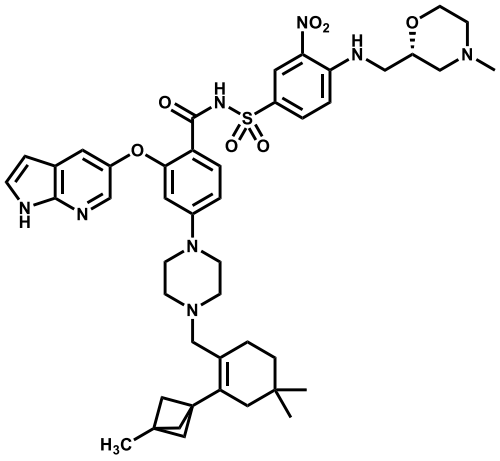
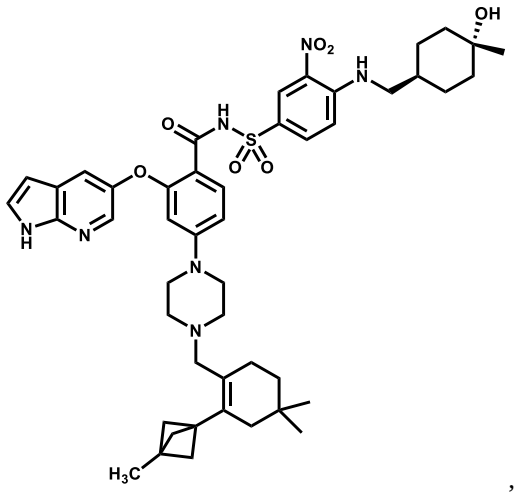
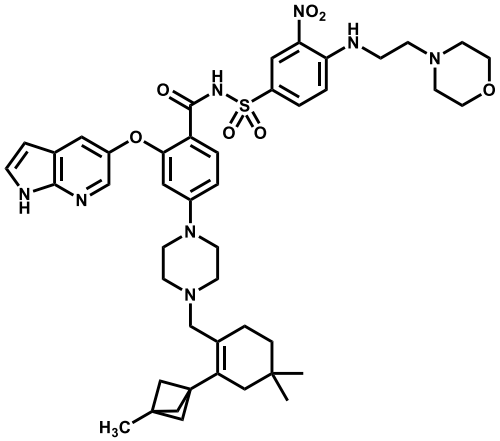
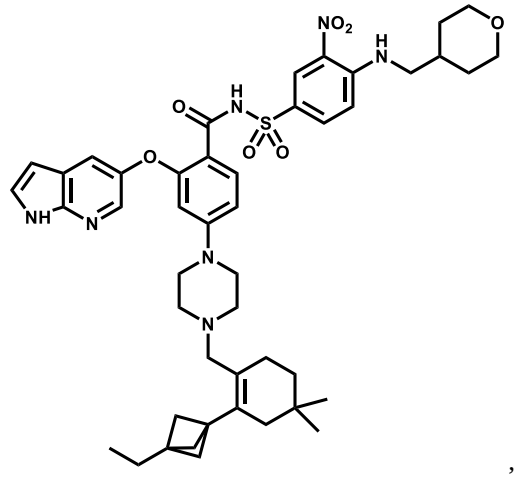
49. The compound of any one of Claims 1-41, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from: , and .

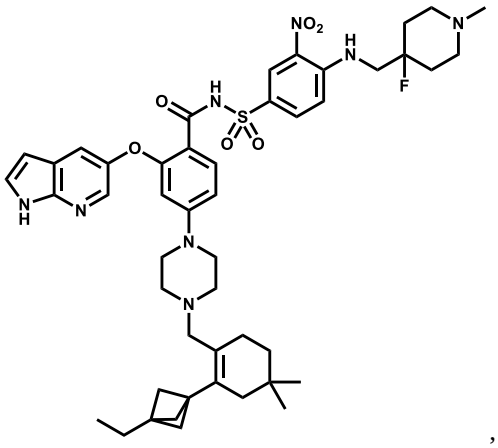
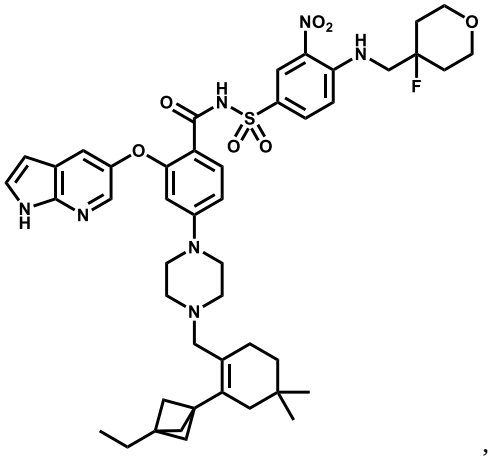
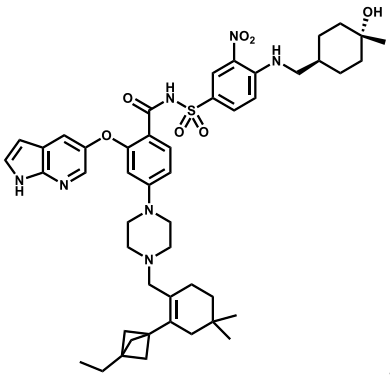
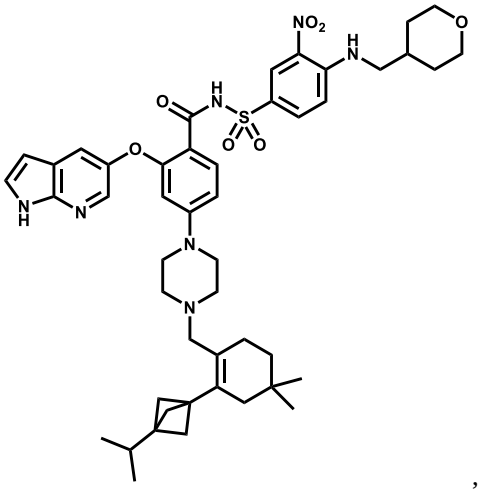
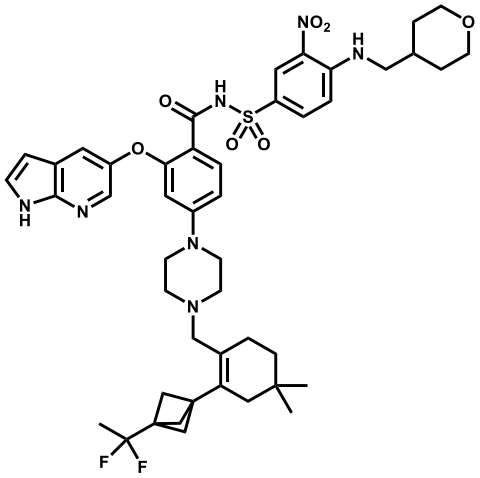
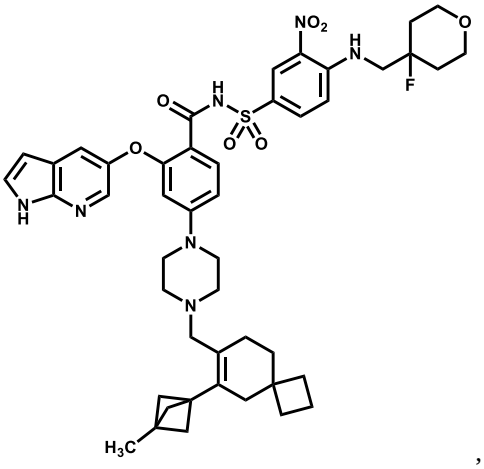
50. The compound of any one of Claims 1-41, or a pharmaceutically acceptable salt thereof, wherein R^7 is selected from: .

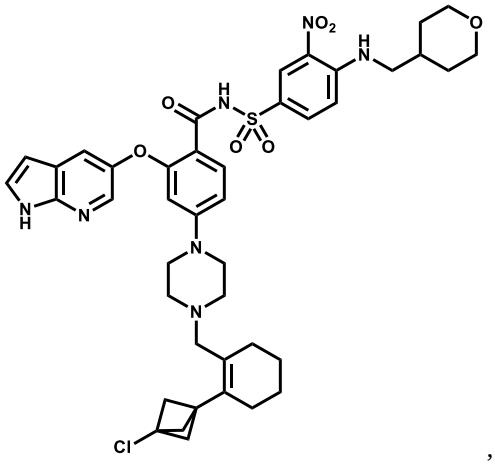
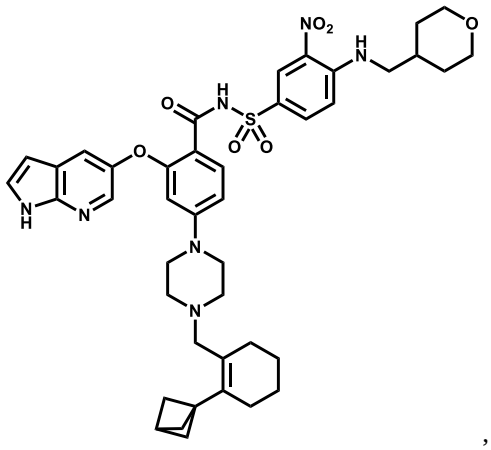
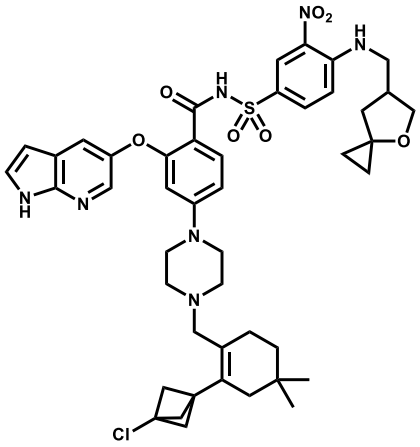
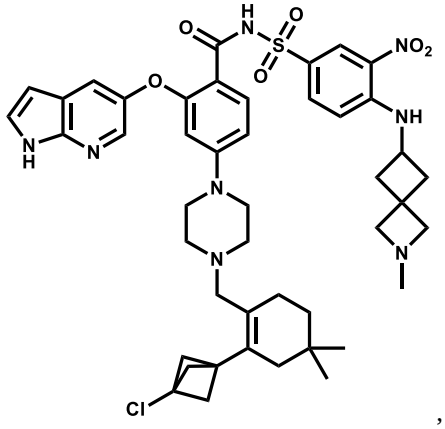
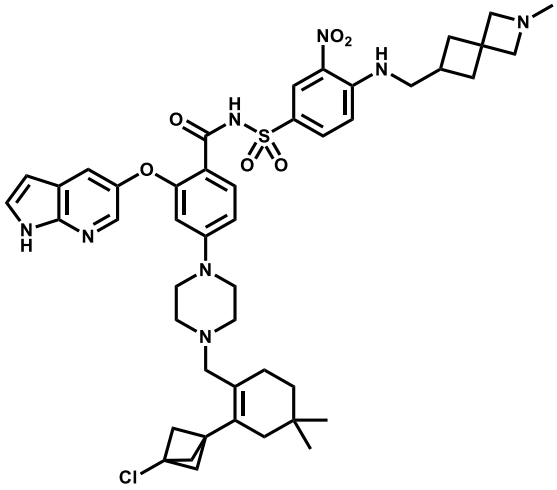
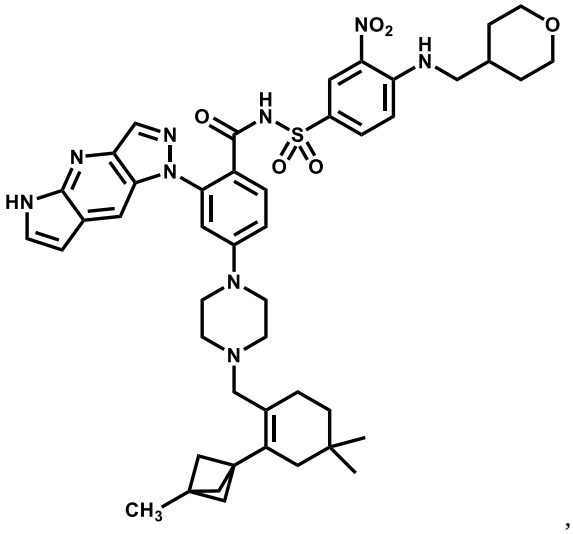
51. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

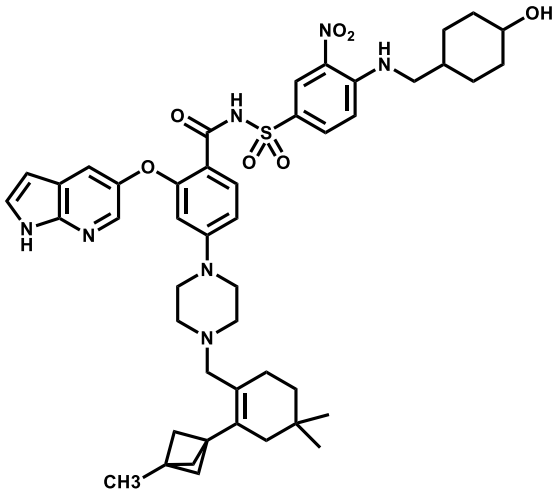
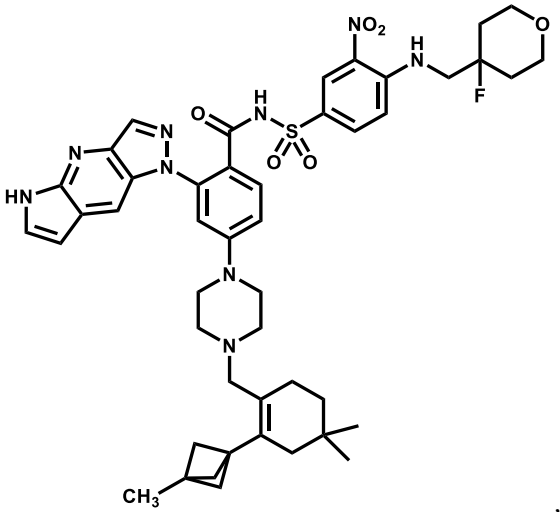
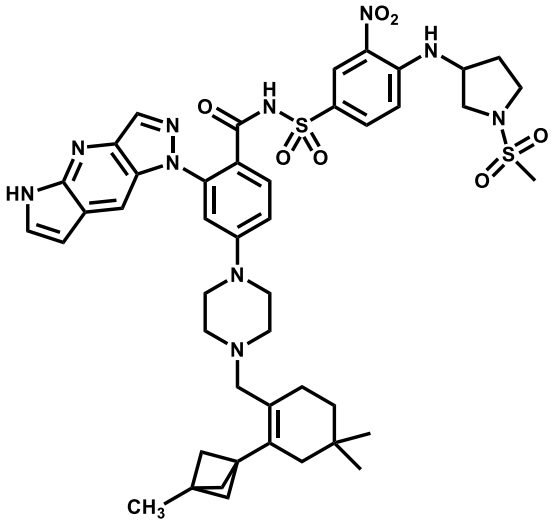
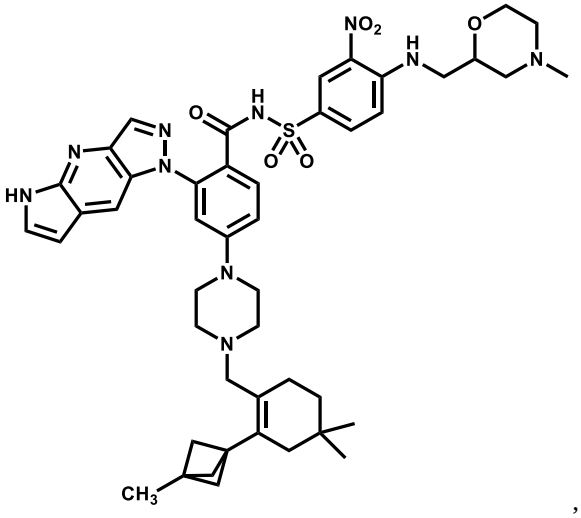
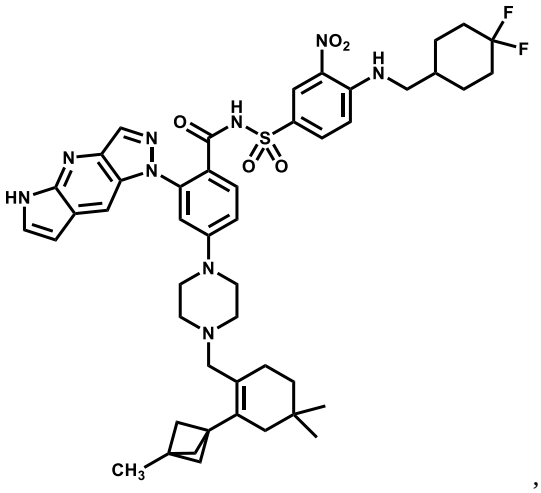
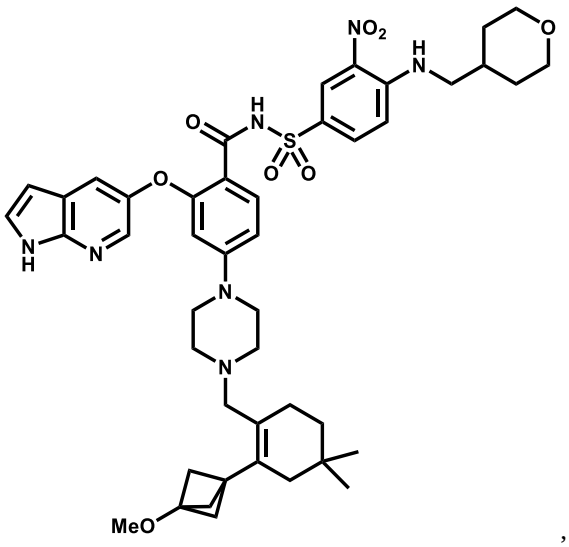

,

,

,

,

,

,

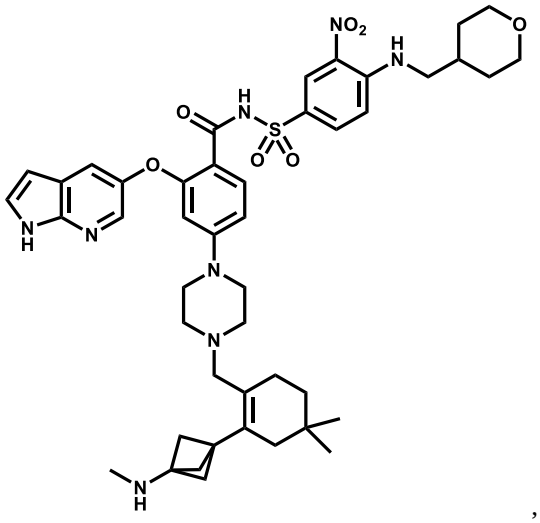
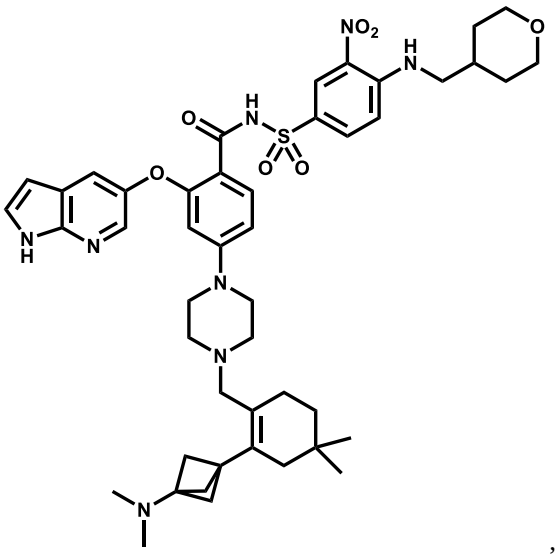
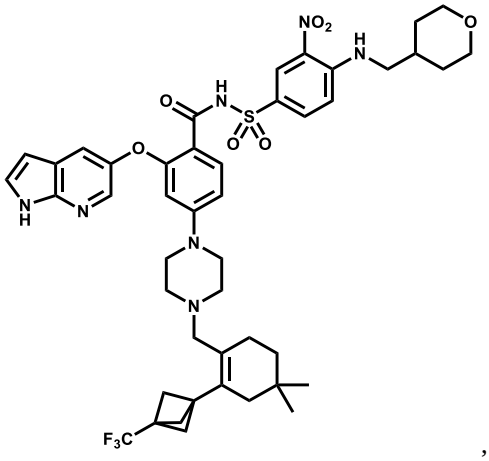
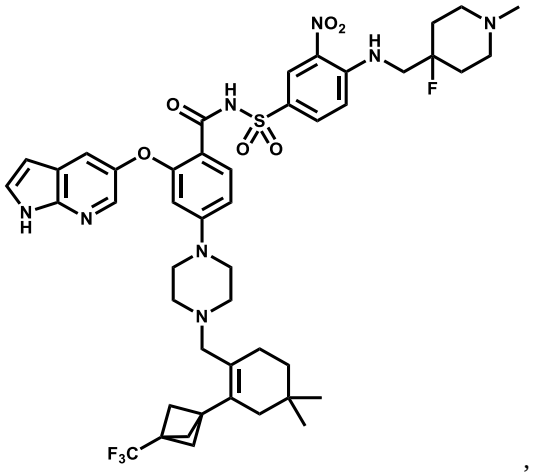
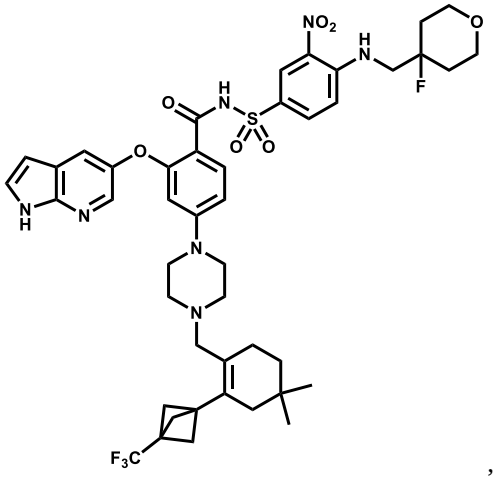
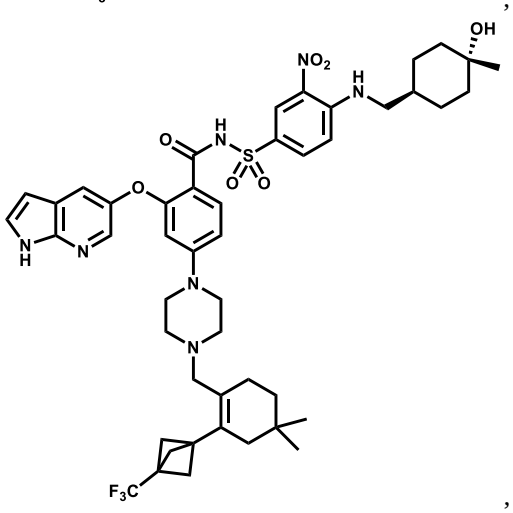

,

,

,

,

,

,

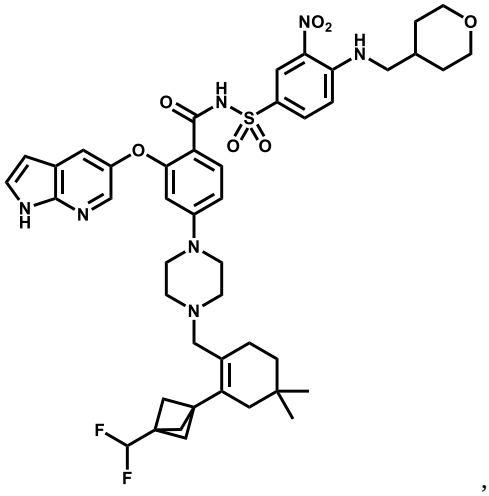
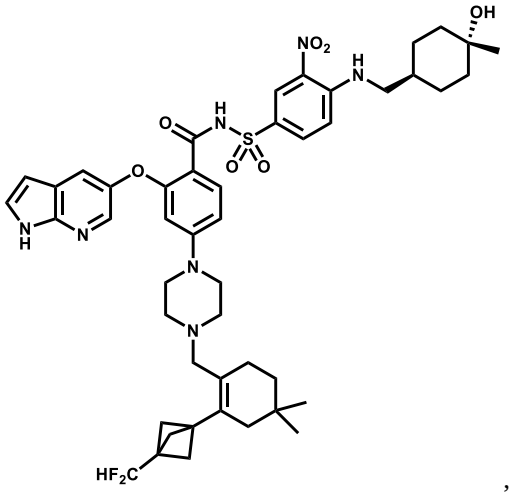
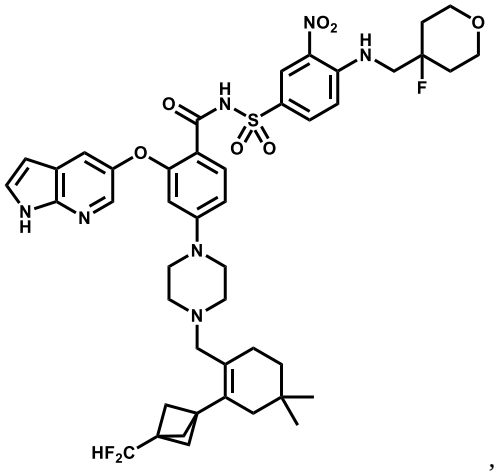
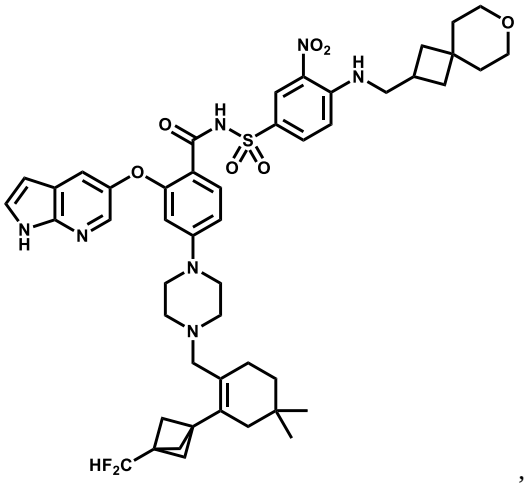
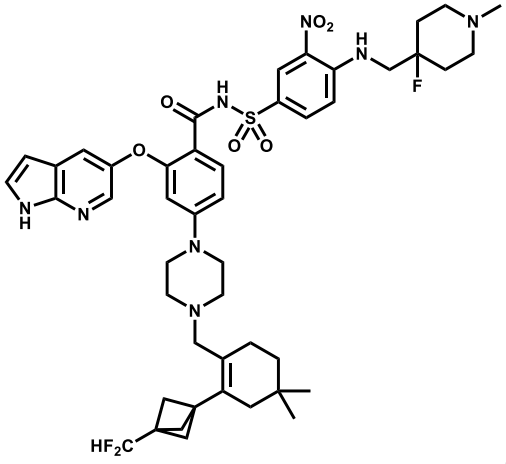
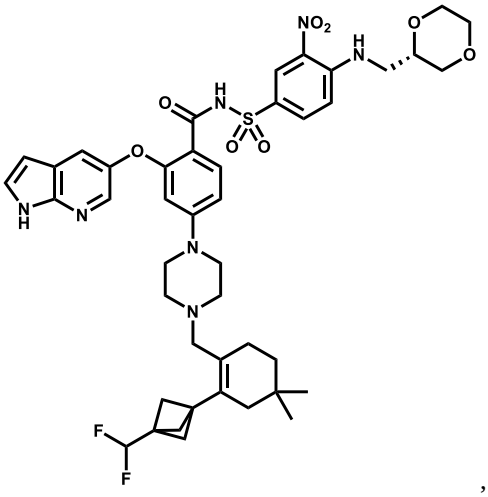

,

,

,

,

,

,

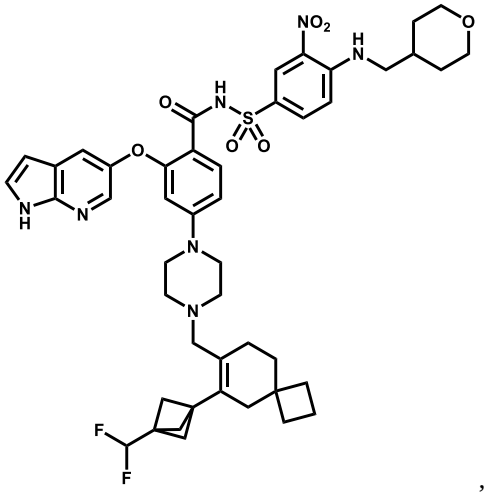
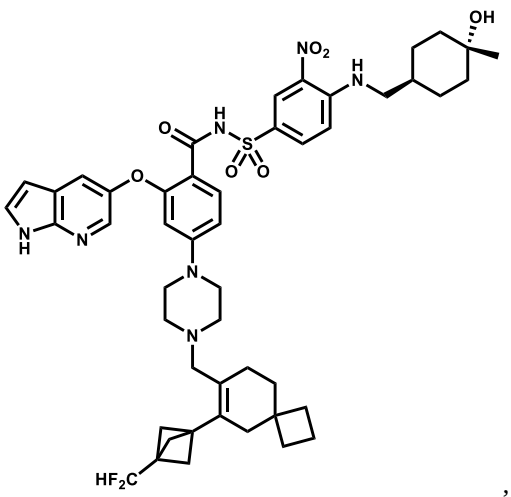
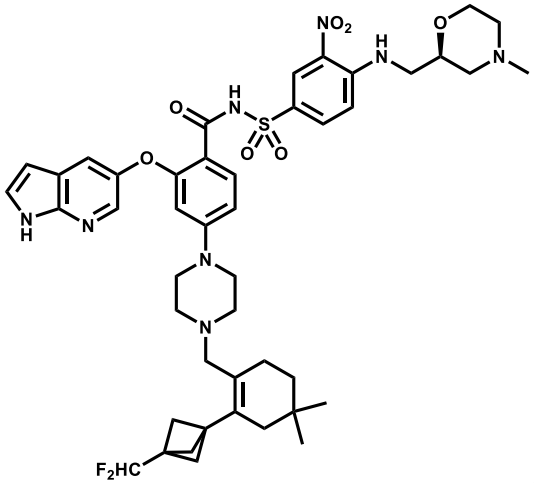

,

,

,

,

,

,


,

,

.

,

,

,

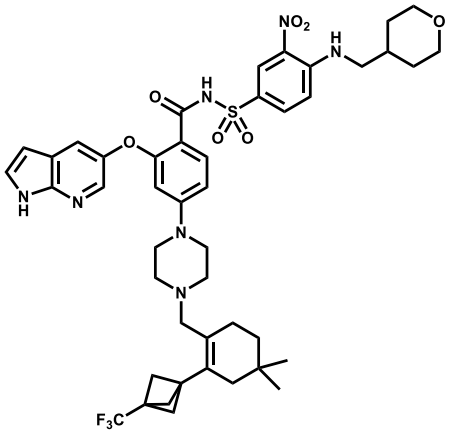
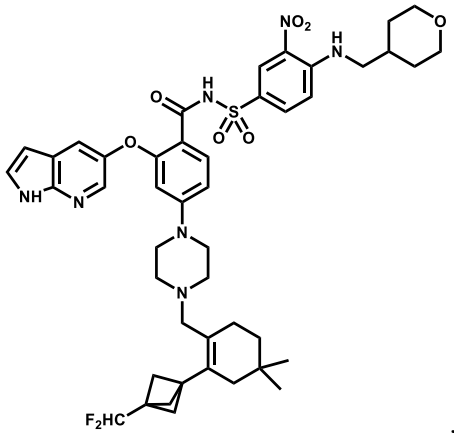

,

,

,

,

,

,

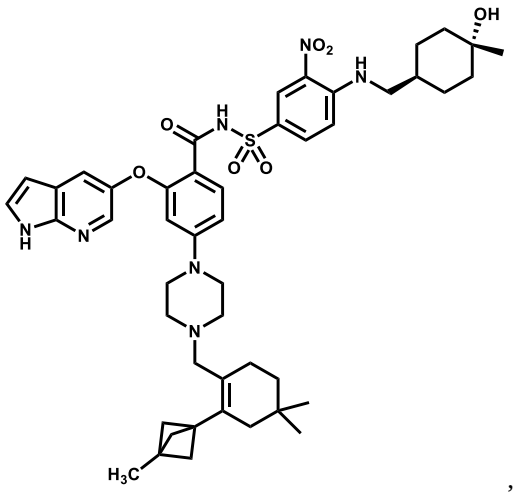

,

,

,

,

,

,

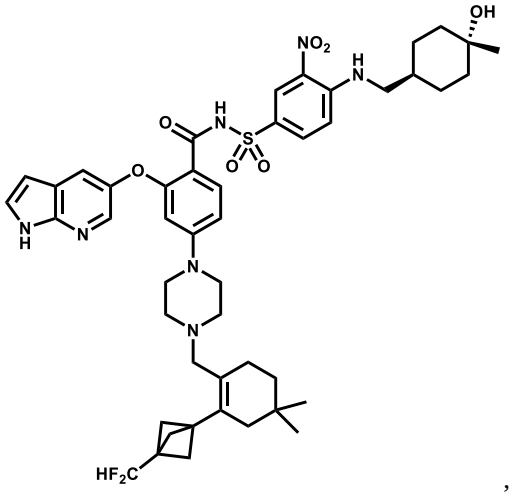

,

,

,

,

,

,

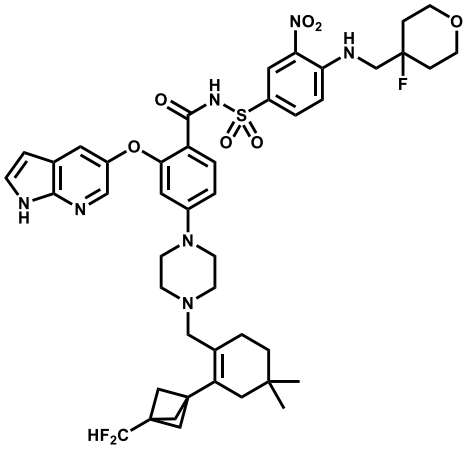

,

, and

.

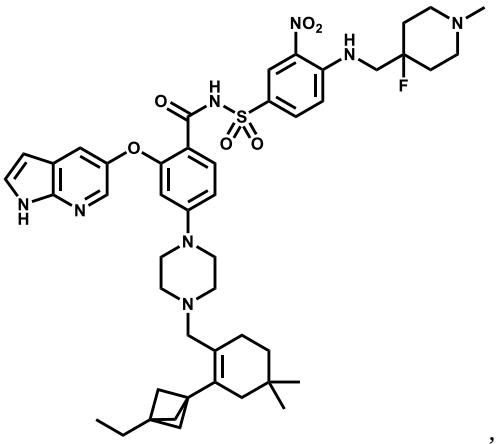
52. The compound of Claim 51, wherein the compound is selected from the group consisting of:

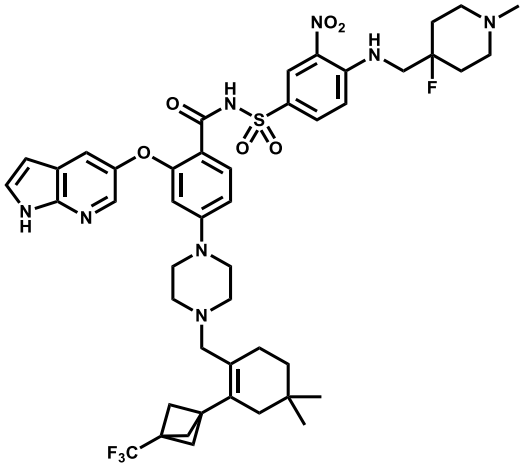

and

, or a pharmaceutically acceptable salt of any of the foregoing.

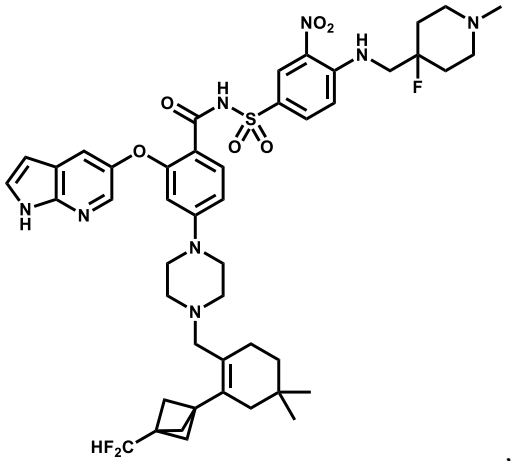
53. The compound of Claim 51, wherein the compound is  , or a pharmaceutically acceptable salt thereof.

54. The compound of Claim 51, wherein the compound is  , or a pharmaceutically acceptable salt thereof.

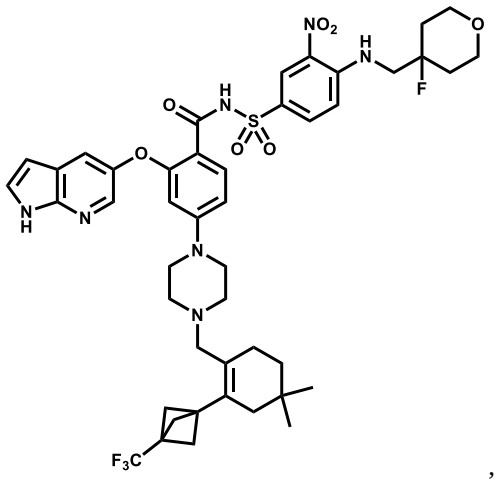
55. The compound of Claim 51, wherein the compound is  or a pharmaceutically acceptable salt thereof.

56. The compound of Claim 51, wherein the compound is  , or a pharmaceutically acceptable salt thereof.

57. The compound of Claim 51, wherein the compound is  , or a pharmaceutically acceptable salt thereof.

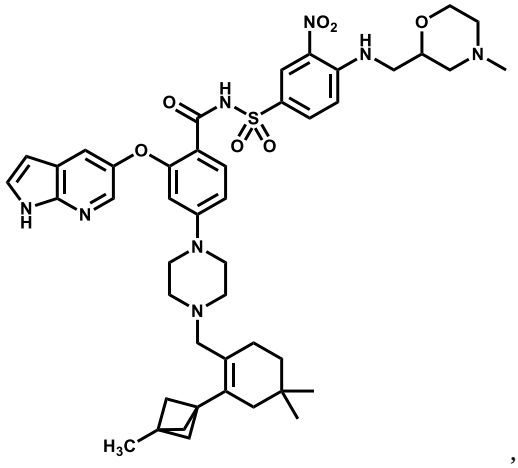
58. The compound of Claim 51, wherein the compound is  , or a pharmaceutically acceptable salt thereof.

59. The compound of Claim 51, wherein the compound is

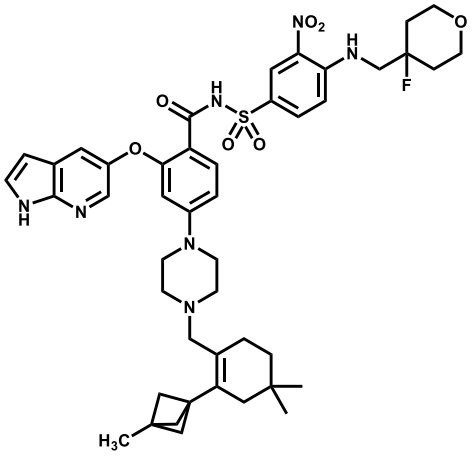


, or a pharmaceutically acceptable salt thereof.

60. The compound of Claim 51, wherein the compound is



, or a pharmaceutically acceptable salt thereof.



61. The compound of Claim 51, wherein the compound is

, or a pharmaceutically acceptable salt thereof.

62. A pharmaceutical composition comprising an effective amount of the compound of any one of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

63. Use of an effective amount of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 62 in the manufacture of a medicament for treating

a cancer or a tumor, wherein the cancer or the tumor is selected from a bladder cancer, a brain cancer, a breast cancer, a bone marrow cancer, a cervical cancer, a colorectal cancer, an esophageal cancer, a hepatocellular cancer, a lymphoblastic leukemia, a follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, a melanoma, a myelogenous leukemia, a Hodgkin's lymphoma, a Non-Hodgkin's lymphoma, a head and neck cancer (including oral cancer), an ovarian cancer, a non-small cell lung cancer, a chronic lymphocytic leukemia, a myeloma, a prostate cancer, a small cell lung cancer, a spleen cancer, a polycythemia vera, a thyroid cancer, an endometrial cancer, a stomach cancer, a gallbladder cancer, a bile duct cancer, a testicular cancer, a neuroblastoma, an osteosarcoma, an Ewings's tumor and a Wilm's tumor.

64. Use of an effective amount of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 62 in the manufacture of a medicament for inhibiting replication of a malignant growth or a tumor, wherein the malignant growth or the tumor is due to a cancer selected from a bladder cancer, a brain cancer, a breast cancer, a bone marrow cancer, a cervical cancer, a colorectal cancer, an esophageal cancer, a hepatocellular cancer, a lymphoblastic leukemia, a follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, a melanoma, a myelogenous leukemia, a Hodgkin's lymphoma, a Non-Hodgkin's lymphoma, a head and neck cancer (including oral cancer), an ovarian cancer, a non-small cell lung cancer, a chronic lymphocytic leukemia, a myeloma, a prostate cancer, a small cell lung cancer, a spleen cancer, a polycythemia vera, a thyroid cancer, an endometrial cancer, a stomach cancer, a gallbladder cancer, a bile duct cancer, a testicular cancer, a neuroblastoma, an osteosarcoma, an Ewings's tumor and a Wilm's tumor.

65. Use of an effective amount of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 62 in the manufacture of a medicament for treating a malignant growth or a tumor, wherein the malignant growth or the tumor is due to a cancer selected from a bladder cancer, a brain cancer, a breast cancer, a bone marrow cancer, a cervical cancer, a colorectal cancer, an esophageal cancer, a hepatocellular cancer, a lymphoblastic leukemia, a follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, a melanoma, a myelogenous leukemia, a Hodgkin's lymphoma, a Non-Hodgkin's lymphoma, a head and neck cancer (including oral cancer), an ovarian cancer, a non-small cell lung cancer, a chronic lymphocytic leukemia, a myeloma, a prostate cancer, a small cell lung cancer, a spleen cancer, a polycythemia vera, a thyroid cancer, an endometrial cancer, a stomach cancer, a gallbladder cancer, a bile duct cancer, a testicular cancer, a neuroblastoma, an osteosarcoma, an Ewings's tumor and a Wilm's tumor.

66. Use of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of Claim 62, and an effective amount of a HIV latency reversing agent, or a pharmaceutically acceptable salt thereof, for preparing a medicament for treating a HIV infection.

67. Use of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of Claim 62, and an effective amount of a HIV latency reversing agent, or a pharmaceutically acceptable salt thereof, for preparing a medicament for reducing the reoccurrence of a HIV infection.

68. Use of a compound of any one of Claims 1-61, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of Claim 62, and an effective amount of a HIV latency reversing agent, or a pharmaceutically acceptable salt thereof, for preparing a medicament suitable for use in reducing the population of HIV infected cells.

69. The use of Claim 68, wherein the cells are CD4+T cells.

70. The use of any one of Claims 66-68, wherein the HIV latency reversing agent is selected from: a protein kinase C agonist, a PD-1 inhibitor, a PD-L1 inhibitor, an HDAC inhibitor, a phorbol ester and a bromodomain inhibitor.

71. The use of Claim 70, wherein the HIV latency reversing agent is selected from: ingenol, rostatin, nivolumab, pembrolizumab, pidilizumab, AMP-224, AMP-514, PDR001, REGN2810, MEDI0680, Durvalumab, Atezolizumab, Avelumab, BMS-936559, BGB-A317, vorinostat, panobinostat, valproic acid, romidepsin, prostratin, phorbol 12-myristate-13-acetate, bryostatin-1, (S)-tert-butyl 2-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)acetate, JQ1, I-BET762, OTX015, I-BET151, CPI203, PFI-1, MS436, CPI-0610, RVX2135, FT-1101, BAY1238097, INCB054329, TEN-010, GSK2820151, ZEN003694, BAY-299, BMS-986158, ABBV-075 and GS-5829.

72. The use of any one of Claims 66-71, further comprising the use of one or more agents selected from the group consisting of a non-nucleoside reverse transcriptase inhibitor (NNRTI), a nucleoside reverse transcriptase inhibitor (NRTI), a protease inhibitor (PI), a fusion/entry inhibitor, an integrase strand transfer inhibitor (INSTI), a HIV vaccine, a HIV other antiretroviral therapy compound and combinations thereof, or a pharmaceutically acceptable salt of any of the aforementioned.