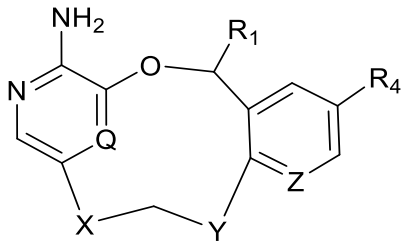
CLAIMS

1. A compound of Formula (I):



(I),

or an enantiomer, a mixture of enantiomers, or a tautomer thereof, or a pharmaceutically acceptable salt thereof, wherein

Q is CH or N;

Z is CR_5 or N;

X is a 5-membered heteroarylene selected from the group consisting of pyrazolylene, isoxazolylene, isothiazolylene, imidazolylene, and triazolylene; wherein the 5-membered heteroarylene is substituted with 0, 1, or 2 occurrences of R_2;

Y is a 5- or 6-membered heteroarylene, comprising 1 to 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur; wherein the 5- or 6-membered heteroarylene is substituted with 0, 1, or 2 occurrences of R_3;

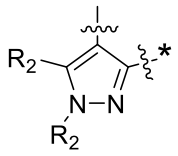
in Y, the point of attachment to the methylene group bonded to X and Y and the point of attachment to the aromatic ring comprising Z are on adjacent atoms, and the 5- to 6-membered heteroarylene ring atom alpha to the point of attachment to the methylene group and beta to the point of attachment to the aromatic ring comprising Z is carbon, oxygen, or sulfur;

R_1 is selected from the group consisting of H, methyl, and hydroxymethyl;

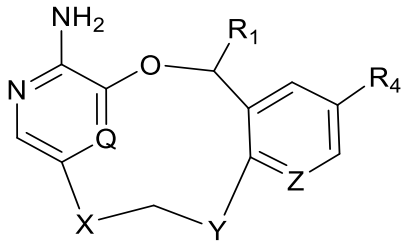
each instance of R_2 is independently selected from the group consisting of H, CN, halo, C_{1-4} alkoxy, C_{1-4} alkyl, halo-C_{1-4} alkyl, C_{3-4} cycloalkylmethyl, C_{3-6} cycloalkyl, and 3- to 6-membered heterocyclyl;

each instance of R_3 is independently selected from the group consisting of H, halo, CN, C_{1-4} alkoxy, halo-C_{1-4} alkyl, and C_{1-4} alkyl; and

each of R_4 and R_5 is independently H or F;

provided that X is not  wherein R_2 is not H, wherein * indicates the point of attachment of X to the methylene group bonded to X and Y.

2. A compound of Formula (I):



(I),

or an enantiomer, a mixture of enantiomers, or a tautomer thereof, or a pharmaceutically acceptable salt thereof, wherein

Q is CH or N;

Z is CR_5 or N;

X is a 5-membered heteroarylene selected from the group consisting of pyrazolylene, isoxazolylene, isothiazolylene, imidazolylene, and triazolylene; wherein the 5-membered heteroarylene is substituted with 0, 1, or 2 occurrences of R_2;

Y is a heteroarylene selected from the group consisting of 2*,3-substituted-furanylene, 2,3*-substituted-furanylene, 3*,4-substituted-furanylene, 1*,2-substituted-imidazolylene, 1*,5-substituted-imidazolylene, 1,5*-substituted-imidazolylene, 4,5*-substituted-1,2,3-oxadiazolylene, 3,4*-substituted-1,2-oxazolylene, 4*,5-substituted-1,2-oxazolylene, 4,5*-substituted-1,2-oxazolylene, 4,5*-substituted-1,3-oxazolylene, 1*,2-substituted-phenylene, 1,5*-substituted-pyrazolylene, 4*,5-substituted-pyrazolylene, 3,4*-substituted-pyridazinylene, 4*,5-substituted-pyridazinylene, 2,3*-substituted-pyridinylene, 3*,4-substituted-pyridinylene, 3,4*-substituted-pyridinylene, 4,5*-substituted-pyrimidinylene, 1*,2-substituted-pyrrolylene, 1,2*-substituted-pyrrolylene, 2,3*-substituted-pyrrolylene, 3*,4-substituted-pyrrolylene, 4,5*-

substituted-1,2,3-thiadiazolylene, 3,4*-substituted-1,2-thiazolylene, 4*,5-substituted-1,2-thiazolylene, 4,5*-substituted-1,2-thiazolylene, 4,5*-substituted-1,3-thiazolylene, 2*,3-substituted-thiophenylene, 2,3*-substituted-thiophenylene, 3*,4-substituted-thiophenylene, 4,5*-substituted-1,2,3-triazinylene, 1,5*-substituted-1,2,3-triazolylene, and 3,4*-substituted-1,2,4-triazolylene; wherein the heteroarylene is substituted with 0, 1, or 2 occurrences of R_3; wherein * indicates the point of attachment of Y to the methylene group bonded to X and Y;

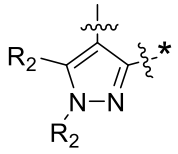
in Y the heteroarylene ring atom alpha to the point of attachment to the methylene group and beta to the point of attachment to the aromatic ring comprising Z is carbon, oxygen, or sulfur;

R_1 is selected from the group consisting of H, methyl, and hydroxymethyl;

each instance of R_2 is independently selected from the group consisting of H, CN, halo, C_{1-4} alkoxy, C_{1-4} alkyl, halo-C_{1-4} alkyl, C_{3-4} cycloalkylmethyl, C_{3-6} cycloalkyl, and 3- to 6-membered heterocyclyl;

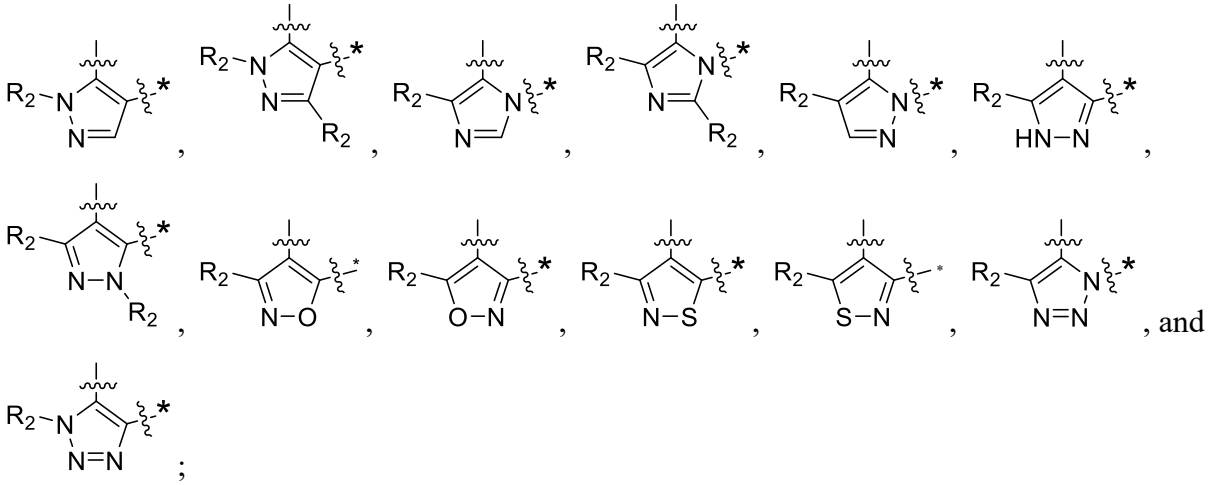
each instance of R_3 is independently selected from the group consisting of H, halo, CN, C_{1-4} alkoxy, halo-C_{1-4} alkyl, and C_{1-4} alkyl; and

each of R_4 and R_5 is independently H or F;

provided that X is not 

wherein R_2 is not H, wherein * indicates the point of attachment of X to the methylene group bonded to X and Y.

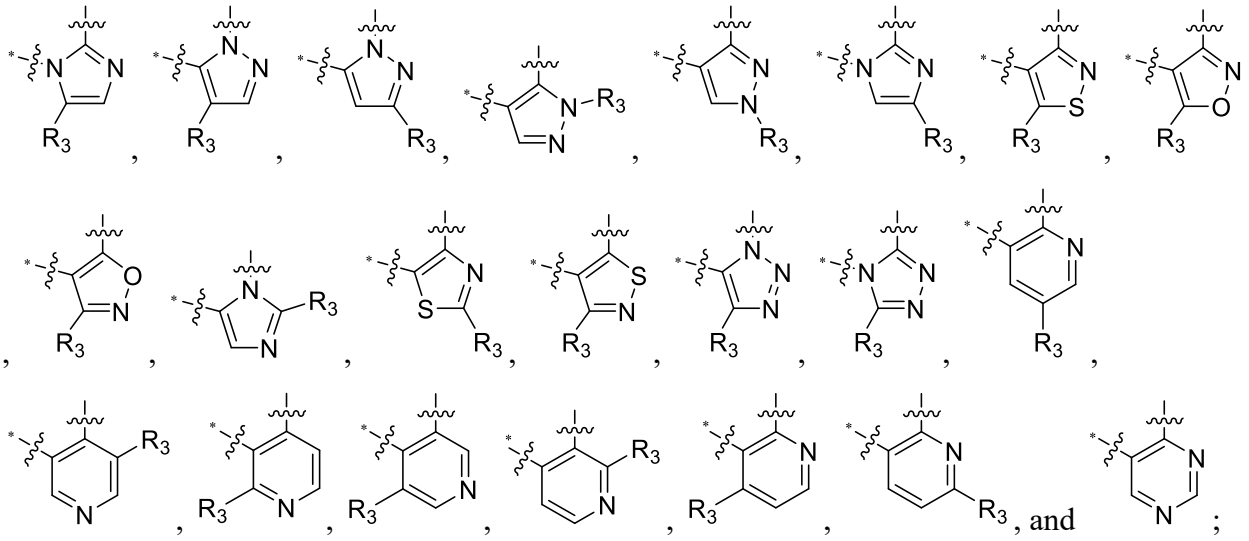
3. The compound of claim 1 or 2, wherein X is a 5-membered heteroarylene selected from the group consisting of:



wherein * indicates the point of attachment of X to the methylene group bonded to X and Y; and

R_2 is independently selected from the group consisting of H, CN, halo, C_{1-4} alkoxy, C_{1-4} alkyl, halo-C_{1-4} alkyl, C_{3-4} cycloalkylmethyl, C_{3-6} cycloalkyl, and 3- to 6-membered heterocyclyl.

4. The compound of any one of claims 1 to 3, wherein Y is a heteroarylene selected from the group consisting of:



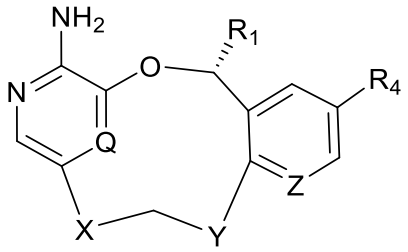
wherein * indicates the point of attachment of Y to the methylene group bonded to X and Y; and

R_3 is selected from the group consisting of H, halo, CN, C_{1-4} alkoxy, halo-C_{1-4} alkyl, and C_{1-4} alkyl.

5. The compound of any one of claims 1 to 4, wherein Q is CH.

6. The compound of any one of claims 1 to 5, wherein Z is CR_5.

7. The compound of any one of claims 1 to 6, which is a compound of Formula (I-B):



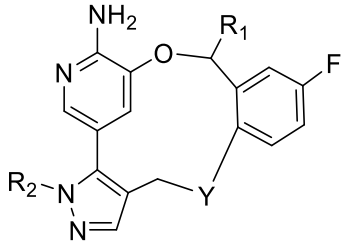
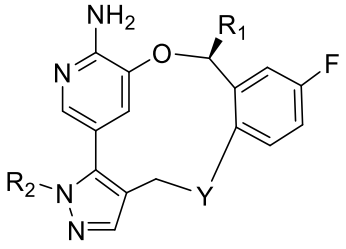
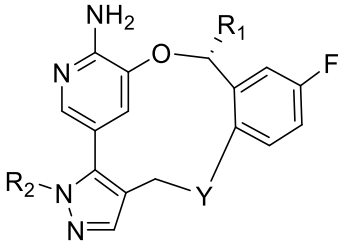
(I-B),

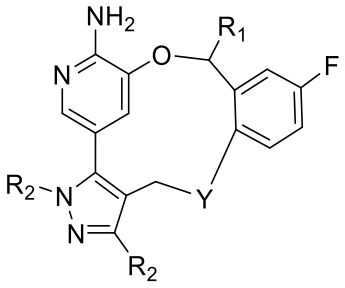
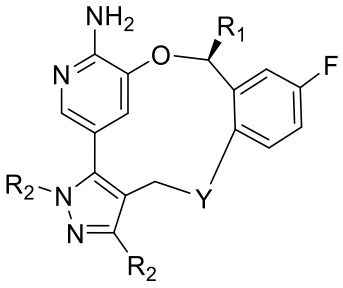
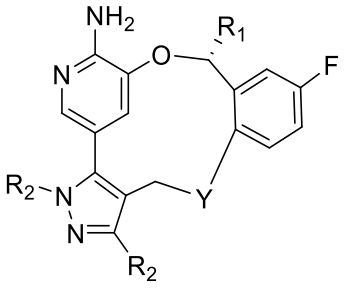
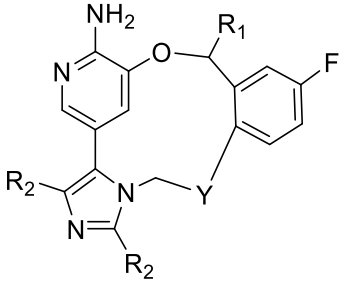
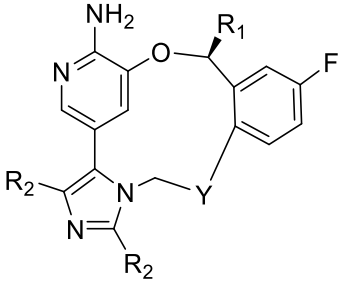
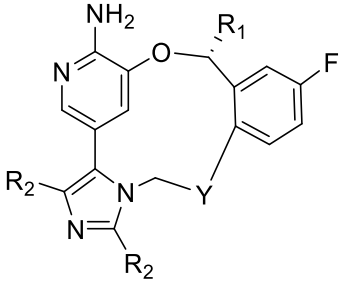
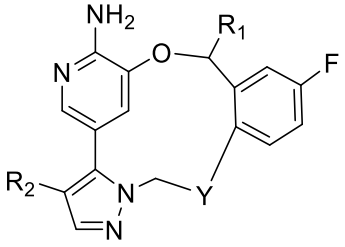
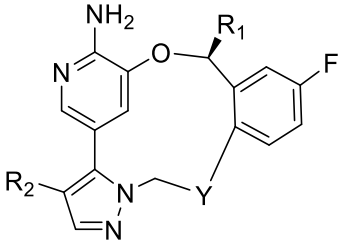
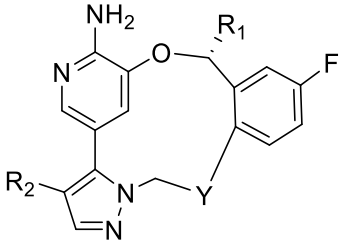
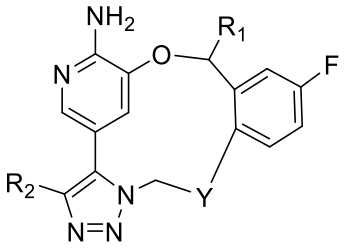
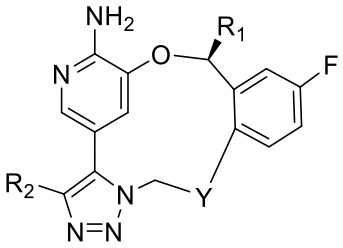
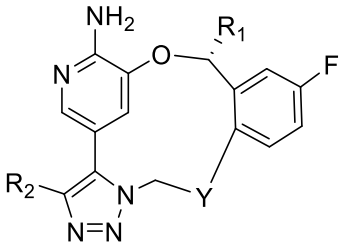
or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

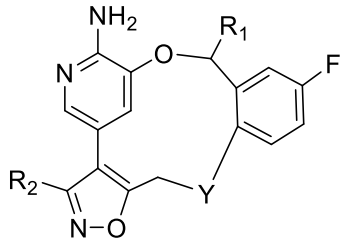
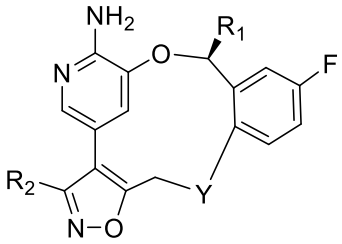
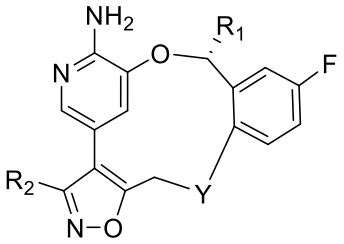
8. The compound of any one of claims 1 to 7, wherein each instance of R_2 is independently selected from the group consisting of H, chloro, fluoro, CN, methyl, ethyl, isopropyl, chloro, methoxy, trifluoromethyl, 2-fluoroethyl, difluoromethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, cyclopropylmethyl, cyclopropyl, cyclobutyl, and oxetanyl.

9. The compound of any one of claims 1 to 8, wherein each instance of R_3 is independently selected from the group consisting of H, fluoro, chloro, bromo, CN, methoxy, difluoromethyl, trifluoromethyl, methyl, and ethyl.

10. The compound of claim 1 or 2, which is a compound of any one of the following formula:

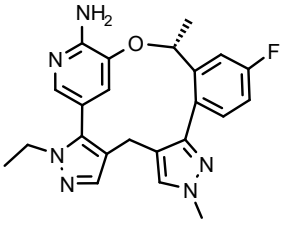
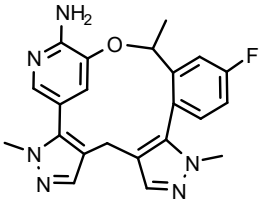
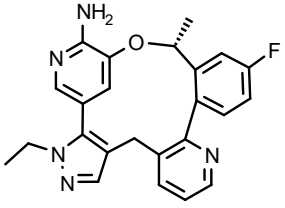
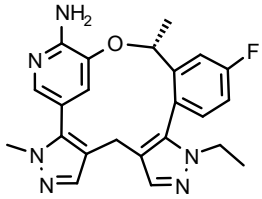
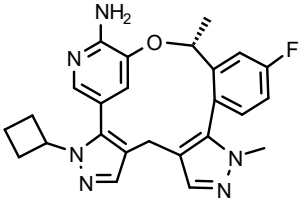
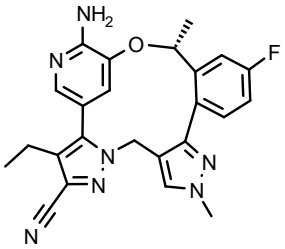
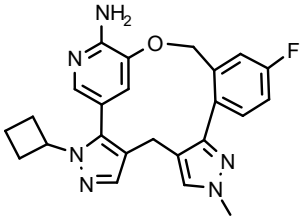
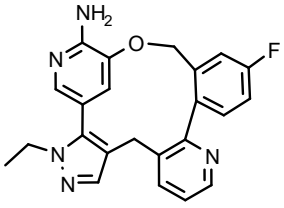
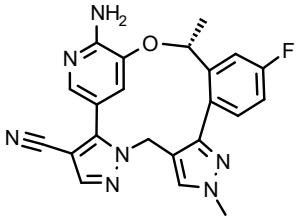
		
(II),	(II-A),	(II-B),

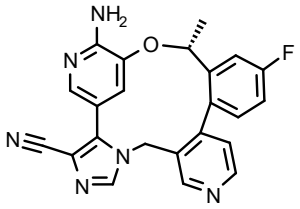
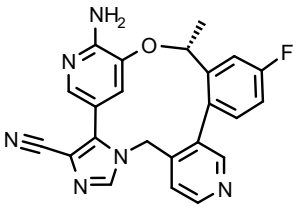
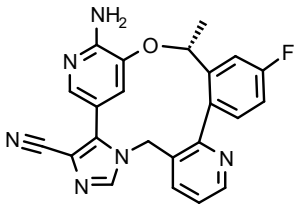
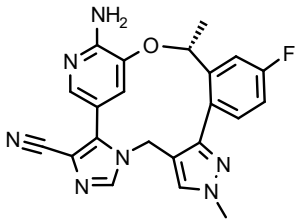
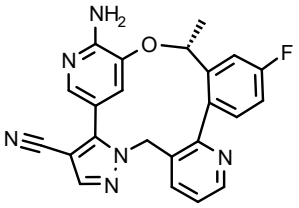
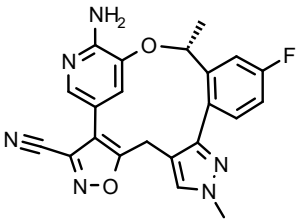
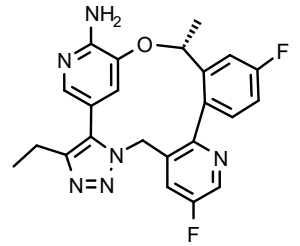
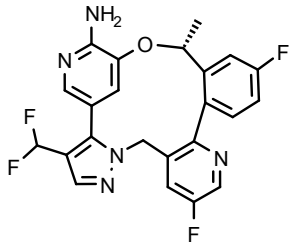
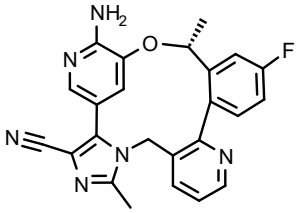
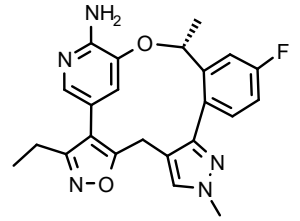
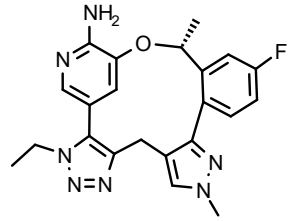
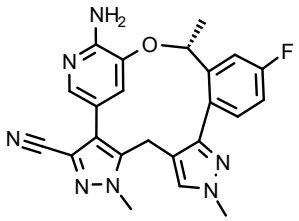
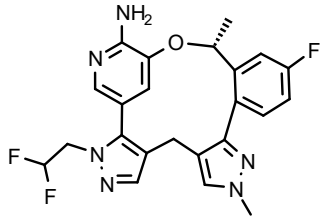
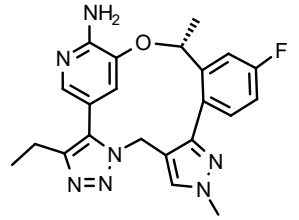
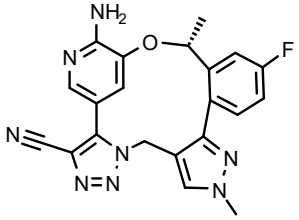
 (III),	 (III-A),	 (III-B),
 (IV),	 (IV-A)	 (IV-B),
 (V),	 (V-A),	 (V-B),
 (VI),	 (VI-A),	 (VI-B),

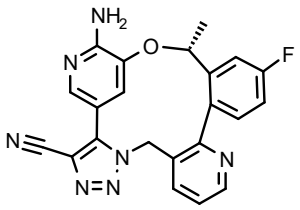
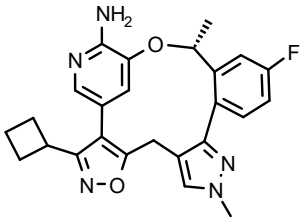
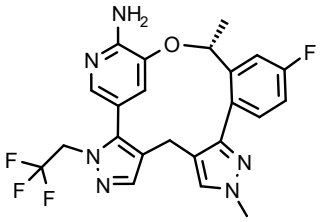
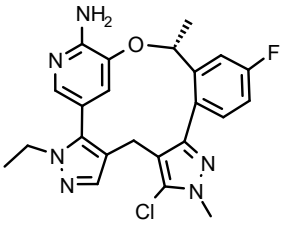
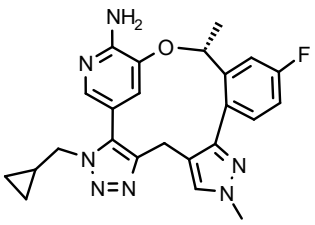
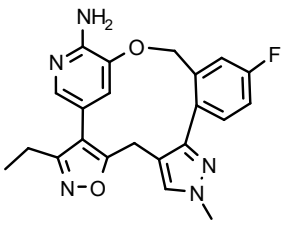
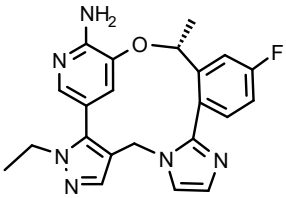
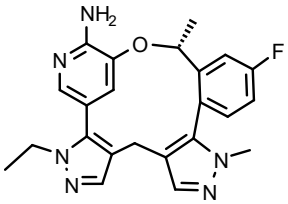
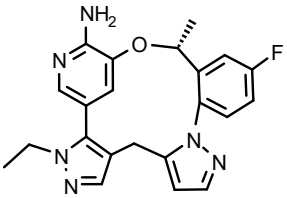
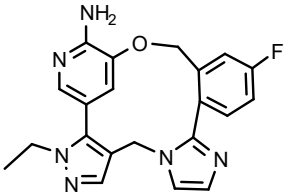
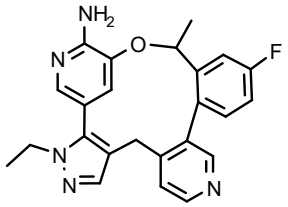
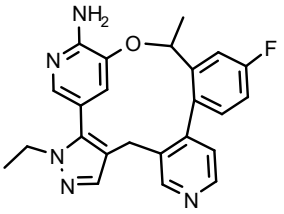
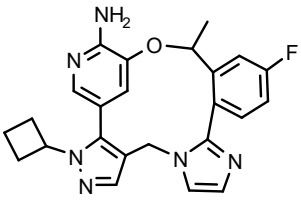
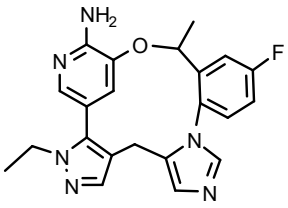
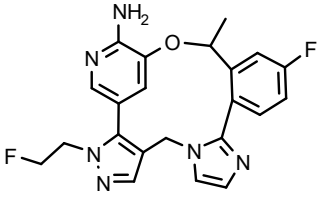
		
(VII),	(VII-A), or	(VII-B),

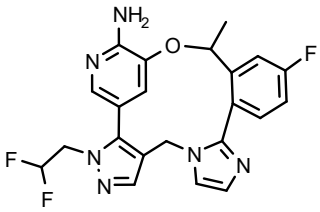
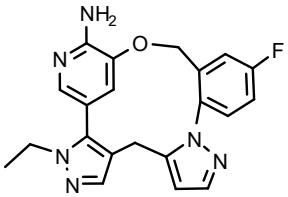
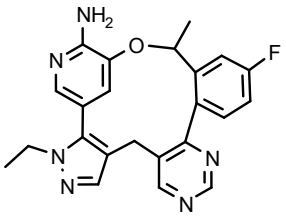
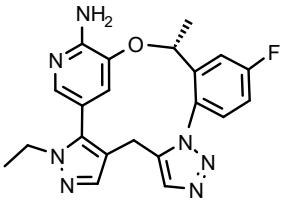
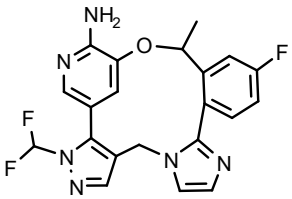
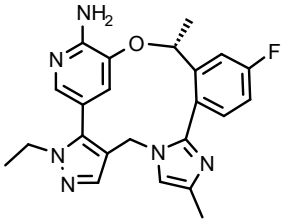
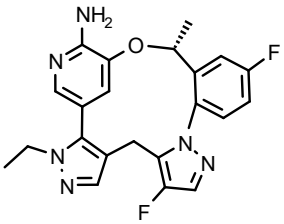
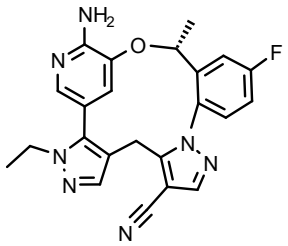
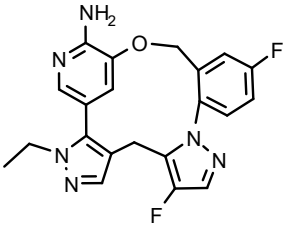
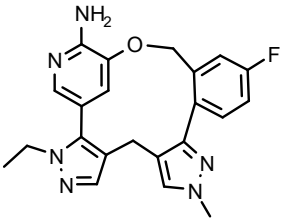
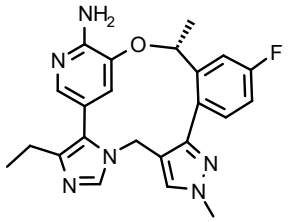
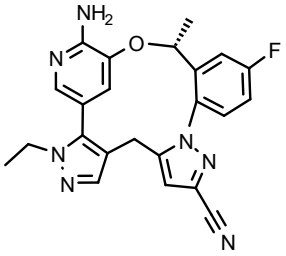
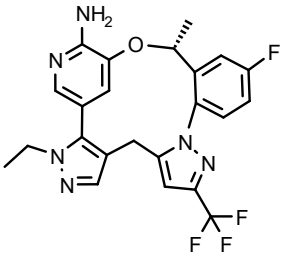
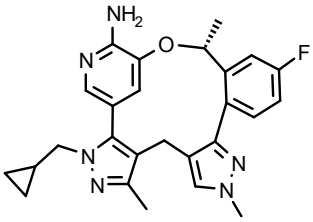
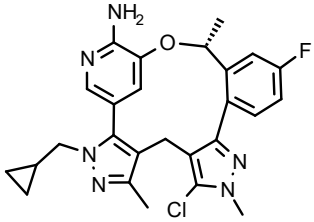
or an enantiomer, a mixture of enantiomers, or a tautomer thereof, or a pharmaceutically acceptable salt thereof.

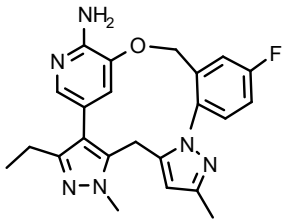
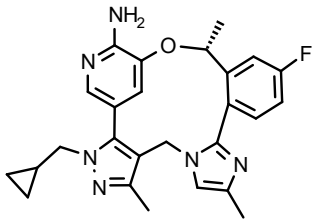
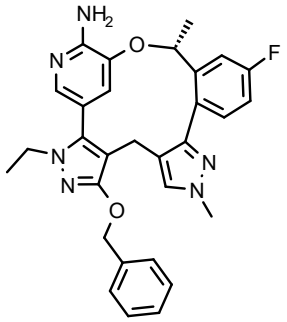
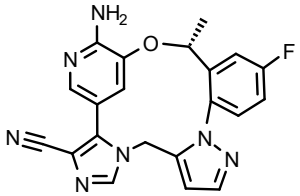
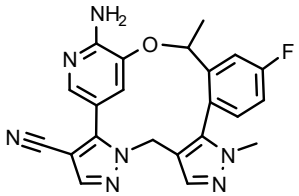
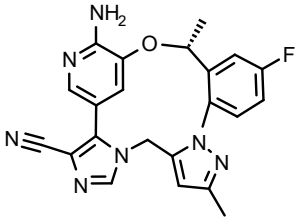
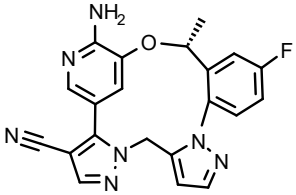
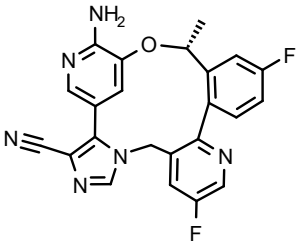
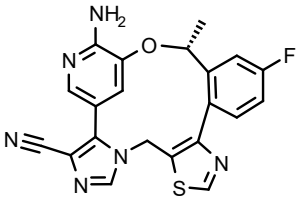
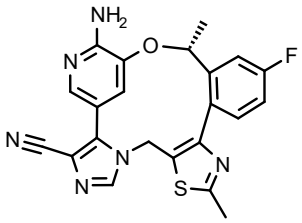
11. A compound, which is:

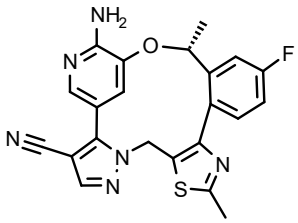
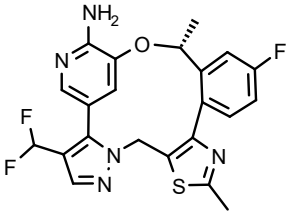
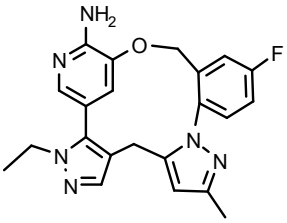
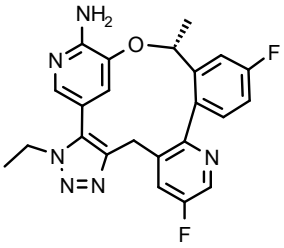
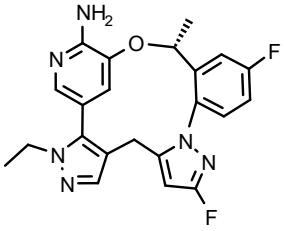
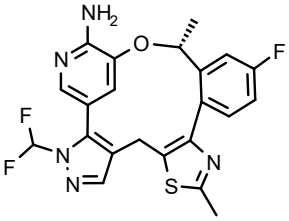
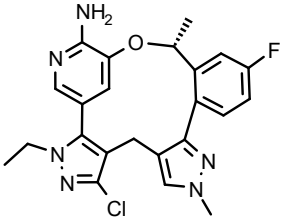
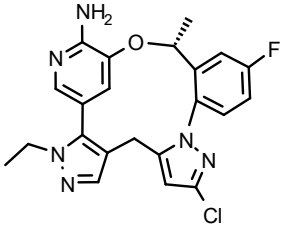
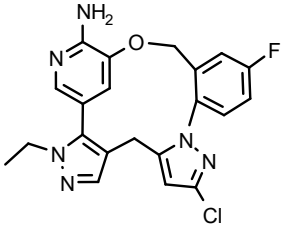
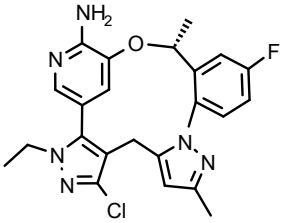
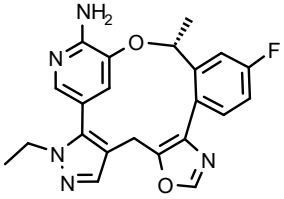
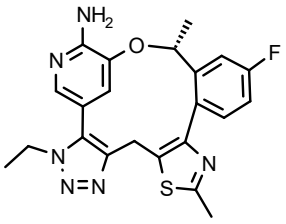
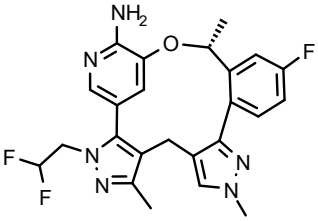
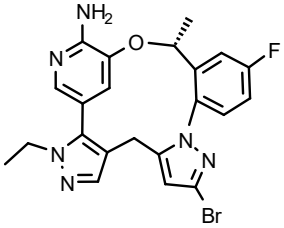
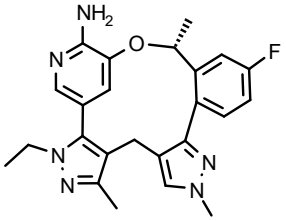
		
1,	2,	3,
		
4,	5,	6,
		
7,	8,	9,

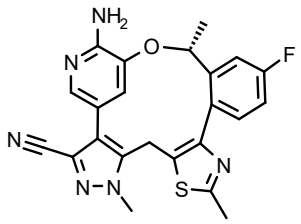
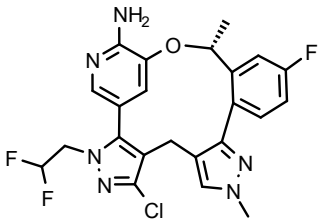
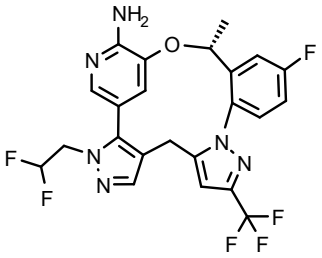
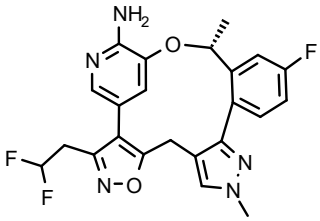
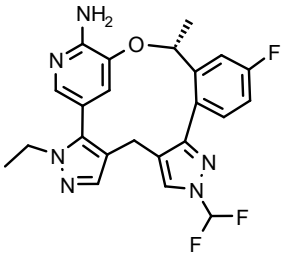
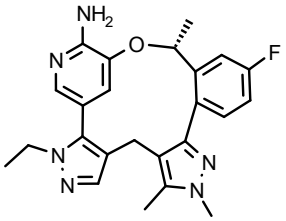
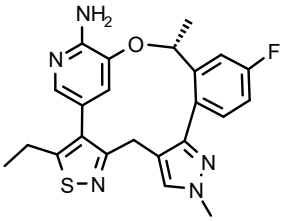
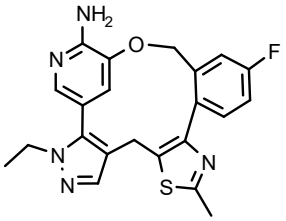
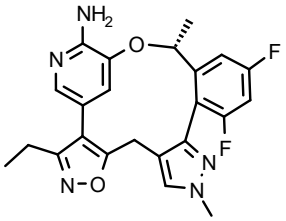
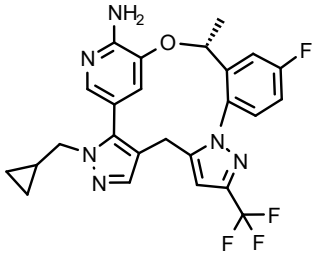
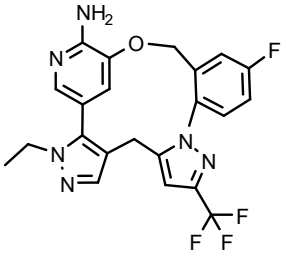
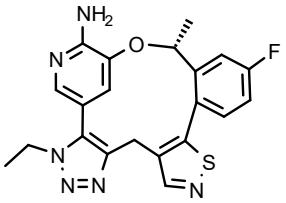
 10,	 11,	 12,
 13,	 14,	 15,
 16,	 17,	 18,
 19,	 20,	 21,
 22,	 23,	 24,

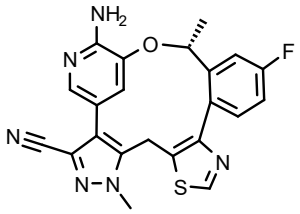
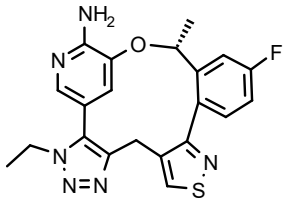
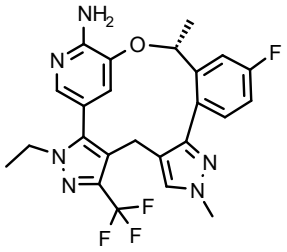
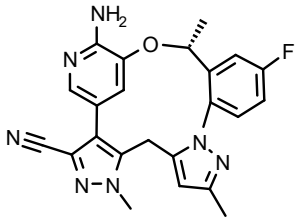
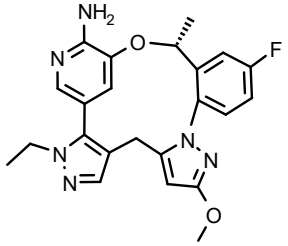
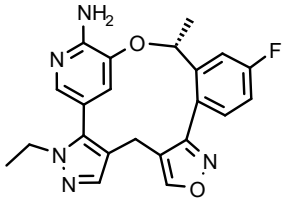
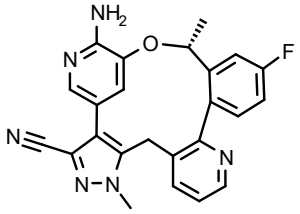
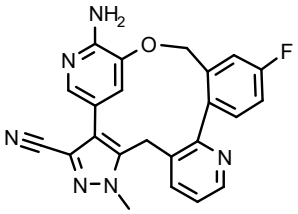
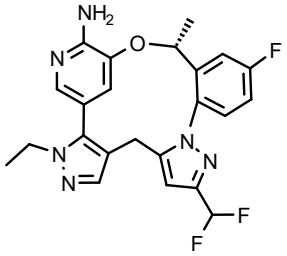
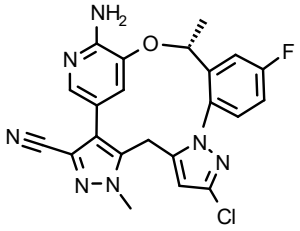
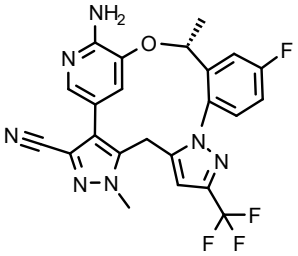
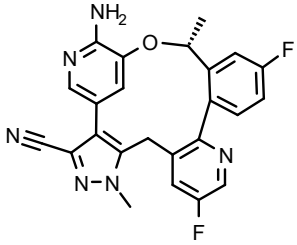
 25,	 26,	 27,
 28,	 29,	 30,
 31,	 32,	 33,
 34,	 35,	 36,
 37,	 38,	 39,

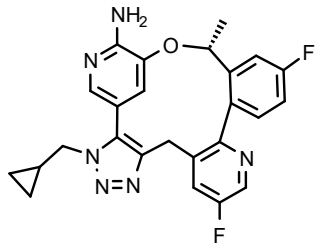
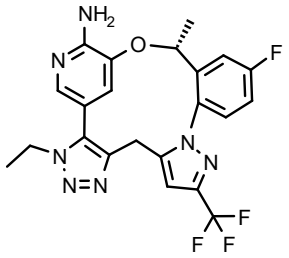
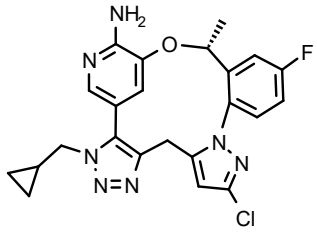
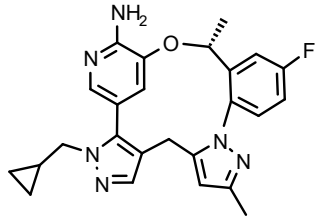
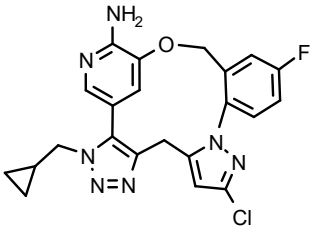
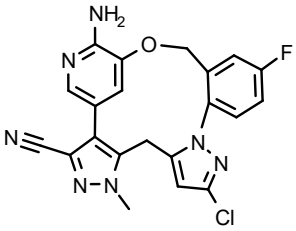
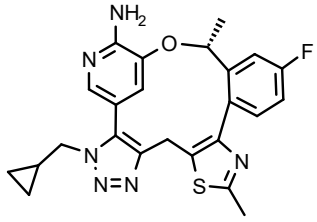
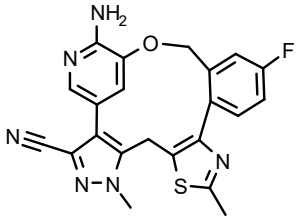
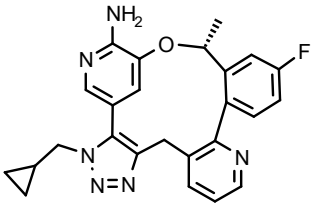
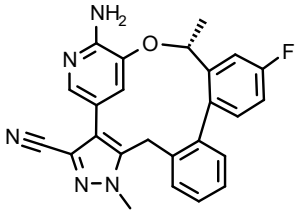
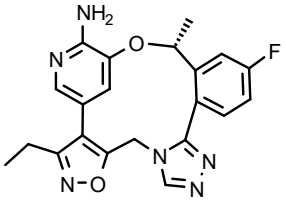
 40,	 41,	 42,
 43,	 44,	 45,
 46,	 47,	 48,
 49,	 50,	 51,
 52,	 53,	 54,

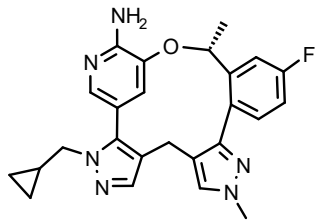
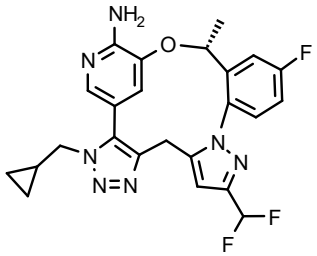
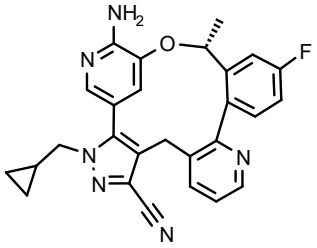
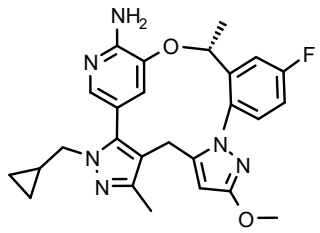
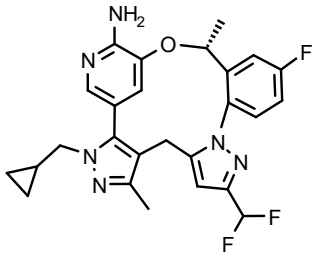
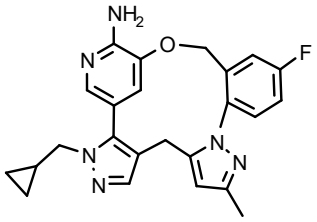
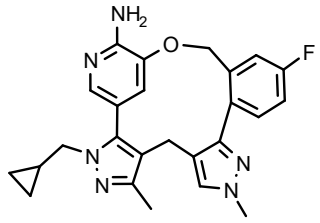
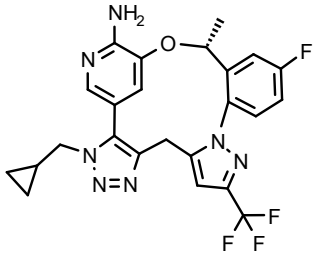
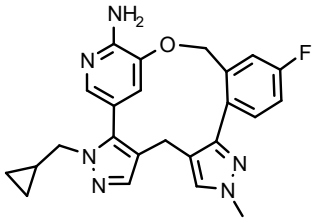
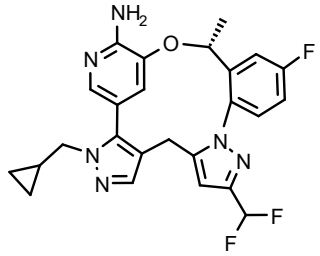
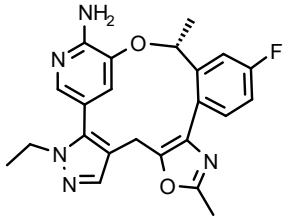
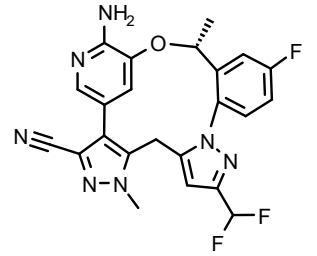
 55,	 56,	 57,
 58,		 60,
 61,	 62,	 63,
 64,	 65,	

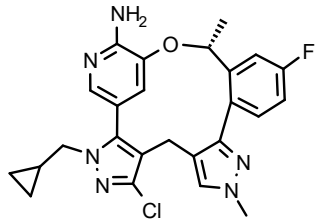
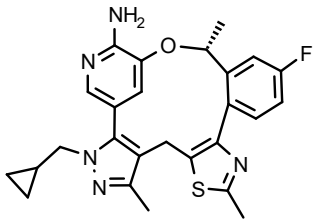
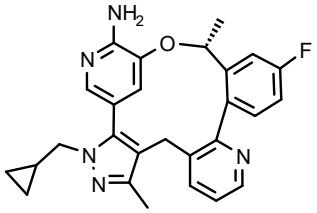
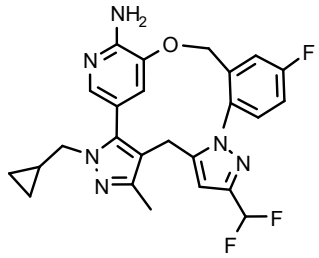
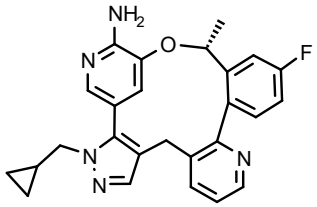
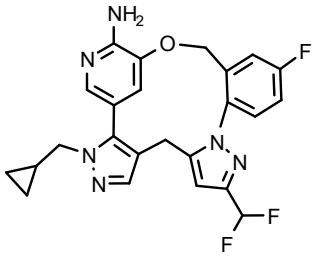
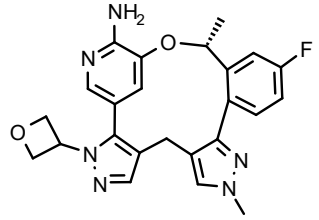
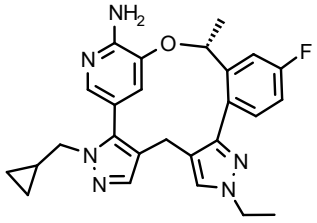
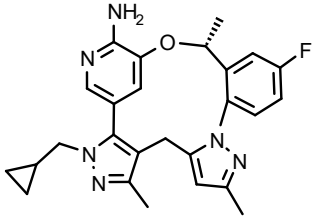
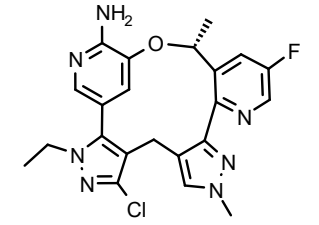
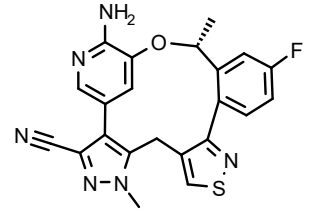
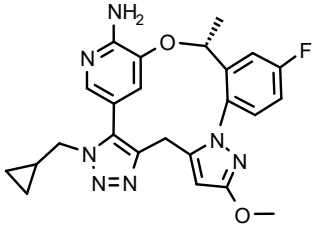
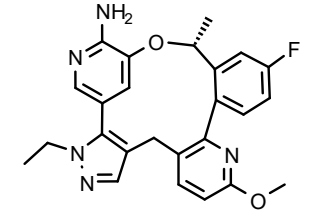
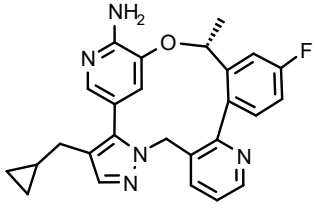
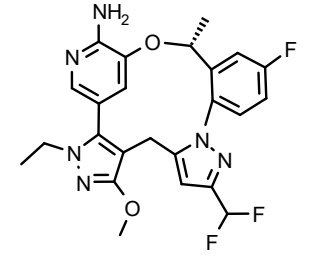
 67,	 68,	 69,
 70,	 71,	 72,
 73,	 74,	 75,
 76,	 77,	 78,
 79,	 80,	 81,

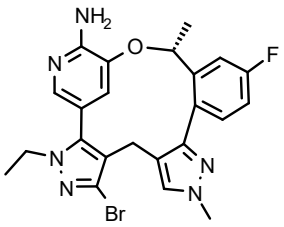
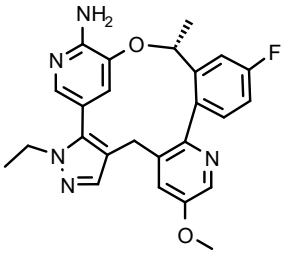
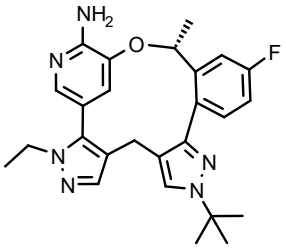
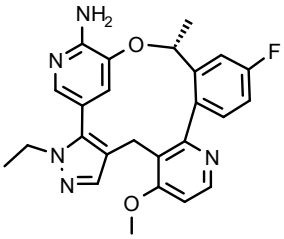
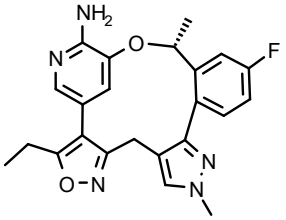
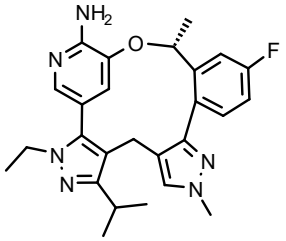
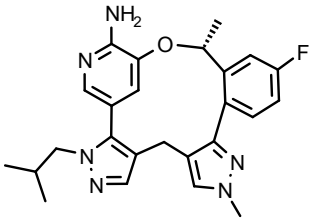
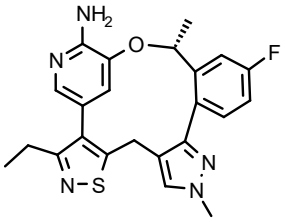
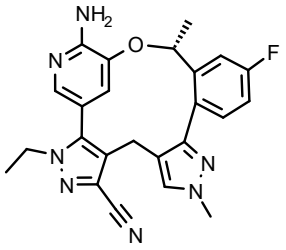
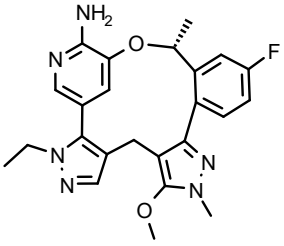
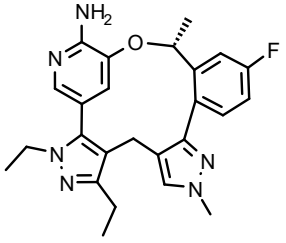
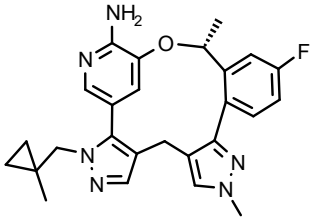
 82,	 83,	 84,
 85,	 86,	 87,
 88,	 89,	 90,
 91,	 92,	 93,

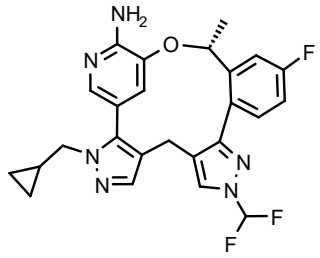
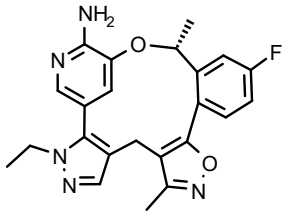
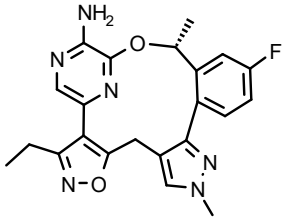
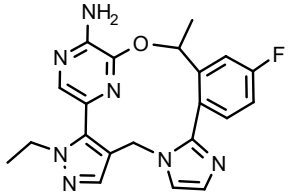
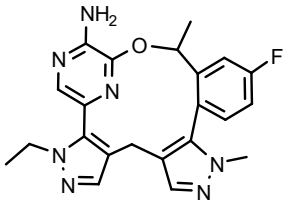
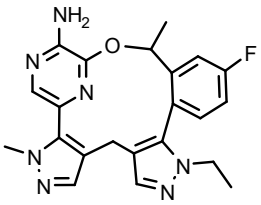
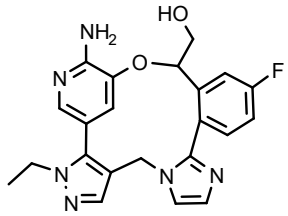
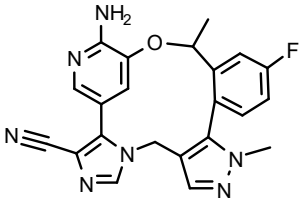
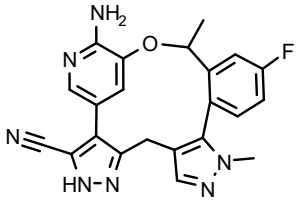
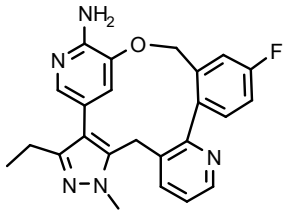
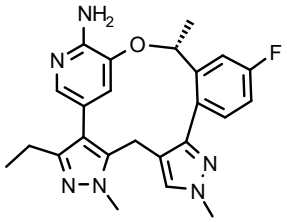
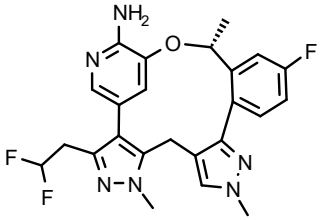
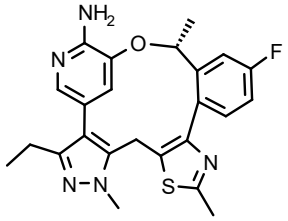
 94,	 95,	 96,
 97,	 98,	 99,
 100,	 101,	 102,
 103,	 104,	 105,

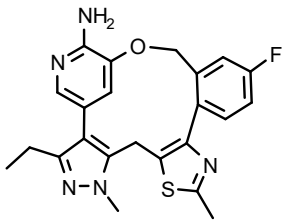
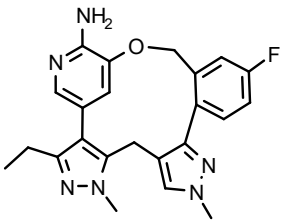
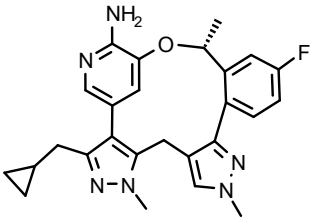
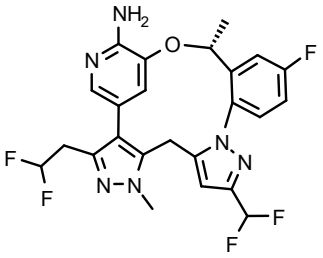
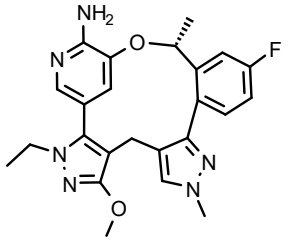
 106,	 107,	 108,
 109,	 110,	
	 113,	 114,
 115,	 116,	 117,
		 120,

		
121,	122,	123,
		
124,	125,	126,
		
127,	128,	129,
		
130,	131,	132,

 133,	 134,	 135,
 136,	 137,	 138,
 139,	 140,	 141,
 142,	 143,	 144,
 145,	 146,	 147,

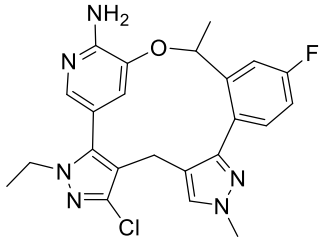
 148,	 149,	 150,
 151,	 152,	 153,
 154,	 155,	 156,
 157,	 158,	 159,

 160,	 161,	 162,
 163,	 164,	 165,
 166,	 167,	 168,
	 170,	 171,
 172,	 173,	

 175,	 176,	
 178,		 180, or
 181,		

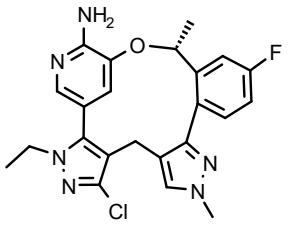
or a pharmaceutically acceptable salt thereof.

12. A compound, which is:

,

or a pharmaceutically acceptable salt thereof.

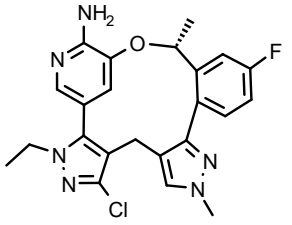
13. A compound, which is:



,

or a pharmaceutically acceptable salt thereof.

14. A compound, which is:



.

15. A pharmaceutical composition, comprising the compound or pharmaceutically acceptable salt of any one of claims 1 to 14; and a pharmaceutically acceptable carrier or excipient.

16. Use of the compound or pharmaceutically acceptable salt of any one of claims 1 to 14, or the pharmaceutical composition of claim 15, in the manufacture of a medicament for treating cancer in a subject.

17. The use of claim 16, wherein the cancer is a solid tumor.

18. The use of claim 17, wherein the solid tumor is lung cancer, glioblastoma, inflammatory myofibroblastic tumor (IMT), bile duct cancer, ovarian cancer, gastric cancer, colorectal cancer, angiosarcoma, melanoma, epithelioid hemangioendothelioma, esophageal cancer, kidney cancer, breast cancer, colon cancer, thyroid cancer, spitzoid tumor, cholangiocarcinoma, or neuroblastoma.

19. The use of claim 16, wherein the cancer is a hematologic malignancy.

20. The use of claim 19, wherein the hematologic malignancy is anaplastic large cell lymphoma (ALCL), diffuse large B-cell lymphoma (DLBCL), or large B-cell lymphoma.

21. The use of claim 16, wherein the cancer is lung cancer.

22. The use of claim 16, wherein the cancer is non-small cell lung cancer.

23. The use of claim 16, wherein the cancer is spitzoid melanoma, esophageal squamous cell carcinoma, renal medullary carcinoma, renal cell carcinoma, papillary thyroid cancer, or serous ovarian carcinoma.

24. The use of any one of claims 16 to 23, wherein the cancer is a ROS1 (ROS proto-oncogene 1, receptor tyrosine kinase) positive cancer.

25. The use of any one of claims 16 to 23, wherein the cancer comprises expression of an oncogenic *ROS1* gene or oncogenic *ROS1* gene-fusion.

26. The use of claim 25, wherein the oncogenic *ROS1* gene or oncogenic *ROS1* gene-fusion contains one or more mutations of the human *ROS1* gene.

27. The use of claim 26, wherein the one or more mutations in the oncogenic *ROS1* gene or oncogenic *ROS1* gene-fusion results in expression of a ROS1 protein with a G2032R mutation.

28. The use of any one of claims 16 to 23, wherein the cancer is an ALK (anaplastic lymphoma kinase) positive cancer.

29. The use of any one of claims 16 to 23, wherein the cancer comprises expression of an oncogenic *ALK* gene or oncogenic *ALK* gene-fusion.

30. The use of claim 29, wherein the oncogenic *ALK* gene or the oncogenic *ALK* gene-fusion contains one or more mutations of the human *ALK* gene.

31. The use of claim 30, wherein the one or more mutations in the oncogenic *ALK* gene or the oncogenic *ALK* gene-fusion results in expression of an ALK protein with one or more mutations selected from the group consisting of G1202R, G1202del, L1196M, L1196Q, L1198F, G1269A, D1203N, I1171N, I1171S, I1171T, F1174C, F1174L, V1180L, C1156Y, S1206Y, E1210K, and R1275Q, or wherein the one or more mutations in the oncogenic *ALK* gene or the

oncogenic *ALK* gene-fusion results in expression of an ALK protein with a co-mutation of G1202R and one or more mutations selected from L1196M, G1269A, and L1198F.

32. The use of any one of claims 16 to 23, wherein the cancer has one or more ALK mutations comprising one or more ALK fusions with NPM1, STRN, HIP1, or EML4.

33. The use of claim 32, wherein ALK mutation is EML4-ALK, EML4-ALK variant 1, EML4-ALK variant 3, EML4-ALK G1202R, EML4-ALK L1196M/G1202R, or EML4-ALK G1202R/G1269A.

34. Use of the compound or pharmaceutically acceptable salt of any one of claims 1 to 14, or the pharmaceutical composition of claim 15, in the manufacture of a medicament for selectively inhibiting ROS1 or ALK over TRK, wherein the inhibition takes place in a subject suffering from cancer.

35. The use of any one of claims 16 to 34, wherein:

(i) the cancer is metastatic, relapsed, or refractory to a prior treatment; and/or

(ii) the cancer is metastatic, relapsed, or refractory to a prior TKI treatment; and/or

(iii) the cancer comprises brain metastases.

36. The use of any one of claims 16 to 35, wherein the medicament is manufactured to be administered in combination with one or more additional therapeutic agents.

37. The use of claim 36, wherein:

(i) the additional therapeutic agent is a TKI, wherein the TKI is crizotinib, ceritinib, alectinib, brigatinib, lorlatinib, entrectinib, repotrectinib, cabozantinib, foretinib, taletrectinib, merestinib, masitinib, or ensartinib; or

(ii) the additional therapeutic agent is a chemotherapeutic agent, an immuno-oncology agent, a SH2 inhibitor, a MEK inhibitor, a MET inhibitor, a SHP2 inhibitor, an anti-PD-1 agent, or a RAS inhibitor.

38. Use of a compound or pharmaceutically acceptable salt of any one of claims 1 to 14 or a pharmaceutical composition of claim 15 for decreasing a level of ROS1 or ALK in a cell.