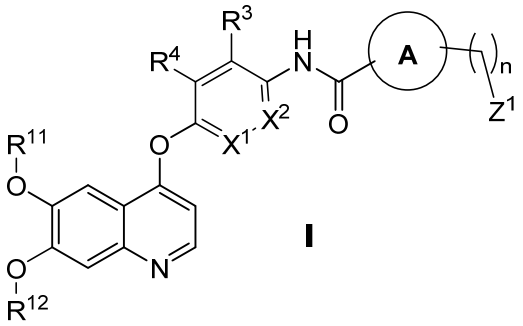
Claims

1. A compound having the general formula I:



I

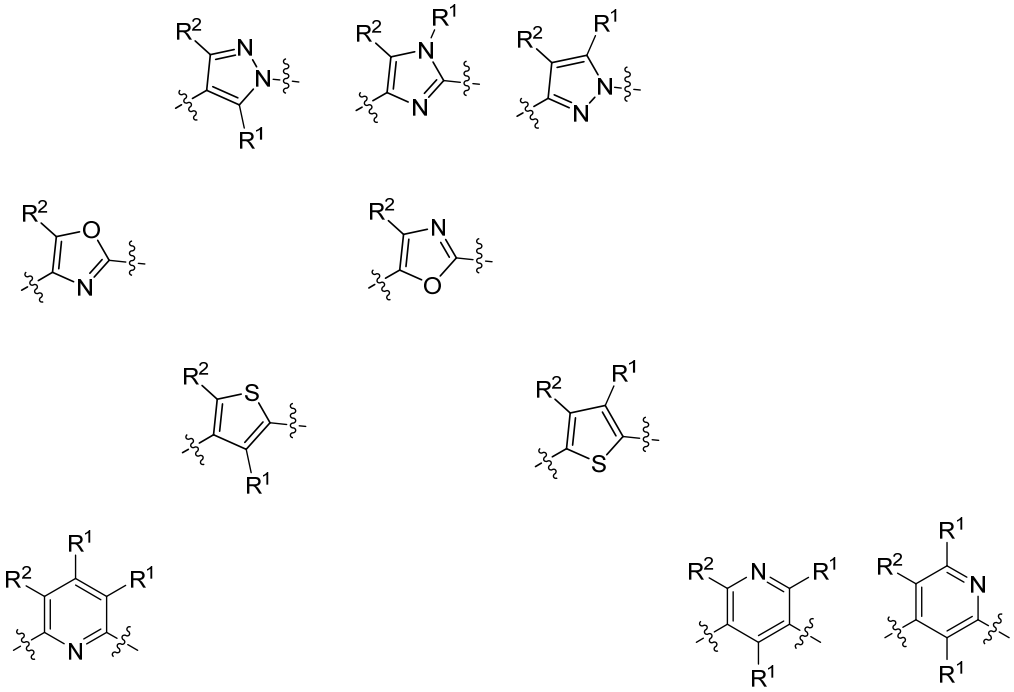
wherein

X^1 is, independently at each occurrence, selected from CR^3 and N;

X^2 is, independently at each occurrence, selected from CR^4 and N;

n is, independently at each occurrence, selected from 0 and 1;

A is, at each occurrence, independently selected from any structure as depicted in the following group W;



Group W

R^1 is, at each occurrence, independently selected from the group consisting of hydrogen; C1-C6 alkyl; C1-C6 alkyl substituted with one or two of OR^5 and NR^5R^6; C3-C10 cycloalkyl; C1-C4 haloalkyl; -(C=O)R^5; any of which is optionally substituted;

R^2 is -OR^8;

R^3 and R^4 are, at each occurrence, independently selected from the group consisting of hydrogen; halogen, e.g Cl or F; C1-C3 alkyl; OR^5; C1-C4 haloalkyl; any of which is optionally substituted;

R^5 and R^6 are, at each occurrence, independently selected from the group consisting of hydrogen; C1-C6 alkyl; C3-C10 cycloalkyl; C1-C4 haloalkyl; any of which is optionally substituted;

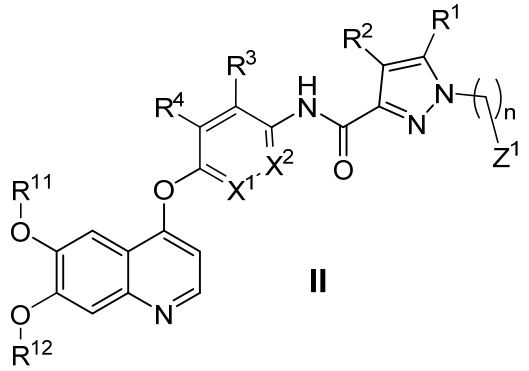
R^8 is, at each occurrence, independently selected from the group consisting of C1-C4 haloalkyl; and C1-C6 alkyl substituted with C1-C4 haloalkyl;

Z^1 is, at each occurrence, independently selected from the group consisting of hydrogen; C1-C6 alkyl; C1-C6 alkyl substituted with one or two of OR^5 and NR^5R^6; C3-C10 cycloalkyl; C3-C10 heterocycloalkyl;

R^{11} and R^{12} are, at each occurrence, independently selected from the group consisting of C1-C6 alkyl; C3-C10 cycloalkyl; C3-C10 heterocycloalkyl; C1-C4 haloalkyl; any of which is optionally substituted;

and pharmaceutically acceptable salts thereof.

2. The compound according to claim 1, having the general formula II:

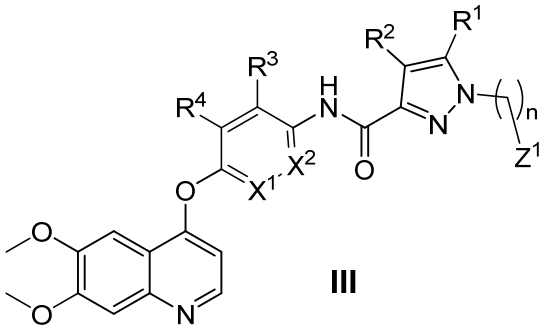


II

wherein

R^1, R^2, R^3, R^4, R^{11}, R^{12}, Z^1, X^1, X^2 and n are as defined in claim 1; and pharmaceutically acceptable salts thereof.

3. The compound according to any of claims 1 and 2, having the general formula III:



III

wherein

R^1, R^2, R^3, R^4, Z^1, X^1, X^2 and n are as defined in claim 1; and pharmaceutically acceptable salts thereof,

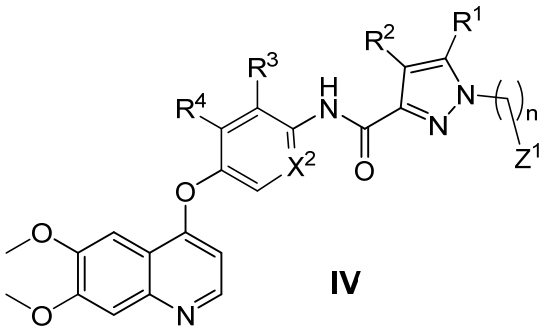
wherein, preferably,

R^3 and R^4 are, at each occurrence, independently selected from the group consisting of hydrogen; halogen, e.g Cl or F; C1-C3 alkyl, which is optionally substituted;

R^8 is, at each occurrence, independently selected from the group consisting of C1-C4 haloalkyl; and C1-C6 alkyl substituted with C1-C4 haloalkyl; and

Z^1 is, at each occurrence, independently selected from the group consisting of hydrogen; C1-C6 alkyl; C1-C6 alkyl substituted with one or two of OR^5 and NR^5R^6; C3-C10 cycloalkyl; C3-C10 heterocycloalkyl; and pharmaceutically acceptable salts thereof.

4. The compound according to any of claims 1 - 3, having the general formula IV:

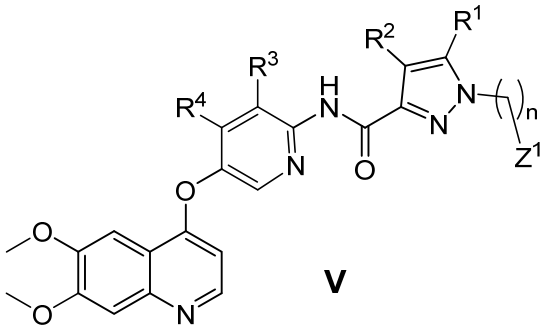


IV

wherein

R^1, R^2, R^3, R^4, Z^1, X^2 and n are as defined in any of claims 1 - 3; and pharmaceutically acceptable salts thereof.

5. The compound according to any of claims 1 - 4, having the general formula V:



V

wherein

R^1, R^2, R^3, R^4, Z^1 and n are as defined in any of claims 1 - 4; and pharmaceutically acceptable salts thereof;

wherein, preferably,

R^3 and R^4 are hydrogen;

and pharmaceutically acceptable salts thereof .

6. The compound according to any of claims 1-5, wherein n = 0 or 1, and Z^1 is selected from C1-C6 alkyl, in particular methyl, ethyl, propyl or isopropyl; C3-C10 cycloalkyl, in particular C3 cycloalkyl; C3-C10 heterocycloalkyl; C1-C6 alkyl substituted with one or two of OR^5 and NR^5R^6; and pharmaceutically acceptable salts thereof.

7. The compound according to any of claims 1-6, wherein R^2 is OR^8, and R^8 is selected from C1-C4 haloalkyl; or C1-C6 alkyl substituted with one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl, difluoroisopropyl, and fluoroisopropyl and pharmaceutically acceptable salts thereof.

8. The compound according to any of claims 6 and 7, wherein
n = 0 or 1, and Z^1 is selected from methyl, ethyl, propyl or isopropyl; C3 cycloalkyl; C3-C10 heterocycloalkyl; C1-C6 alkyl substituted with one or two of OR^5 and NR^5R^6; wherein R^5 and R^6 are, at each occurrence, independently selected from the group consisting of hydrogen; C1-C6 alkyl; C3-C10 cycloalkyl; C1-C4 haloalkyl; any of which is optionally substituted;
and

R^2 is OR^8, and R^8 is selected from C1-C4 haloalkyl; or C1-C6 alkyl substituted with one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl, difluoroisopropyl, and fluoroisopropyl

and pharmaceutically acceptable salts thereof.

9. The compound according to any of the foregoing claims, wherein
R^2 is OR^8, and R^8 is selected from C1-C4 haloalkyl, in particular one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl,

difluoroisopropyl, and fluoroisopropyl; or C1-C6 alkyl substituted with C1-C4 haloalkyl, in particular one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl, difluoroisopropyl, and fluoroisopropyl

10. The compound according to any of the foregoing claims, wherein n = 0 or 1; and Z^1 is selected from methyl; ethyl; propyl; isopropyl; C3 cycloalkyl; C4 cycloalkyl; and C5 cycloalkyl.

11. The compound according to any of claims 9 and 10, wherein n = 0 or 1; Z^1 is selected from methyl; ethyl; propyl; isopropyl; C3 cycloalkyl; C4 cycloalkyl; and C5 cycloalkyl; and
R^2 is OR^8; and R^8 is selected from C1-C4 haloalkyl, in particular one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl, difluoroisopropyl, and fluoroisopropyl; or C1-C6 alkyl substituted with C1-C4 haloalkyl, in particular one of trifluoromethyl, difluoromethyl, fluoromethyl, trifluoroethyl, difluoroethyl, fluoroethyl, trifluoropropyl, difluoropropyl, fluoropropyl, trifluoroisopropyl, difluoroisopropyl, and fluoroisopropyl

12. The compound according to any of the foregoing claims having one of the structures as shown hereafter:

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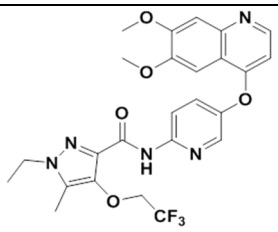
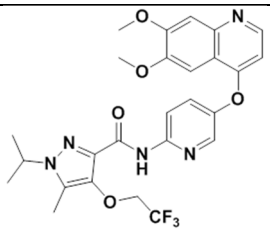
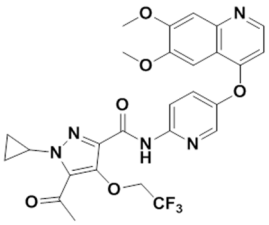
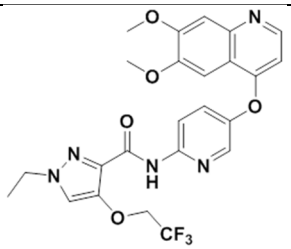
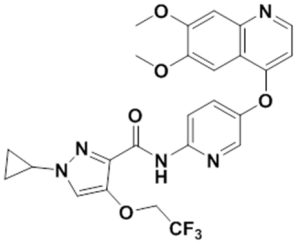
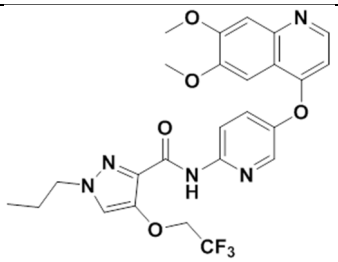
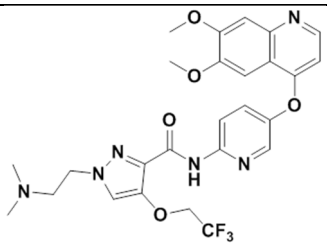
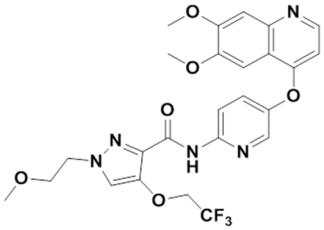
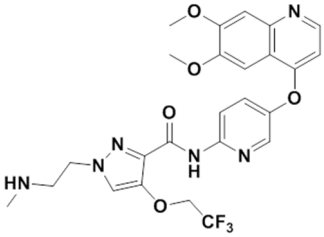
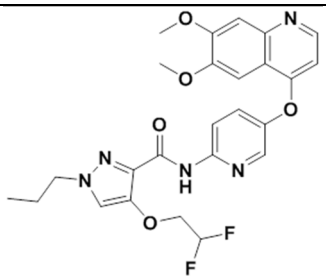
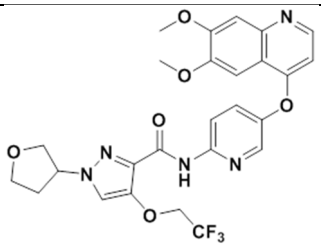
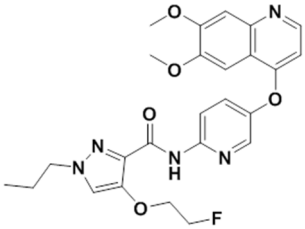
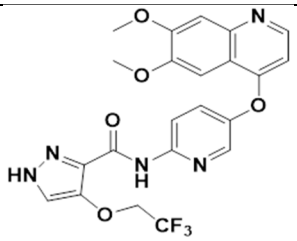
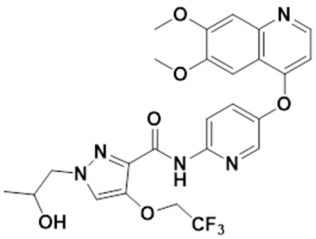
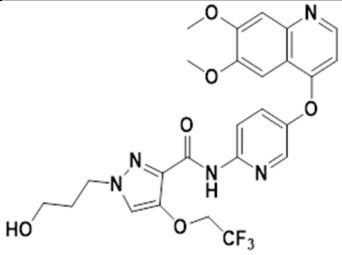
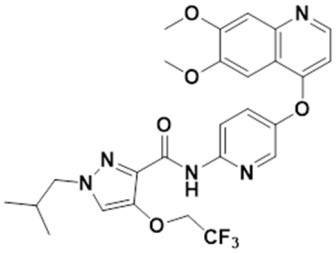
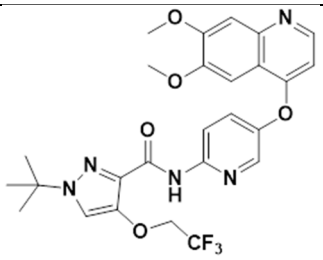
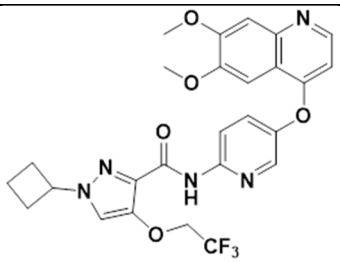
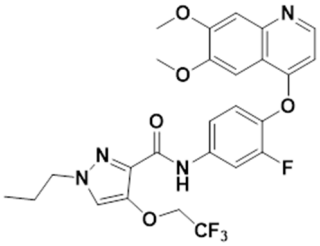
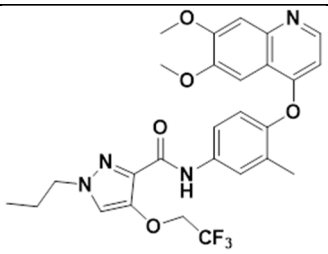
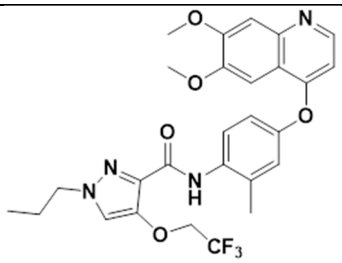
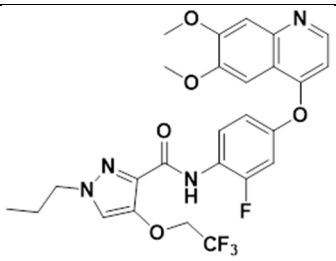
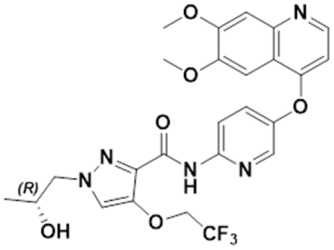
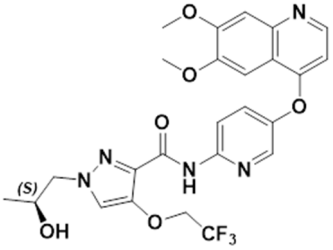
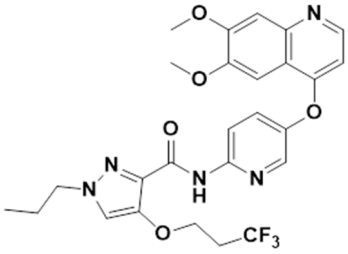
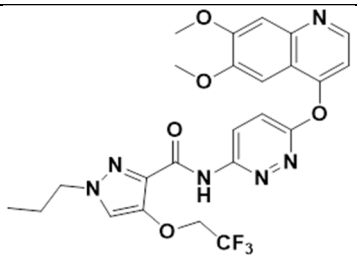
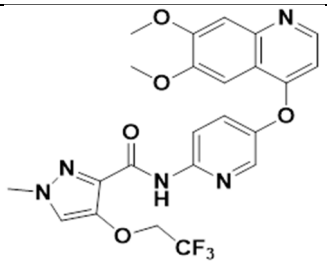
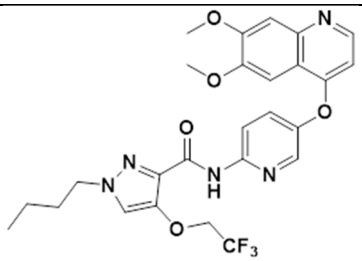
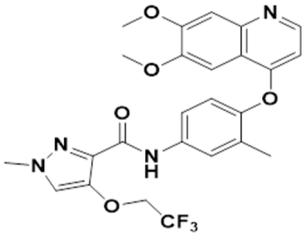
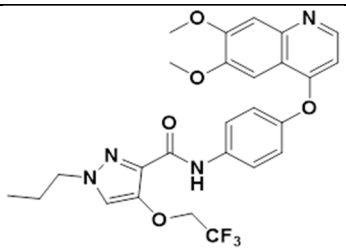
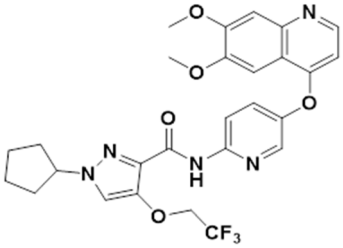
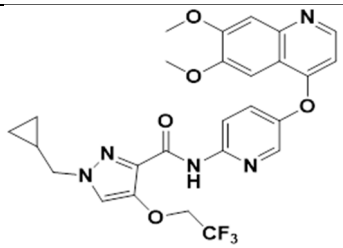
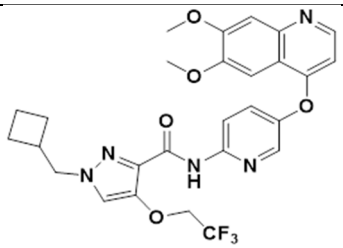
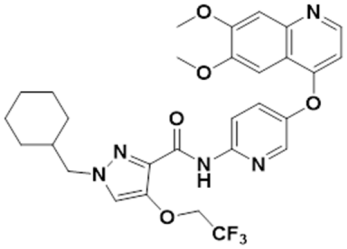
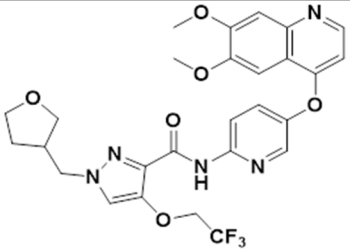
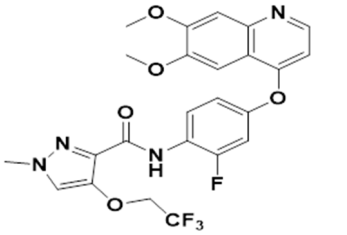
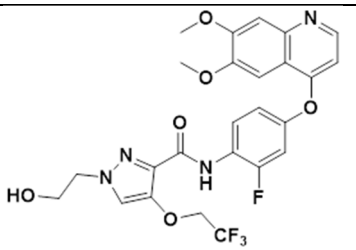
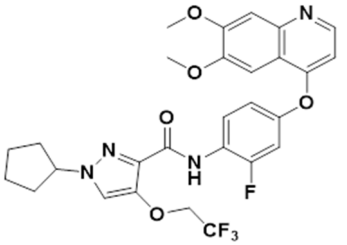
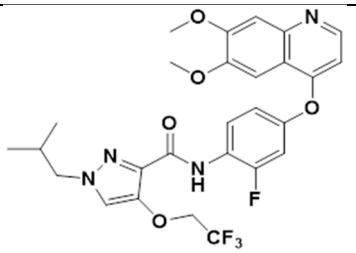
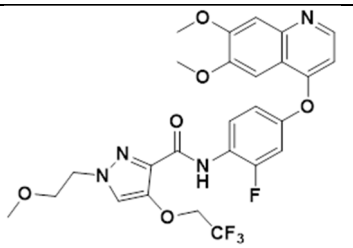
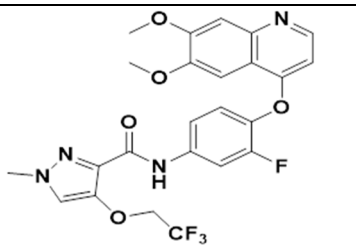
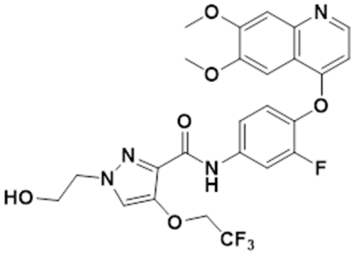
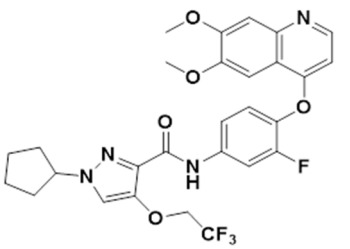
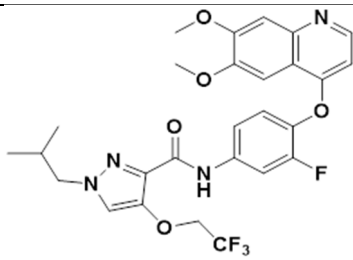
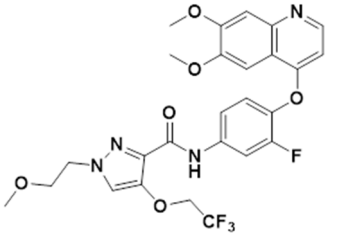
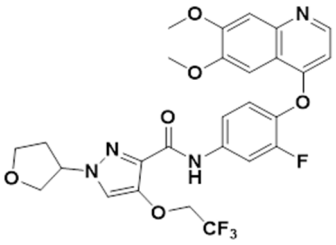
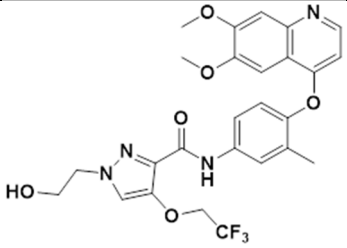
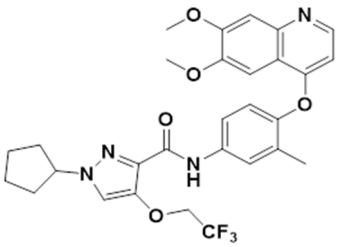
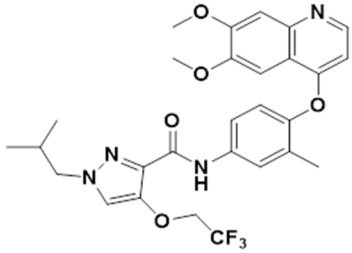
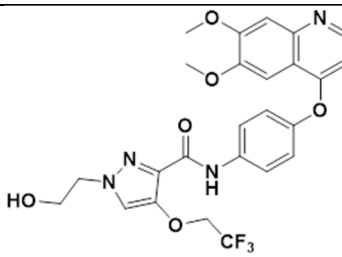
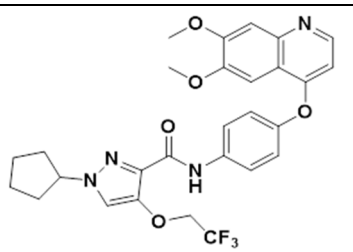
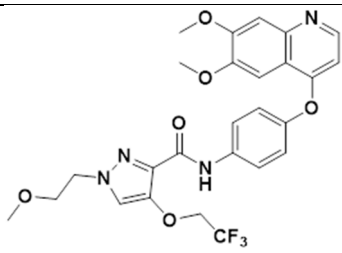
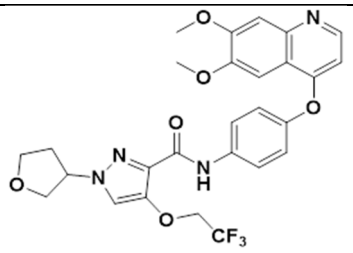
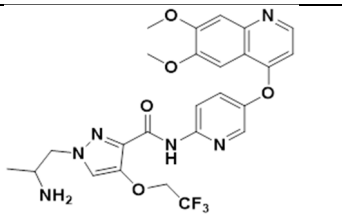
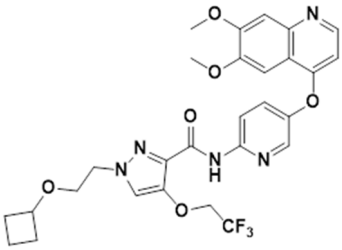
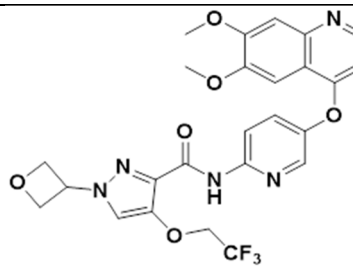
1		2	
3		4	

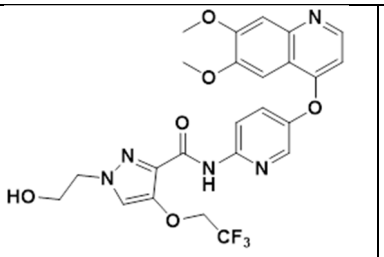
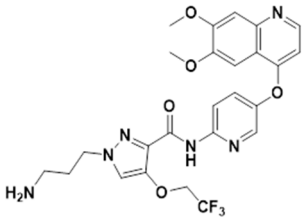
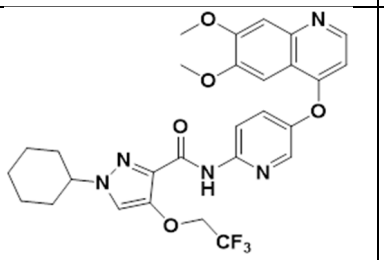
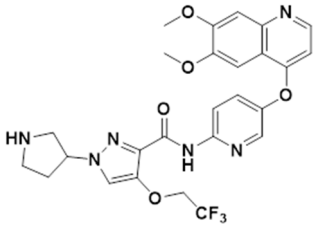
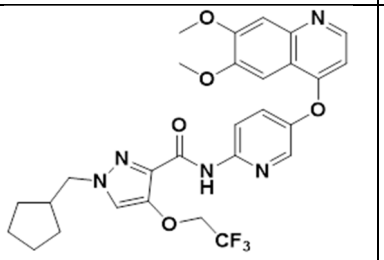
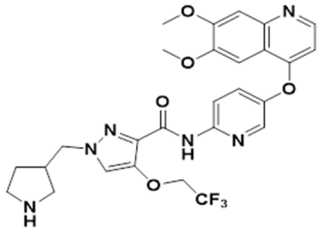
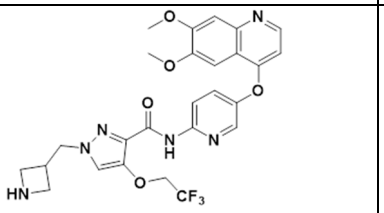
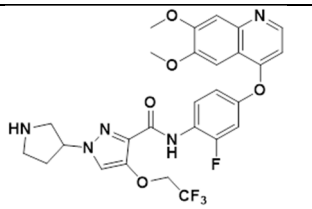
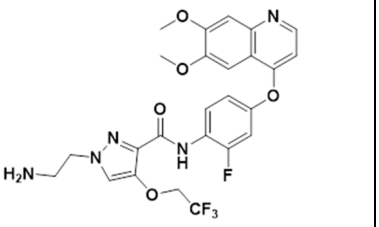
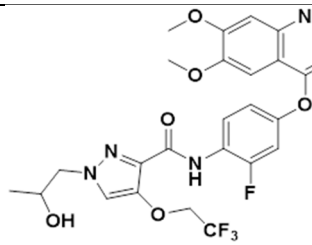
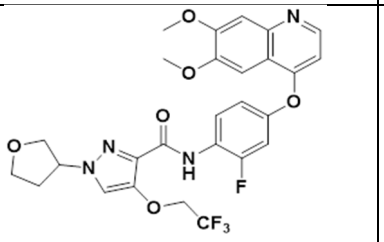
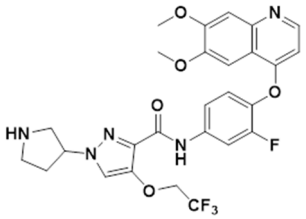
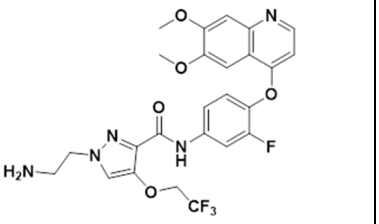
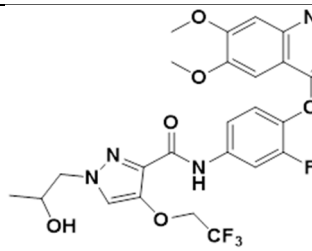
5			
7			
9		10	
11		12	
13		14	
		16	

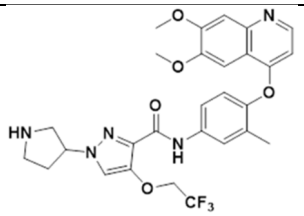
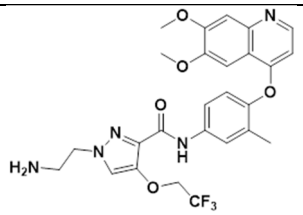
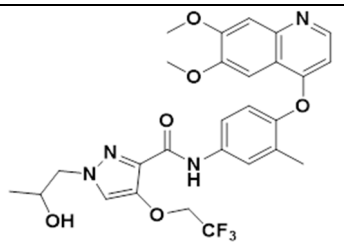
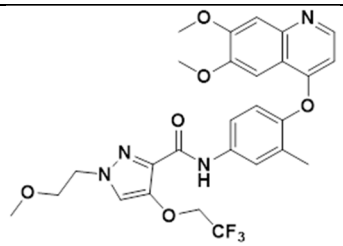
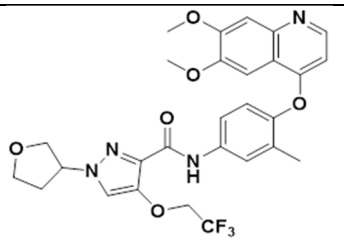
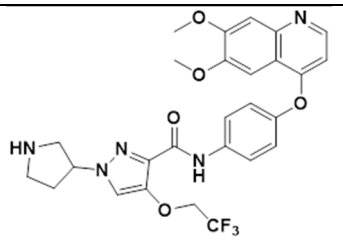
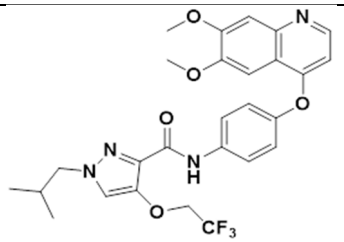
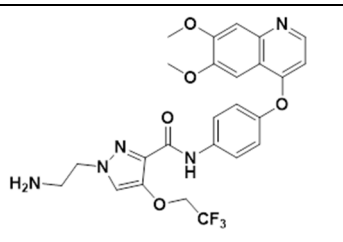
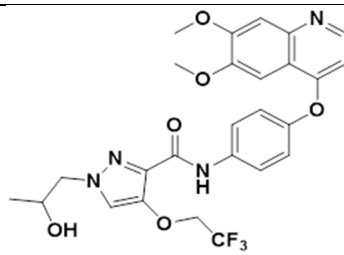
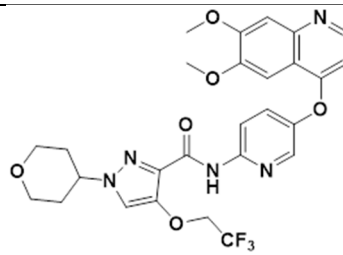
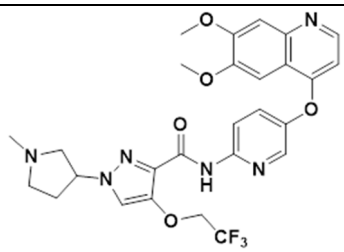
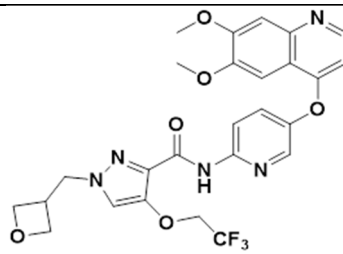
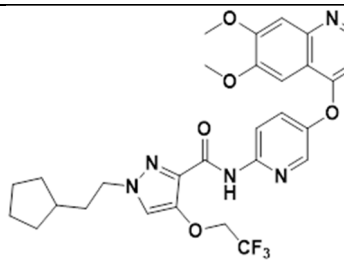
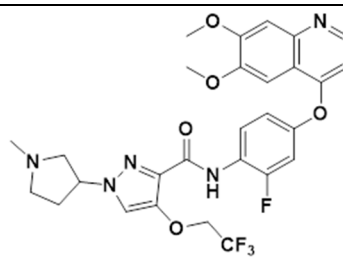
17		18	
21		22	
		24	
25		26	
27		28	
29		30	

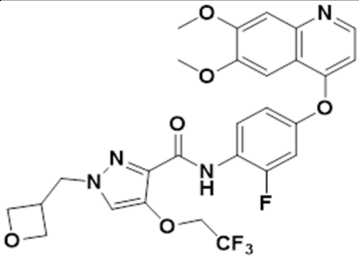
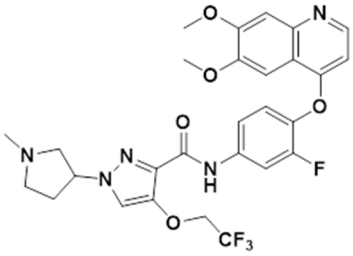
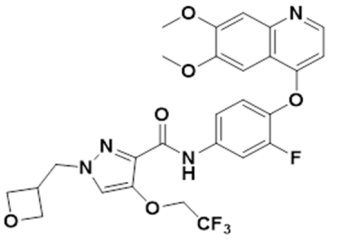
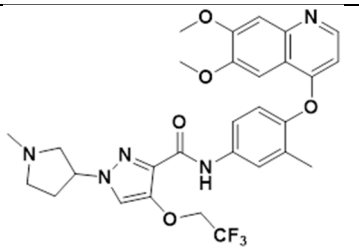
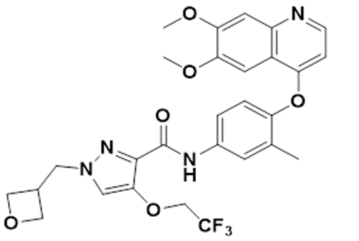
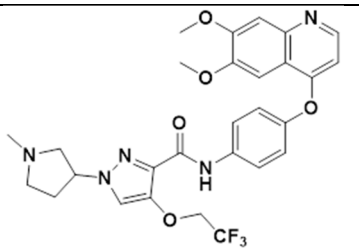
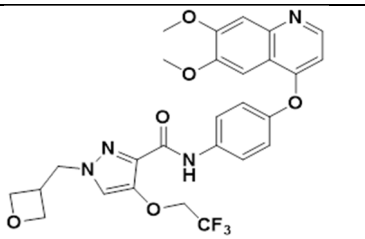
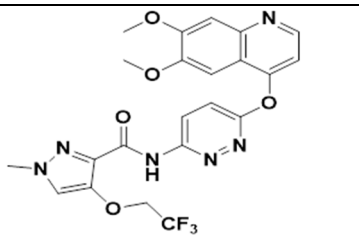
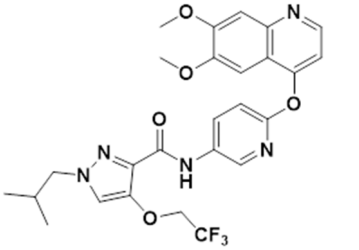
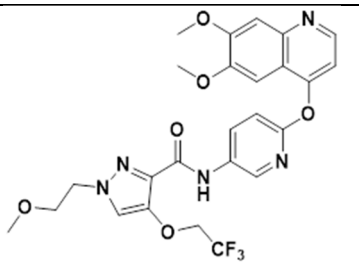
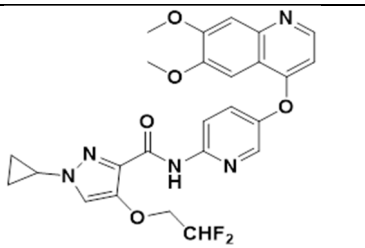
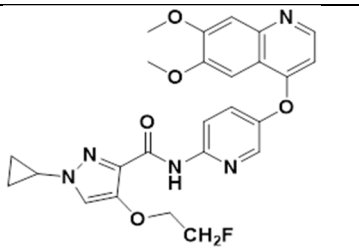
31		32	
33			
		36	
37		38	
		40	
41		42	

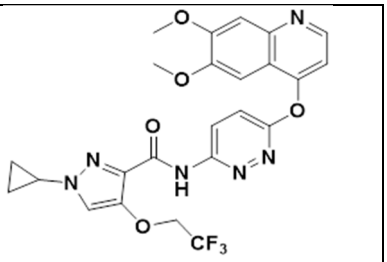
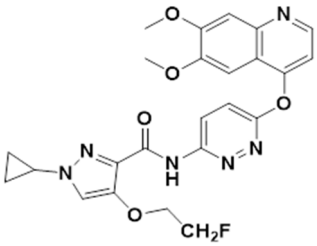
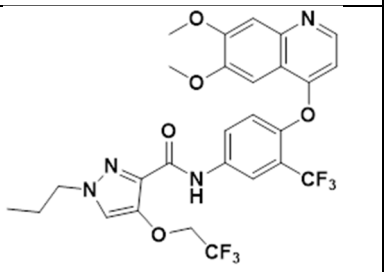
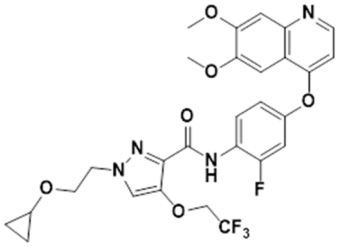
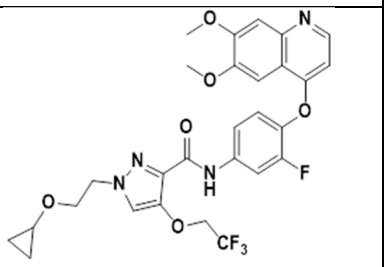
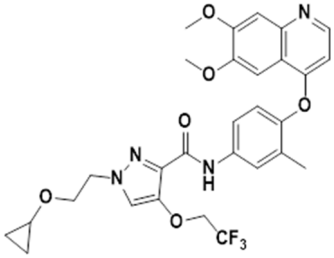
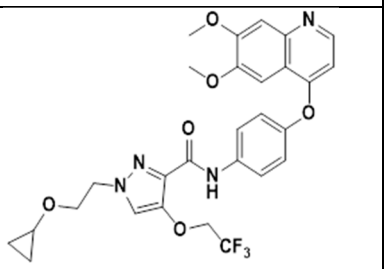
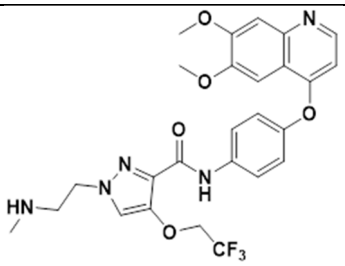
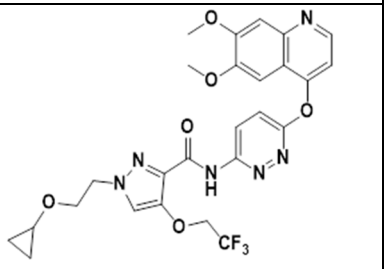
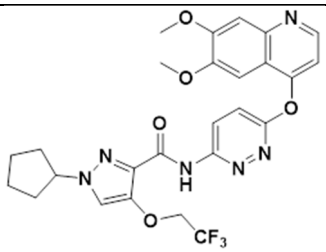
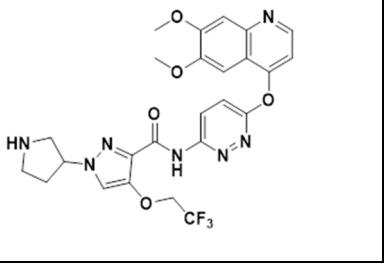
43		44	
45		46	
47		48	
49		50	
51		52	
53		54	

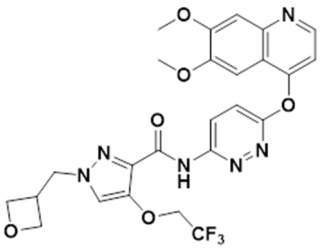
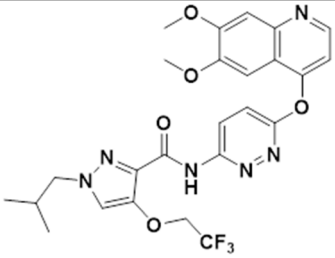
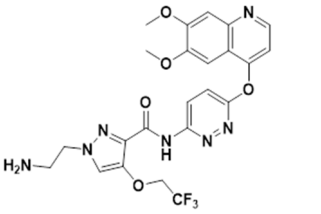
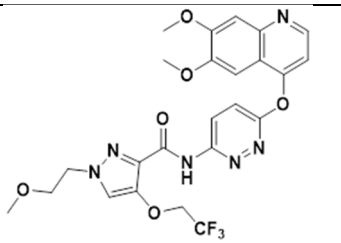
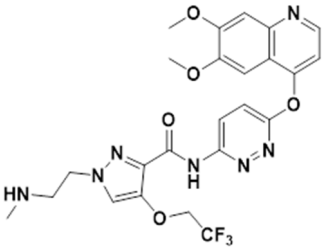
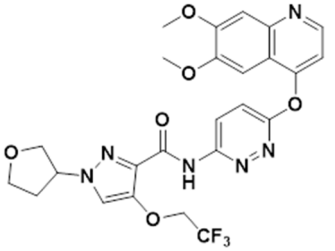
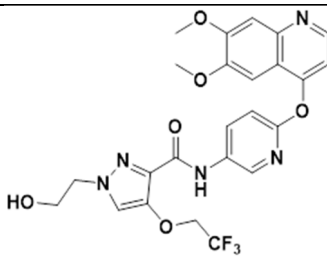
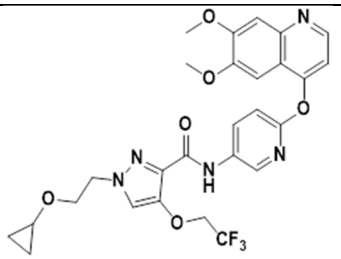
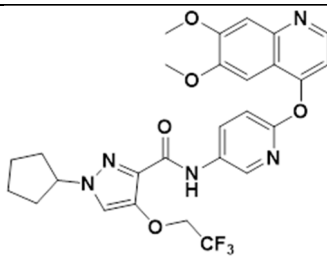
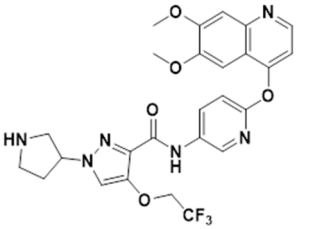
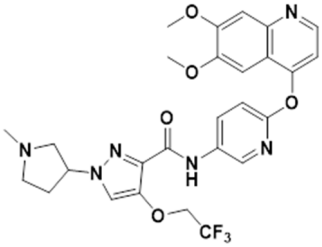
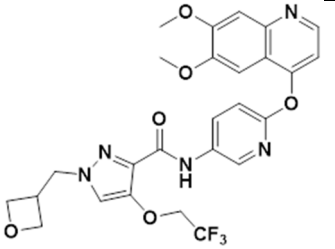
55		56	
57		58	
59		60	
61		62	
63			
65		66	

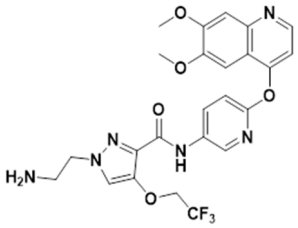
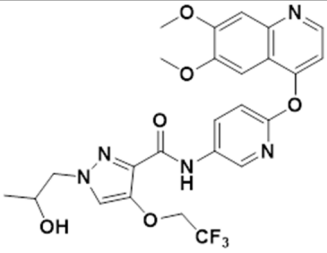
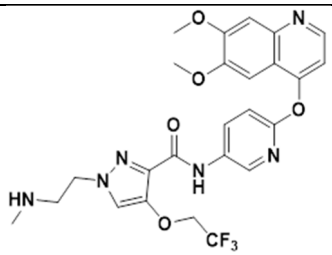
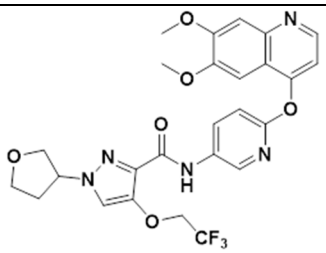
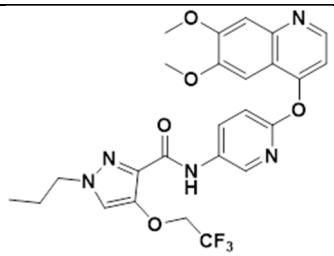
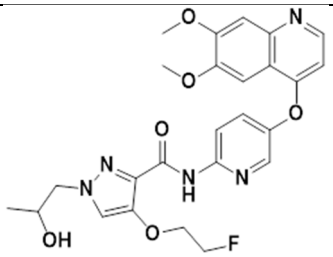
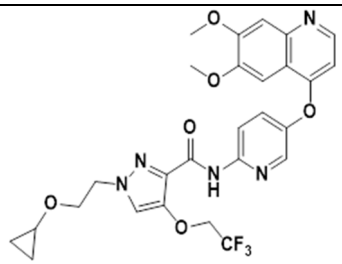
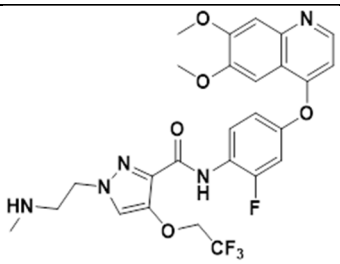
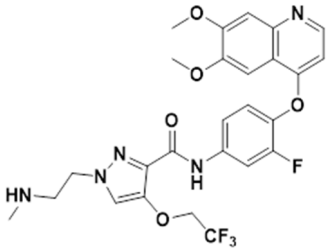
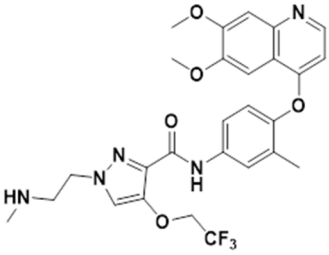
67		68	
69		70	
71		72	
73		74	
75		76	
77		78	
79		80	

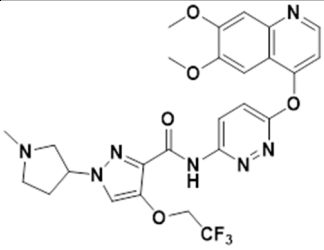
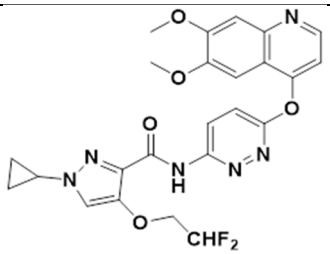
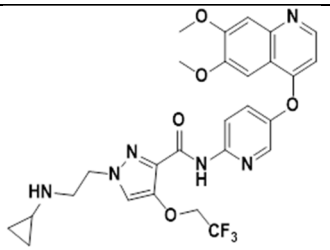
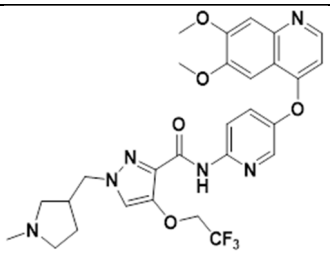
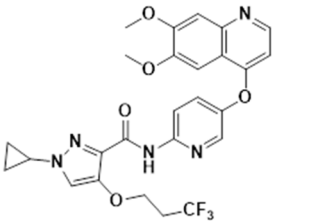
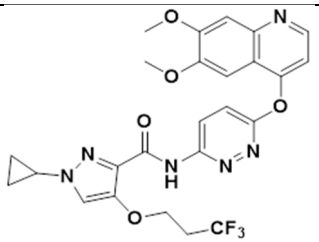
81		82	
83		84	
85		86	
87		88	
89		90	
91		92	
93		94	

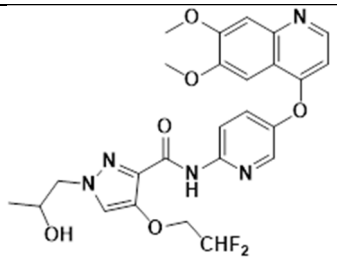
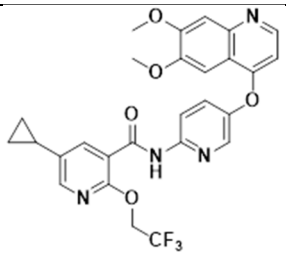
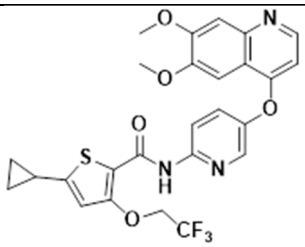
95		96	
97		98	
99		100	
101		102	
103		104	
109		110	

		112	
113		114	
115		116	
117		118	
119		120	
121		122	

123		124	
125		126	
127		128	
129		130	
131		132	
133		134	

135		136	
137		138	
139			
		152	
153		154	
155		156	

157			
		162	
		168	
169		170	
173			

175			
		178	
179			

13. A composition comprising at least one compound according to any of claims 1-12, together with at least one pharmaceutically acceptable carrier, excipient and/or diluent.

14. The composition according to claim 13, further comprising at least one other pharmaceutically active agent.

15. The compound according to any of claims 1-12 or the composition according to any of claims 13-15, for use in therapy.

16. Use of the compound according to any of claims 1-12 or the composition according to any of claims 13 - 14 in the manufacture of a medicament for treating a disorder; wherein said disorder is selected from hyperproliferative disorders, inflammatory disorders and neurodegenerative disorders.

17. The use according to claim 16, wherein the disorder is a disorder associated with, accompanied by, caused by or induced by a Axl/Mer and CSF1R receptor tyrosine kinase, in particular associated with, accompanied by, or caused by Axl/Mer and CSF1R (colony-stimulating factor-1-receptor), preferably associated with, accompanied by, or caused by a hyperfunction of said Axl/Mer and a hyperfunction of said CSF1R.

18. The use according to claim 16, wherein said hyperproliferative disorder is a cancer, preferably a cancer selected from adenocarcinoma, acoustic neuroma, acute lymphoblastic leukemia, acute myeloid leukemia, adrenocortical carcinoma, aids-related cancers, aids-related lymphoma, anal cancer, appendix cancer, astrocytomas, atypical teratoid/rhabdoid tumor, ampullary carcinoma, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer, osteosarcoma and malignant fibrous histiocytoma, brain stem glioma, brain tumor, central nervous system atypical teratoid/rhabdoid tumor, craniopharyngioma, ependymoblastoma, ependymoma, medulloblastoma, medulloepithelioma, pineal parenchymal tumors of intermediate differentiation, supratentorial primitive neuroectodermal tumors and pineoblastoma, brain and spinal cord tumors, breast cancer, urachal tumors, burkitt lymphoma, carcinoid tumor, choroidal melanoma, gastrointestinal cancer, central nervous system lymphoma, cervical cancer, corpus cancer, chordoma, chronic lymphocytic leukemia, chronic myelogenous leukemia, chronic myeloproliferative disorders, colon cancer, colorectal cancer, cutaneous t-cell lymphoma, desmoid tumor, mycosis fungoides, endometrial cancer, esophageal cancer, esthesioneuroblastoma, Ewing sarcoma family of tumors, extracranial germ cell tumor, extragonadal germ cell tumor, extrahepatic bile duct cancer, ear tumors, intraocular melanoma, retinoblastoma, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gastrointestinal stromal cell tumor, gynecologic tumors, ovarian germ cell tumor, gestational trophoblastic tumor, glioma, gallbladder carcinomas, hairy cell leukemia, head and neck cancer, heart cancer, hepatocellular cancer, histiocytosis, hypopharyngeal cancer, hematologic neoplasias, islet cell tumors (endocrine pancreas), renal cell

cancer, kidney cancer, langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lung cancer, non-small cell lung cancer, small intestinal tumors, small cell lung cancer, hodgkin lymphoma, non-hodgkin lymphoma, primary central nervous system lymphoma, macroglobulinemia, malignant fibrous histiocytoma of bone and osteosarcoma, melanoma, merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, spinalioms, multiple endocrine neoplasia syndromes, myelodysplastic syndromes, myelodysplastic/myeloproliferative neoplasms, myeloid leukemia, multiple myeloma, myeloproliferative disorders, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cavity cancer, oropharyngeal cancer, osteosarcoma and malignant fibrous histiocytoma of bone, ovarian cancer, ovarian epithelial cancer, ovarian low malignant potential tumor, oligodendroglioma, plasmacytomas, pancreatic cancer, papillomatosis, parathyroid cancer, penile cancer, pharyngeal cancer, pituitary tumor, plasma cell neoplasm/multiple myeloma, pleuropulmonary blastoma, prostate cancer, rectal cancer, renal cell cancer, transitional cell cancer, respiratory tract cancer, rhabdomyosarcoma, salivary gland cancer, sarcoma, skin testis cancer, ewing sarcoma, kaposi sarcoma, uterine sarcoma, non-melanoma skin cancer, melanoma skin cancer, skin carcinoma, small intestine cancer, soft tissue sarcoma, squamous cell carcinoma, squamous neck cancer, stomach cancer, soft tissue tumors, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, trophoblastic tumor, testicle cancer, gestational cancer, urologic tumors, ureter and renal pelvis cancer, urethral cancer, urothelial carcinoma, uterine cancer, vaginal cancer, vulvar cancer, waldenström macroglobulinemia and wilms tumor, tumors that cause effusions in potential spaces of the body, pleural effusions, pericardial effusions, peritoneal effusion aka ascites, giant cell tumor (GCT), GCT of bone, pigmented villonodular synovitis (PVNS), tenosynovial giant cell tumor (TGCT), TGCT of tendon sheath (TGCT-TS).

19. The use according to claim 16, wherein said inflammatory disorder is selected from osteoarthritis, inflammatory bowel syndrome, tramsplant

rejection, systemic lupus erythematosis, ulcerative colitis, crohn's disease, chronic obstructive pulmonary disease, emphysema, Kawasaki's Disease, hemophagocytic syndrome (macrophage activation syndrome), multicentric reticulohistiocytosis, atherosclerosis, primary progressive multiple sclerosis, tenpsy Type I diabetes, Type Il diabetes, insulin resistance, hyperglycemia, obesity, lipolysis, hypcreosinophilia, osteoporosis, increased risk of fracture, Paget's disease, hypercalcemia, infectionmediated osteolysis (e.g. osteomyelitis), peri-prosthetic or wear-debris-mediated osteolysis, endometriosis, inflammatory pain, chronic pain, and bone pain.

20. The use according to claim 16, wherein said neurodegenerative disorder is selected from Binswanger type dementia, prosencephaly, microcephaly, cerebral palsy, congenital hydrocephalus, abdominal dropsy, progress supranuclear palsy, glaucoma, Wilson disease, Alzheimer's disease and other dementias, Parkinson’s disease (PD) and PD-related disorders, multi infarct dementia, Frontotemporal dementia, pseudo-dementia, Prion disease, Motor neuron diseases, Huntington's disease, spinocerebellar ataxia, and spinal muscular atrophy.

21. The use according to any of claims 16-20, wherein said use is in combination with another pharmaceutically active drug or therapy, in particular radiation therapy, chemotherapy agents, targeted drugs and immune check point inhibitor drugs.