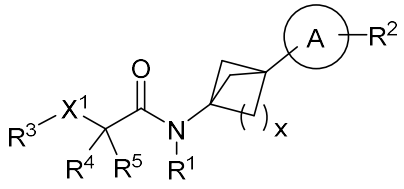
What is claimed is:

1. A compound of Formula II:



II

or a pharmaceutically acceptable salt, isotopically enriched analog, stereoisomer, mixture of stereoisomers or prodrug thereof, wherein:

ring A is heteroaryl or optionally substituted heterocyclyl, provided that when ring A is optionally substituted heterocyclyl and bound to the bridged cycloalkyl via a nitrogen ring atom, a carbon atom on ring A adjacent to the point of attachment is not substituted with =O or =S;

x is 1 or 2;

X^1 is O or a bond;

R^1 is hydrogen, or $C_{2\text{-}12}$ alkynyl;

R^2 is $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, aryl or heteroaryl, each of which, is optionally substituted with one or more R^{11};

R^3 is $C_{1\text{-}12}$ alkyl, $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted with one or more R^{11};

each of R^4 and R^5 is independently hydrogen or $C_{1\text{-}12}$ alkyl, wherein each is independently optionally substituted hydroxyl;

or R^3 and R^4, together with the atoms to which they are attached, join to form a $C_{3\text{-}10}$ cycloalkyl or heterocyclyl, each of which is optionally substituted with one or more R^{11};

each of R^6, R^7 and R^8 is independently hydrogen, $C_{1\text{-}12}$ alkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, aryl, heteroaryl, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-C(O)NR^{20}R^{21}$, $-S(O)_{1\text{-}2}R^{20}$ or
$-S(O)_{1\text{-}2}NR^{20}$, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl and heteroaryl of R^6, R^7 and R^8 is independently optionally substituted with one or more R^{12}; or

two of R^6, R^7 and R^8 are taken together with the atoms to which they are attached to form heterocyclyl independently optionally substituted by one or more halo, oxo, or $C_{1\text{-}12}$ alkyl independently optionally substituted by one or more oxo, halo, hydroxyl or amino;

each R^{11} is independently halo, cyano, nitro, oxo, $-OR^6$, $-SR^6$, $-SF_5$, $-NR^6R^7$, $C_{1\text{-}12}$ alkyl, $C_{2\text{-}12}$ alkenyl, $C_{2\text{-}12}$ alkynyl, $C_{3\text{-}10}$ cycloalkyl, heterocyclyl, aryl, heteroaryl, $-C(O)R^6$, $-C(O)OR^6$, $-OC(O)OR^6$, $-OC(O)R^6$, $-C(O)NR^6R^7$, $-OC(O)NR^6R^7$, $-NR^6C(O)NR^7R^8$, $-S(O)_{1\text{-}2}R^6$, $-S(O)_{1\text{-}2}NR^6$, $-NR^6S(O)_{1\text{-}2}R^7$, $-NR^6S(O)_{1\text{-}2}NR^7R^8$, $-NR^6C(O)R^7$ or $-NR^6C(O)OR^7$, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl of R^{11} is independently optionally substituted with one or more R^{12};

each R^{12} is independently halo, cyano, nitro, oxo, $-OR^{30}$, $-SR^{30}$, $-SF_5$, $-NR^{30}R^{31}$, C_{1-12} alkyl,

C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-C(O)R^{30}$, $-C(O)OR^{30}$, $-OC(O)OR^{30}$, $-OC(O)R^{30}$, $-C(O)NR^{30}R^{31}$, $-OC(O)NR^{30}R^{31}$, $-NR^{30}C(O)NR^{30}R^{31}$, $-S(O)_{1-2}R^{30}$, $-S(O)_{1-2}NR^{30}$, $-NR^{30}S(O)_{1-2}R^{31}$, $-NR^{30}S(O)_{1-2}NR^{30}R^{31}$, $-NR^{30}C(O)R^{31}$, or $-NR^{30}C(=O)OR^{31}$, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl of R^{12} is independently optionally substituted with one or more halo or C_{1-12} alkyl independently optionally substituted by one or more oxo, halo, hydroxyl, or amino;

each R^{20} and R^{21} is independently hydrogen or C_{1-12} alkyl independently optionally substituted with one or more oxo, halo, hydroxyl or amino; or

R^{20} and R^{21} are taken together with the atoms to which they are attached to form heterocyclyl independently optionally substituted by one or more halo or C_{1-12} alkyl independently optionally substituted by one or more oxo, halo, hydroxyl or amino; and

each R^{30} and R^{31} is independently hydrogen or C_{1-12} alkyl independently optionally substituted with one or more oxo, halo, hydroxyl, or amino; or

R^{30} and R^{31} are taken together with the atoms to which they are attached to form heterocyclyl independently optionally substituted by one or more halo or C_{1-12} alkyl independently optionally substituted by one or more oxo, halo, hydroxyl, or amino.

2. The compound of claim 1, wherein X^1 is O.

3. The compound of any one of the preceding claims, wherein x is 1.

4. The compound of any one of the preceding claims, wherein L or ring A is an optionally substituted heteroaryl ring.

5. The compound of any one of the preceding claims, wherein ring A is a five membered C_{2-4} heteroaryl ring.

6. The compound of any one of the preceding claims, wherein ring A is a five membered C_{2-4} heteroaryl ring having 1 to 3 nitrogen ring atoms and optionally 1 or 2 oxygen and/or sulfur atoms.

7. The compound of any one of the preceding claims, wherein ring A is a triazole, oxazole, imidazole, oxadiazole, benzoxazole, pyrazole, triazole, thiadiazole, tetrazole, or isoxazole.

8. The compound of any one of claims 1-3, wherein ring A is an optionally substituted heterocyclyl ring.

9. The compound of any one of claims 1-3, wherein ring A is an optionally substituted five membered C_{2-4} heterocyclyl.

10. The compound of any one of claims 1-3, wherein ring A is an optionally substituted five membered C_{2-4} heterocyclyl ring having 1 to 3 nitrogen ring atoms and optionally 1 or 2 oxygen and/or sulfur atoms.

11. The compound of any one of claims 1-3, wherein ring A is an optionally substituted pyrrolidine, imidazolidine, dihydropyrrole, oxathiazolidine, dihydroisoxazole or oxazolidine.

12. The compound of any one of claims 2-11, wherein ring A is a heterocyclyl, ring A can be further substituted with one to five R^{13} where each R^{13} is independently selected from halo, cyano, oxo, thioxo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy.

13. A compound of any one of claims 2-11, wherein ring A is not further substituted and R^2 is C_{3-10} cycloalkyl optionally substituted with one or more R^{11}.

14. The compound of any one of the preceding claims wherein R^2 is C_{3-10} cycloalkyl, heterocyclyl, or aryl, each of which is optionally substituted with one to six R^{11}.

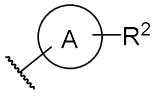
15. The compound of any one of the preceding claims wherein R^2 is C_{3-10} cycloalkyl optionally substituted with one or more R^{11}.

16. The compound of any one of the preceding claims wherein R^2 is cyclopropyl, cyclobutyl, cyclopentyl, phenyl, azetidinyl, pyrrolidinyl, or tetrahydrofuranyl, each of which is optionally substituted with one to six R^{11}.

17. The compound of claim 16, wherein R^2 is substituted with at least one R^{11}.

18. The compound of any one of the preceding claims wherein R^{11} is hydroxyl, halo(C_{1-6} alkoxy), halo, cycloalkyl, cycloalkoxy, phenyl, C_{1-6} alkoxycarbonyl, cyano, halo(C_{1-6} alkyl), halo(C_{1-6} alkoxy)cycloalkoxy, halo(C_{1-6} alkoxy)alkyl, halo(heterocyclyl) or halophenoxy.

19. The compound of claim 1, wherein R^2 is is 1-fluorocyclopropyl, 2-methylcyclopropyl, 2,2-difluorocyclopropyl, 3-(difluoromethoxy)cyclobutyl, 3-(trifluoromethoxy)cyclobutyl, 3-(trifluoromethyl)cyclobutyl, 3-cyanocyclobutyl, 4-chloro-3-fluoro-phenyl, 4-chlorophenyl, 2-cyanocyclobutyl, cyclobutyl, cyclopentyl, cyclopropyl, hydroxycyclobutyl, N-tert-butoxy(carbonyl)azetidin-3-yl, N-tert-butoxy(carbonyl)pyrrolidin-3-yl, tetrahydrofuranyl, (trifluoromethoxy)cyclobutoxy, 3-(1,1-difluoroethyl)cyclobutyl, 3-(1,1,1-trifluoroethyl)azetidinyl, 3-(triazol-2-yl)cyclobutyl, 3-(trifluoromethylthio)cyclobutyl, or 3-(cyclopropyl)cyclobutyl.

20. The compound of claim 1 wherein the moiety 

is 1-(3-cyanocyclobutyl)triazol-4-yl, 1-(3-hydroxycyclobutyl)triazol-4-yl, 1-(4-chlorophenyl)triazol-4-yl, 1-cyclobutyltriazol-4-yl, 2-(3-cyanocyclobutyl)triazol-4-yl, 2-cyclobutyltriazol-4-yl, 3-[(trifluoromethoxy)cyclobutoxy]-imidazol-1-yl, 3-cyanocyclobutyl)triazol-4-yl, 3-cyclobutylisoxazol-5-yl, 4-[3-(trifluoromethoxy)cyclobutyl]imidazol-1-yl, 4-cyclobutylimidazol-1-yl, 4-cyclobutyloxazol-2-yl, 5-(1-fluorocyclopropyl)-1,3,4-oxadiazol-2-yl, 5-(2,2-difluorocyclopropyl)-1,3,4-oxadiazol-2-yl, 5-(3-cyanocyclobutyl)-1,3,4-oxadiazol-2-yl, 5-(4-chloro-3-fluoro-phenyl)-1,3,4-oxadiazol-2-yl, 5-[2-methylcyclopropyl]-1,3,4-oxadiazol-2-yl, 5-[3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl, 5-[3-(trifluoromethyl)cyclobutyl]-1,3,4-oxadiazol-2-yl, 5-[N-(1,1,1-trifluoroethyl)azetidin-3-yl]-1,3,4-oxadiazol-2-yl, 5-[N-(1,1,1-trifluoroethyl)pyrrolidin-3-yl]-1,3,4-

oxadiazol-2-yl, 5-[N-tert-butoxy(carbonyl)azetidin-3-yl]-1,3,4-oxadiazol-2-yl, 5-[N-tert-butoxy(carbonyl)pyrrolidin-3-yl]-1,3,4-oxadiazol-2-yl, 5-cyclobutyl-1,3,4-oxadiazol-2-yl, 5-cyclobutyl-4,5-dihydroisoxazol-3-yl, 5-cyclobutylisoxazol-3-yl, 5-cyclobutyloxazol-2-yl, or 5-cyclopentyl-4,5-dihydroisoxazol-3-yl.

21. The compound of any one of the preceding claims, wherein R^3 is C_{1-12} alkyl, which is optionally substituted with one or more R^{11}.

22. The compound of any one of the preceding claims, wherein R^3 is C_{3-10} cycloalkyl, heterocyclyl, aryl or heteroaryl, each of which is optionally substituted with one or more R^{11}.

23. The compound of any one of the preceding claims, wherein R^3 is C_{3-10} cycloalkyl, aryl, or heteroaryl, each of which is optionally substituted with one or more R^{11}.

24. The compound of any one of the preceding claims, wherein R^3 is cyclobutyl, triazolyl or phenyl, each of which is optionally substituted with one or more R^{11}.

25. The compound of any one of the preceding claims, wherein R^3 isphenyl which is optionally substituted with one or more R^{11}.

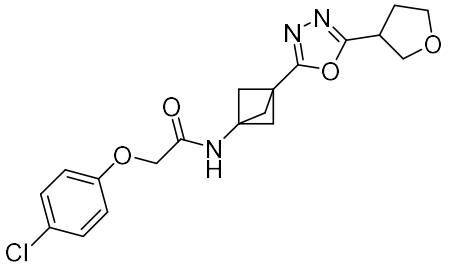
26. The compound of claim 25, wherein R^3 is phenyl optionally substituted with one or more substituents independently selected from halo, cyano, C_{1-12} alkyl optionally substituted with one or more halo, and C_{1-12} alkoxy optionally substituted with one or more halo.

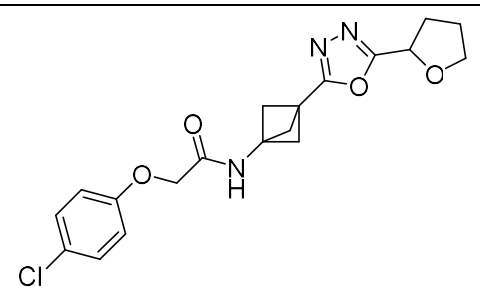
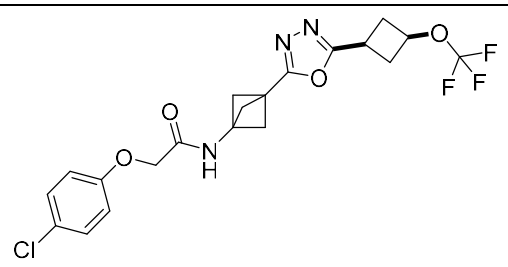
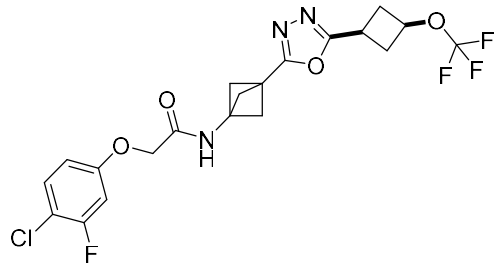
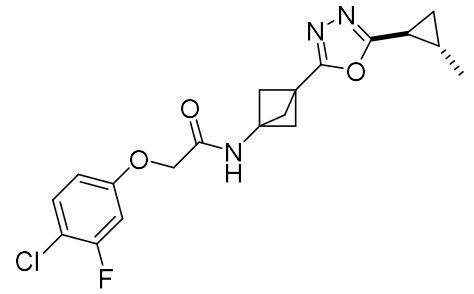
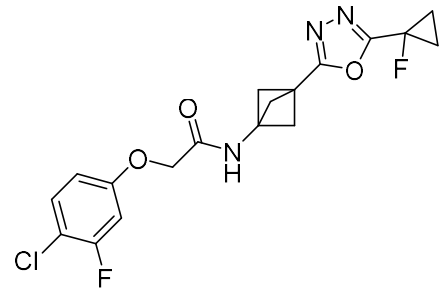
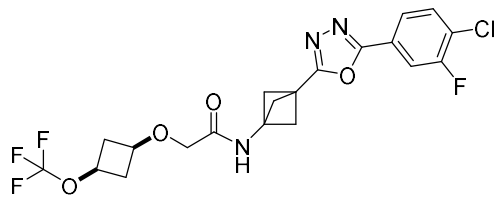
27. The compound of any one of the preceding claims, wherein R^3 is phenyl substituted with chloro, fluoro or a combination thereof.

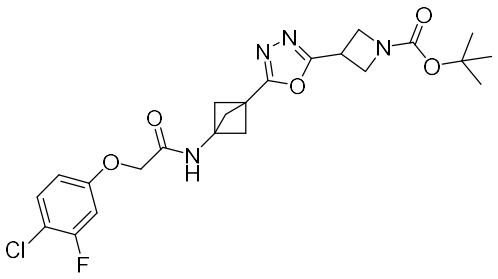
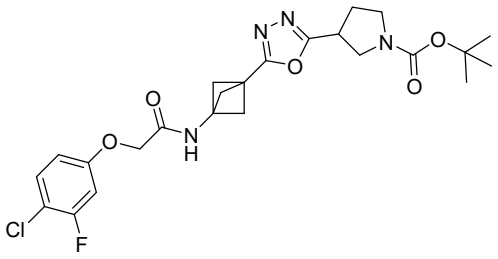
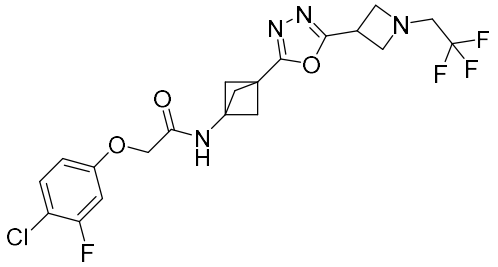
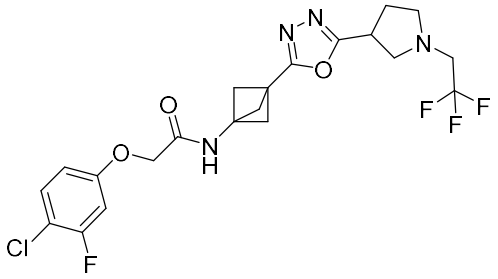
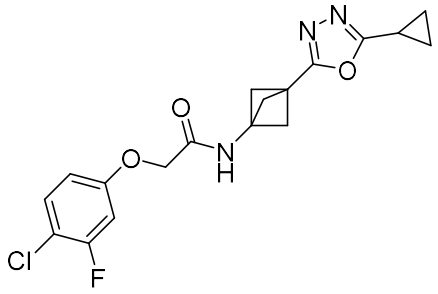
28. The compound of any one of the preceding claims, wherein R^3 4-chlorophenyl, 4-chloro-3-fluorophenyl or trifluoromethoxycyclobut-2-yl.

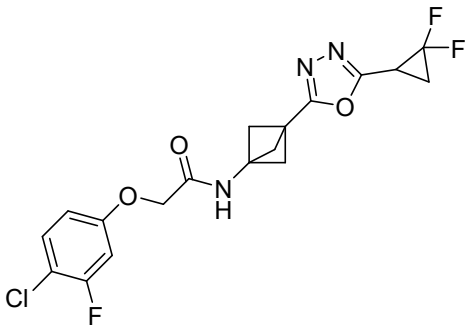
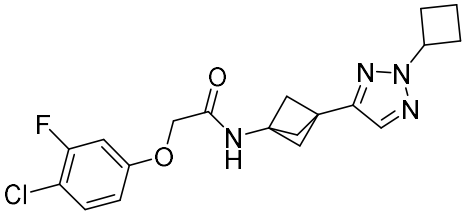
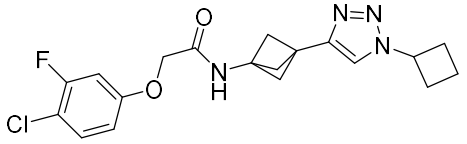
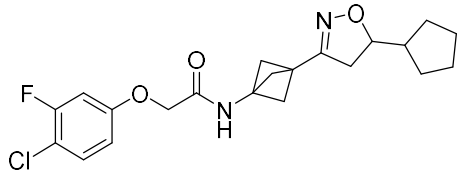
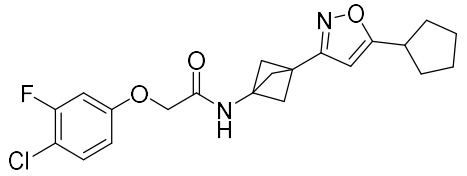
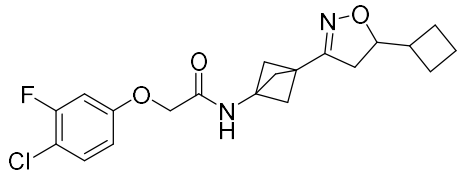
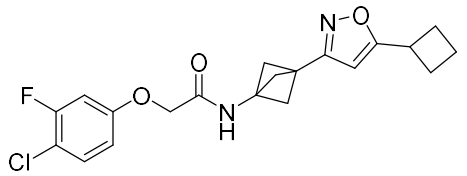
29. The compound of any one of the preceding claims, wherein R^1 is H.

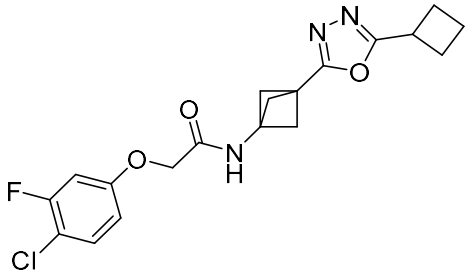
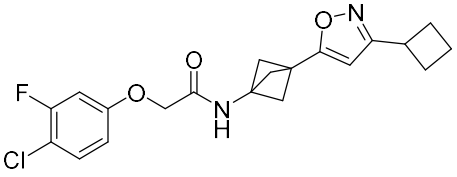
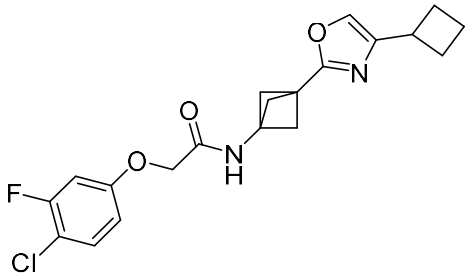
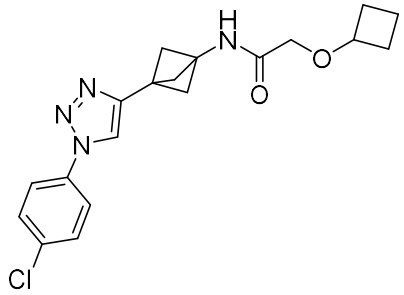
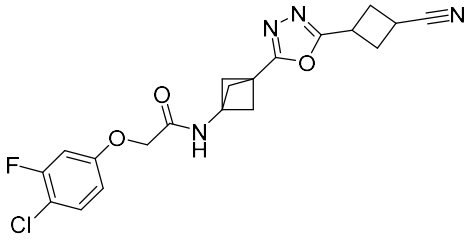
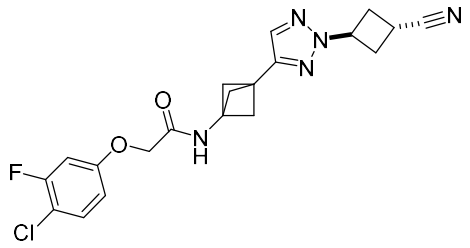
30. A compound or a pharmaceutically acceptable salt, isotopically enriched analog, stereoisomer, mixture of stereoisomers or prodrug thereof selected from :

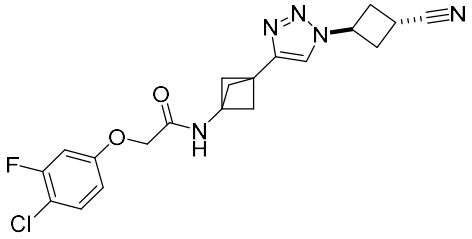
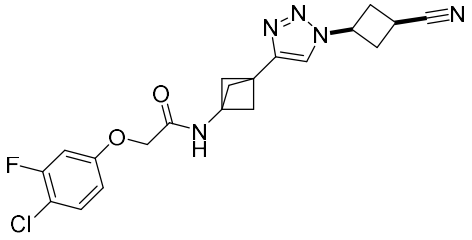
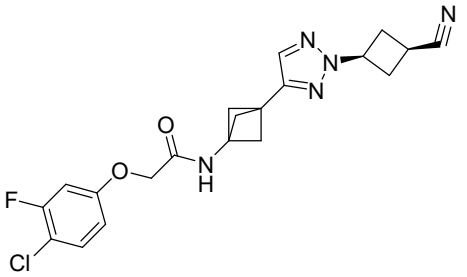
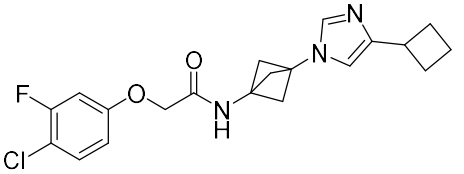
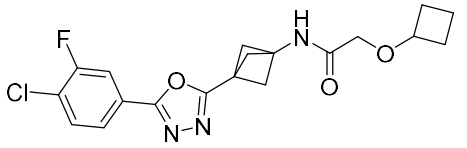
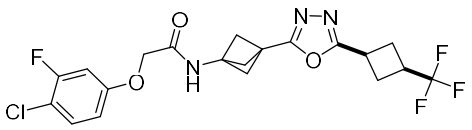
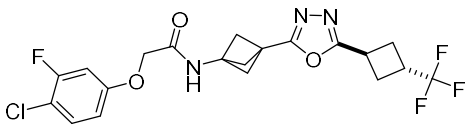
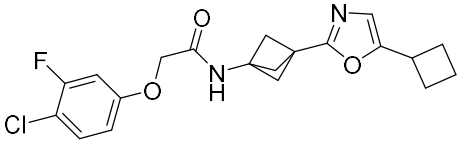
Ex.	Compound
1	

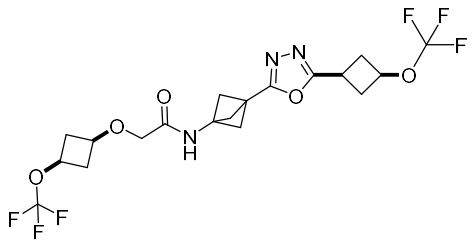
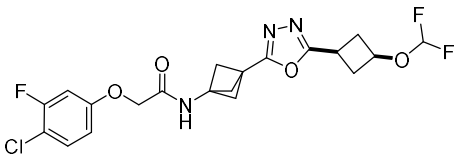
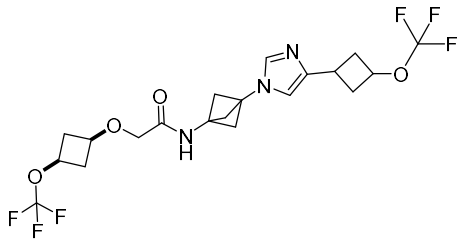
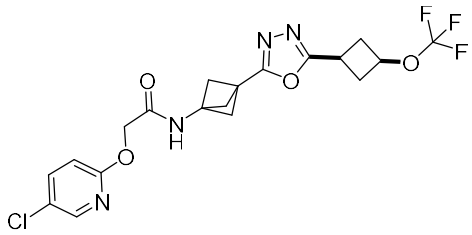
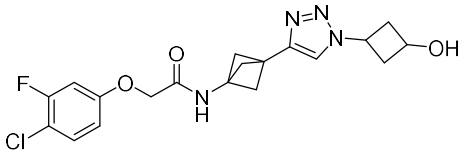
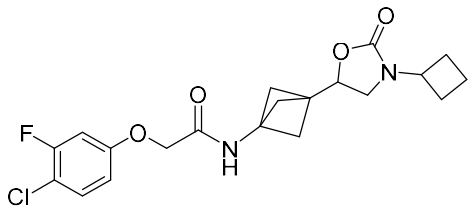
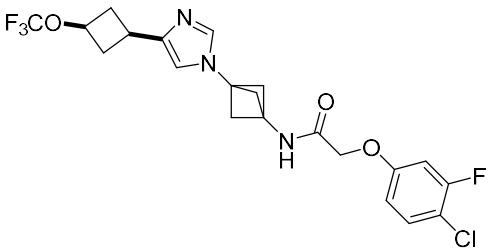
Ex.	Compound
2	
3	
6	
9	
10	
12	

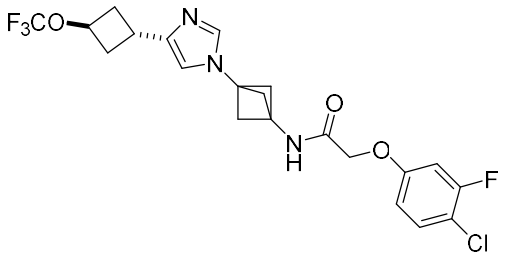
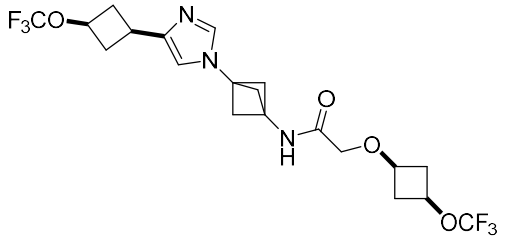
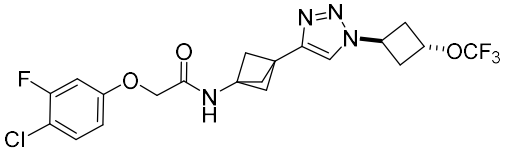
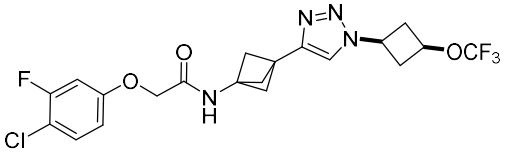
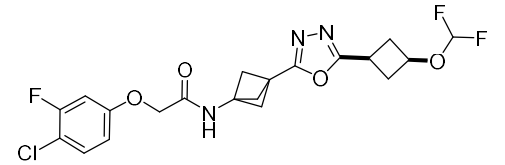
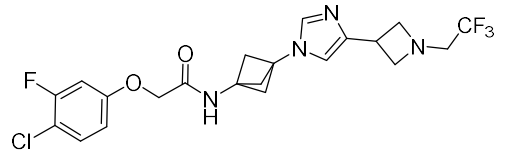
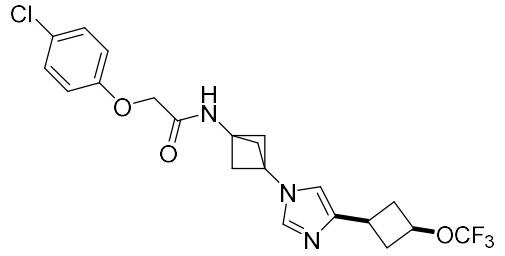
Ex.	Compound
13	
14	
15	
16	
17	

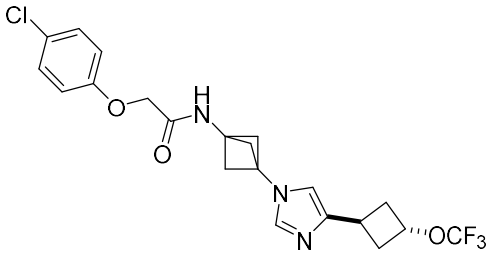
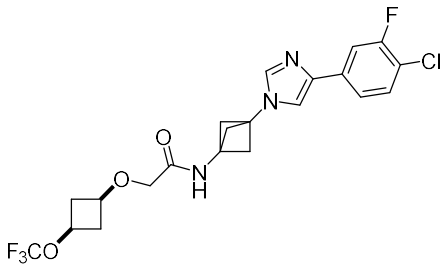
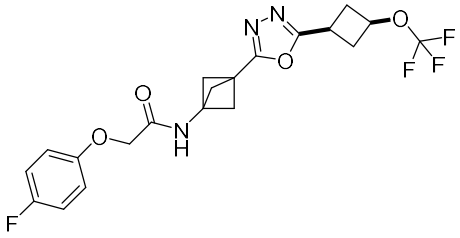
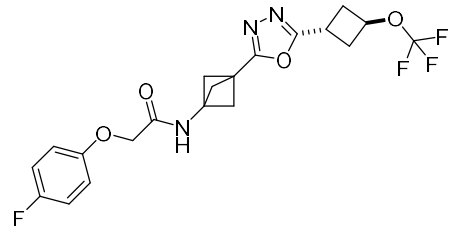
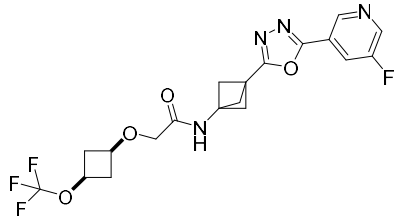
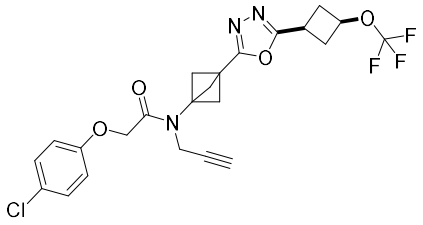
Ex.	Compound
18	
19	
20	
21	
22	
23	
24	

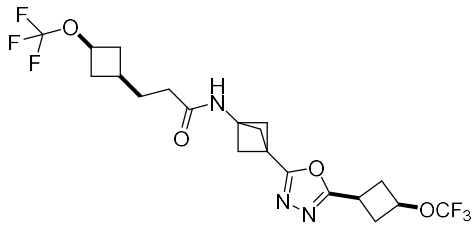
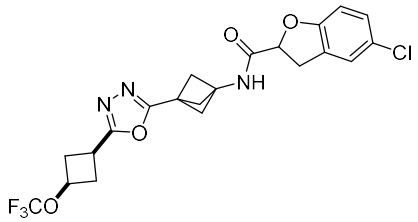
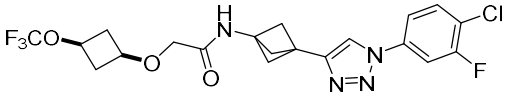
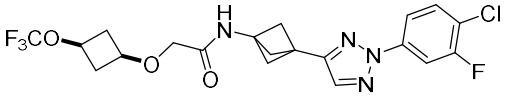
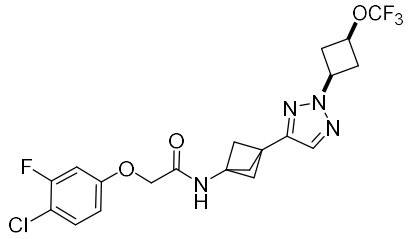
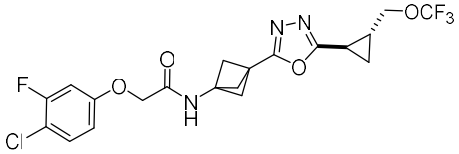
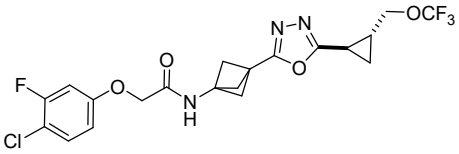
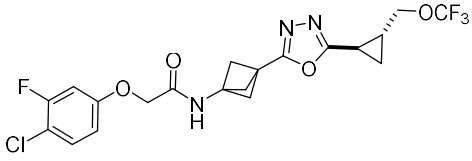
Ex.	Compound
25	
26	
27	
28	
29	
33	

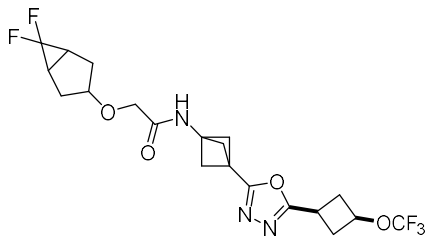
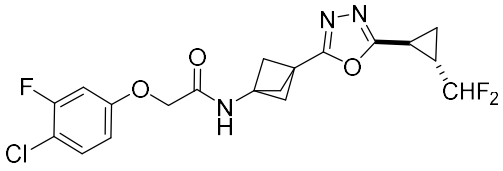
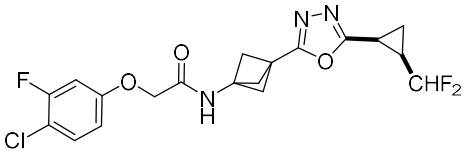
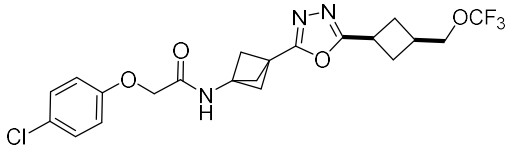
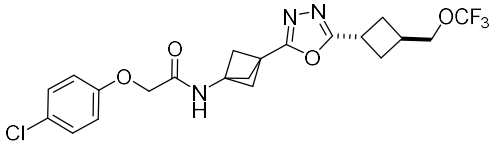
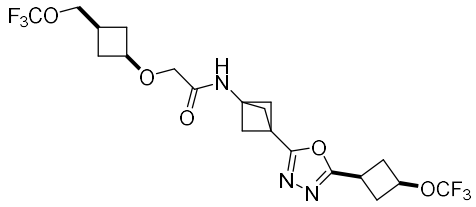
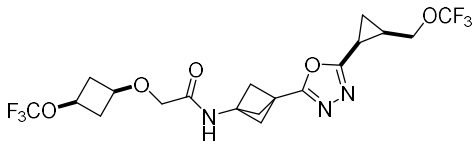
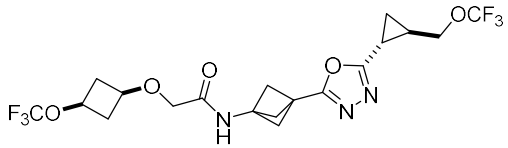
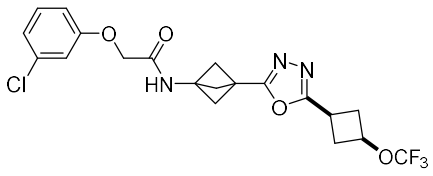
Ex.	Compound
34	
35	
36	
39	
42	
43	
44	
47	

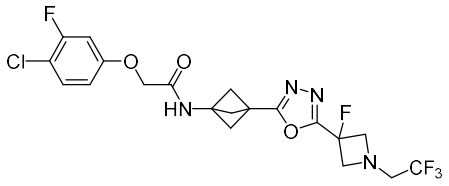
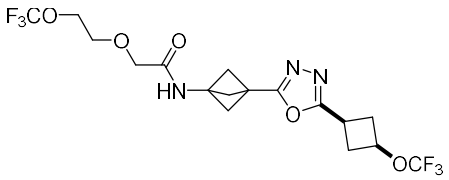
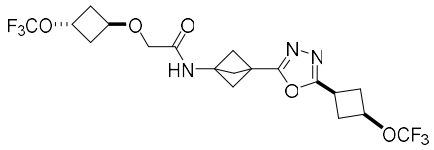
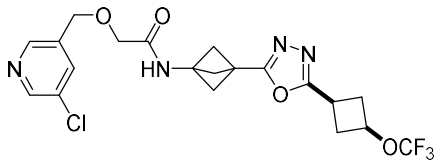
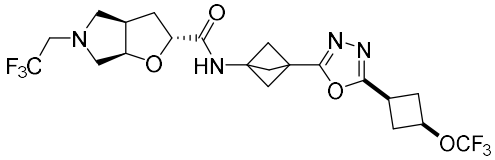
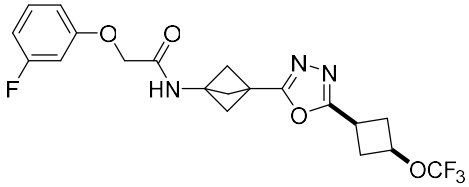
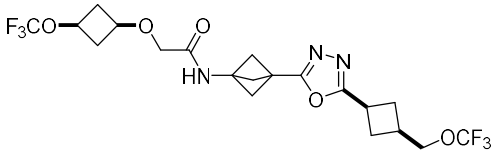
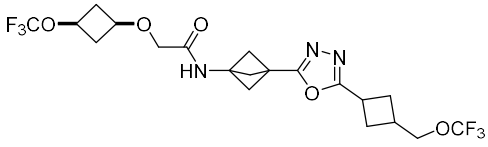
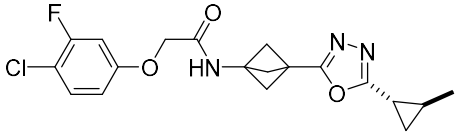
Ex.	Compound
50	
51	
52	
56	
57	
59	
61	

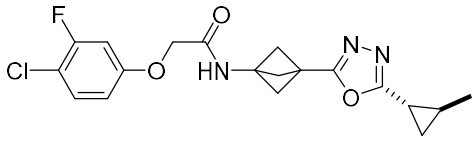
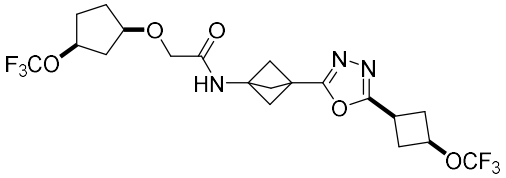
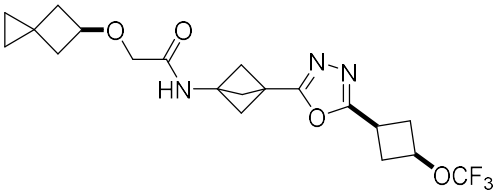
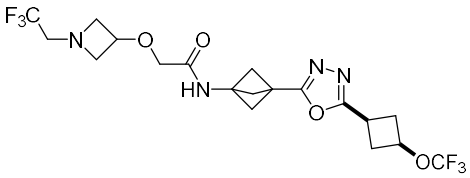
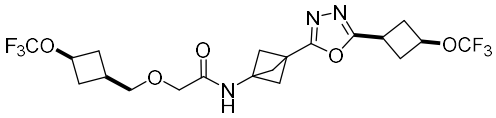
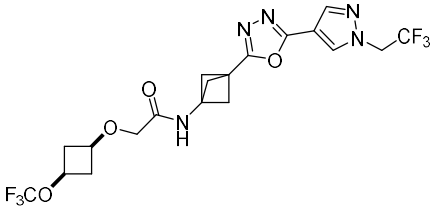
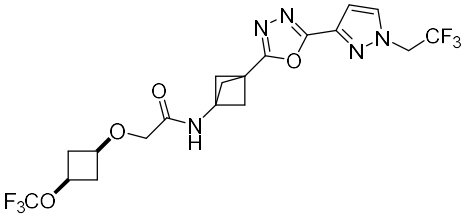
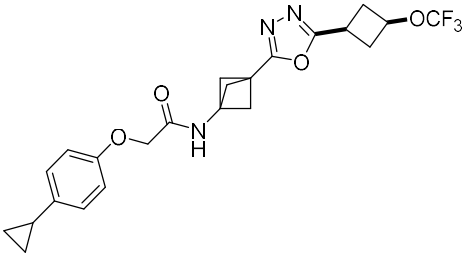
Ex.	Compound
62	
63	
64	
65	
66	
67	
68	

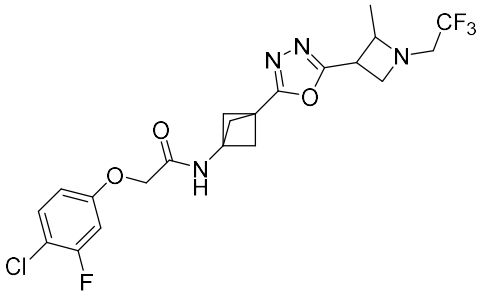
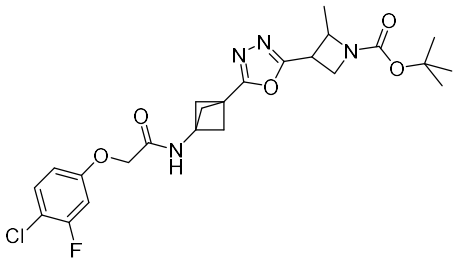
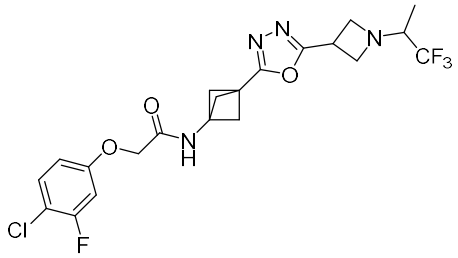
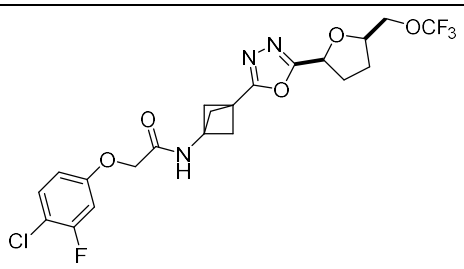
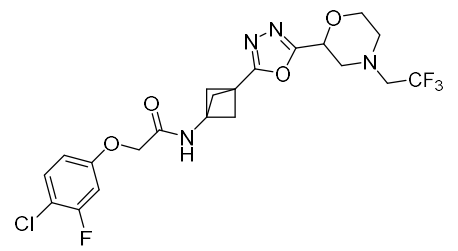
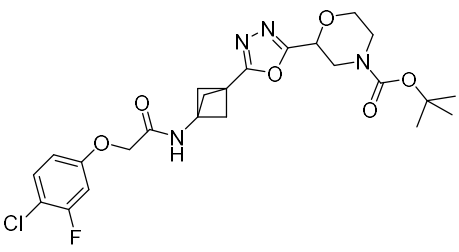
Ex.	Compound
69	
70	
71	
72	
73	
74	

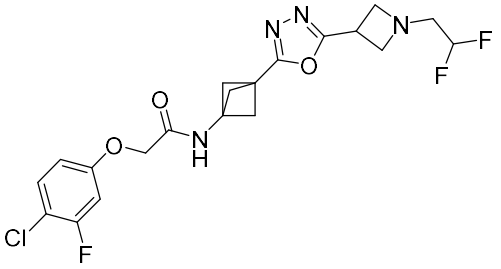
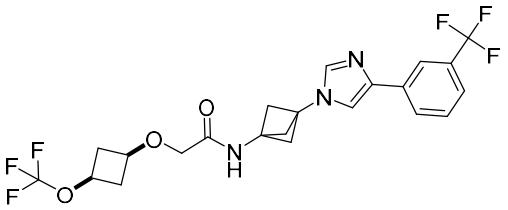
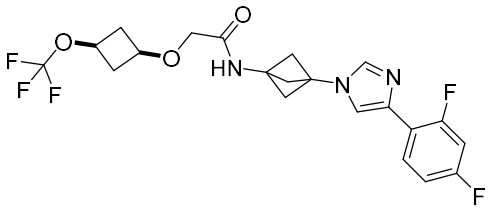
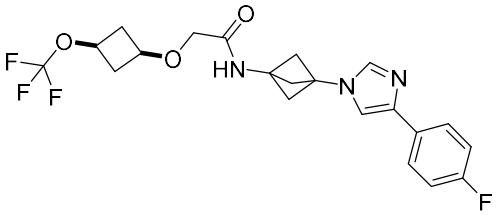
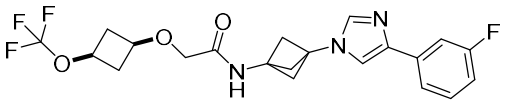
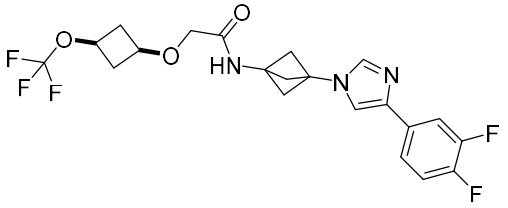
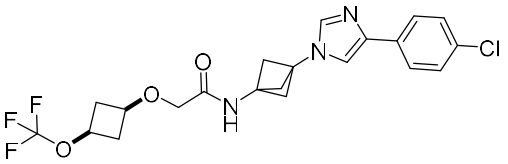
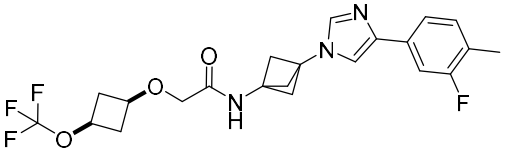
Ex.	Compound
75	
76	
77	
78	
79	
80	
81	
82	

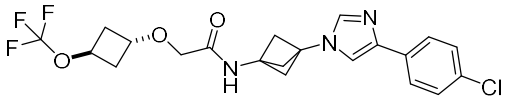
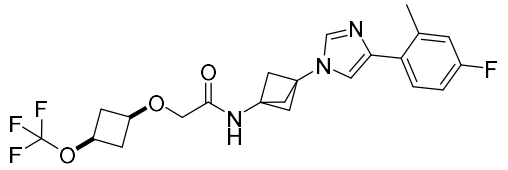
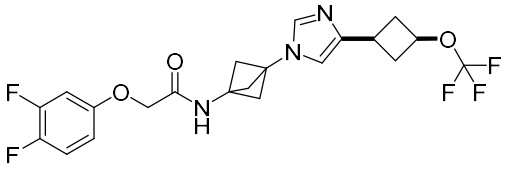
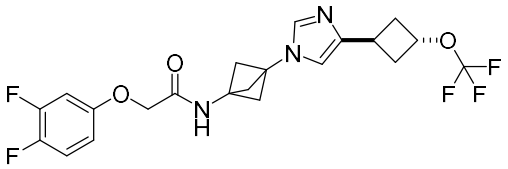
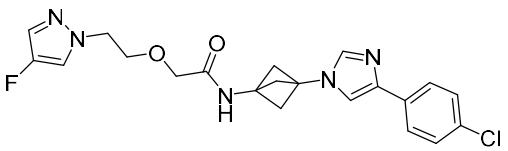
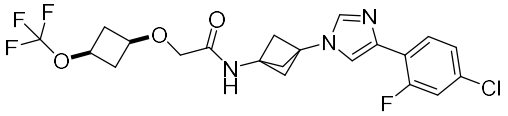
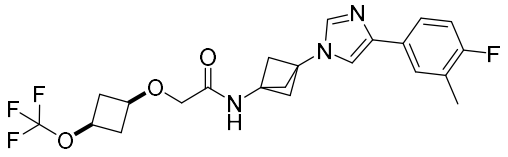
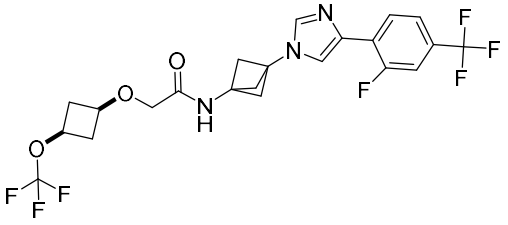
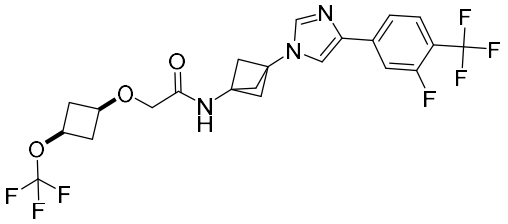
Ex.	Compound
83	
84	
85	
86	
87	
89	
90	
91	
92	

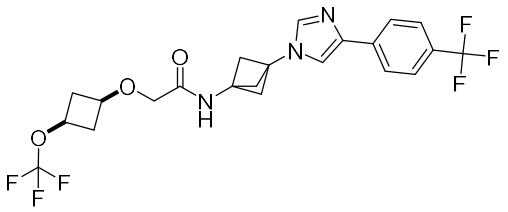
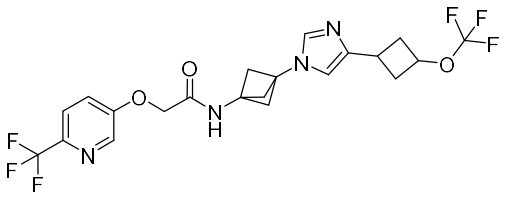
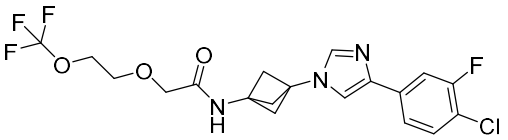
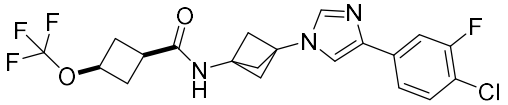
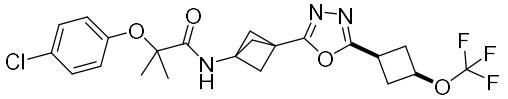
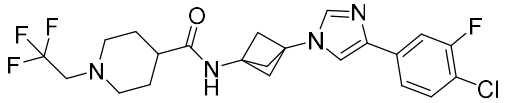
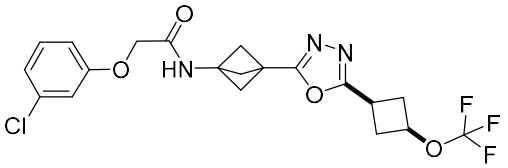
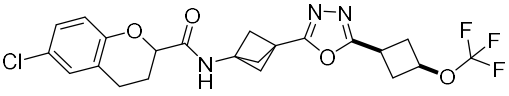
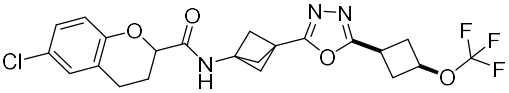
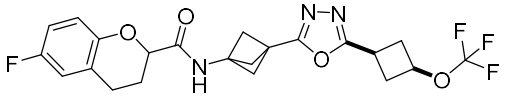
Ex.	Compound
93	
94	
95	
97	
102	
105	
106	
107	
112	 (first eluting enantiomer)

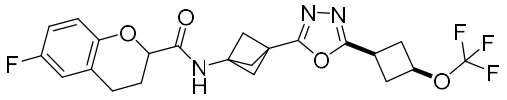
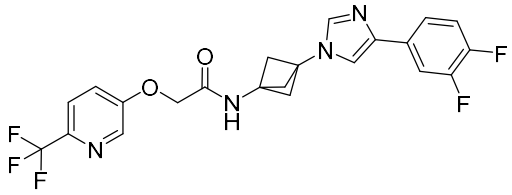
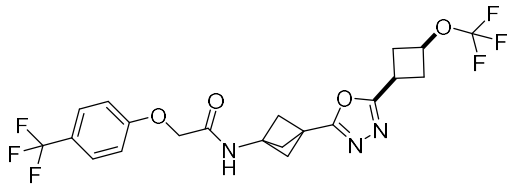
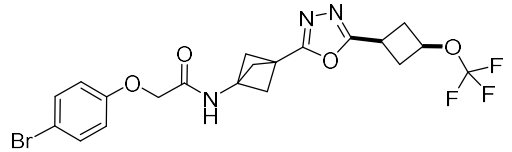
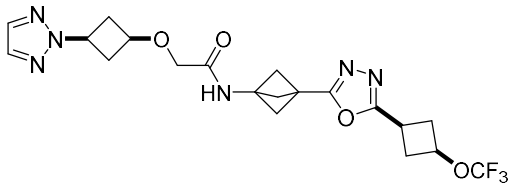
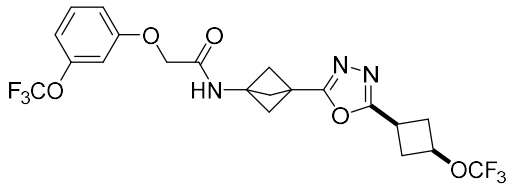
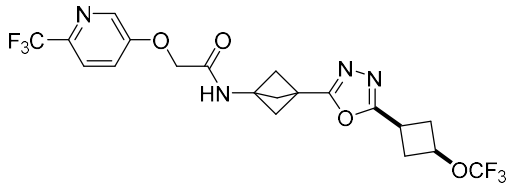
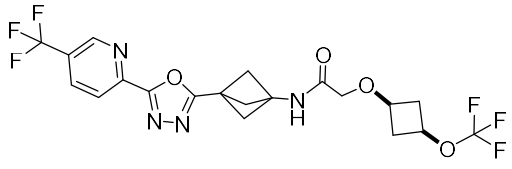
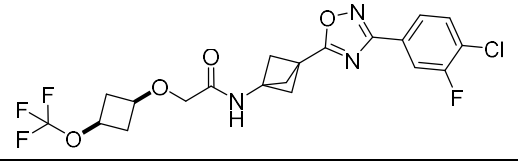
Ex.	Compound
113	 (second eluting enantiomer)
114	
115	
116	
117	
118	
119	
120	

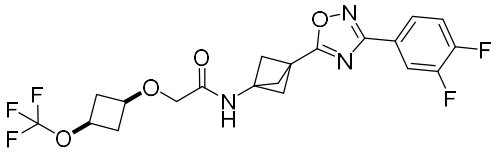
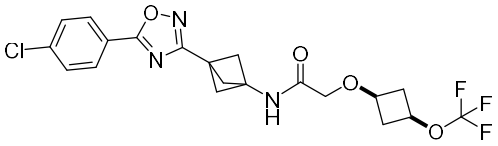
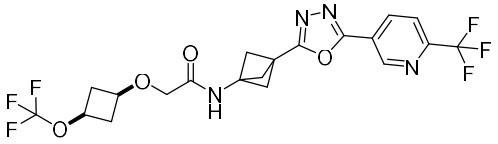
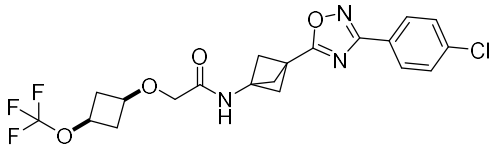
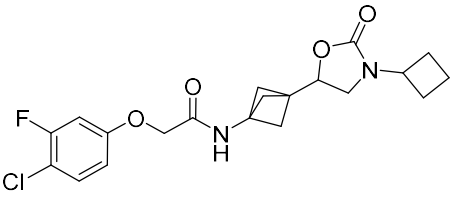
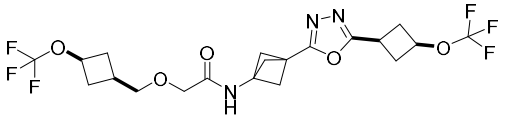
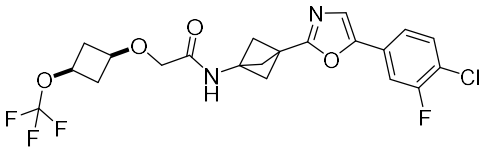
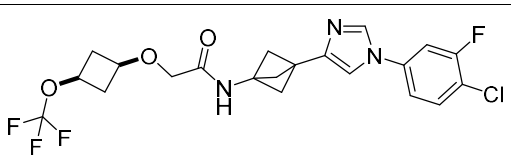
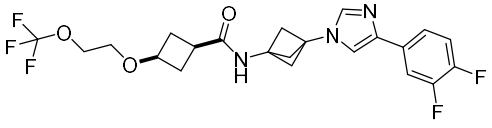
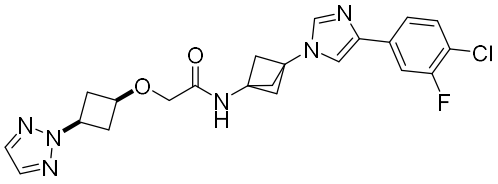
Ex.	Compound
121	
122	
123	
124	
127	
128	

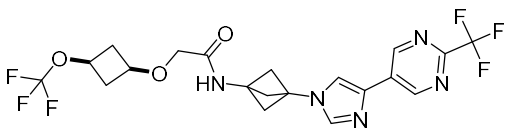
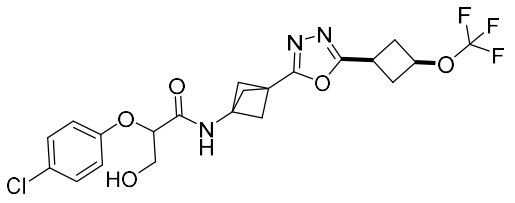
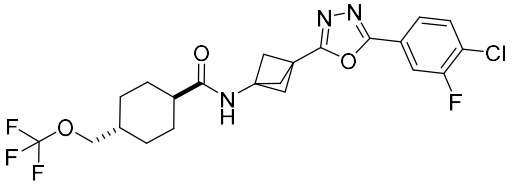
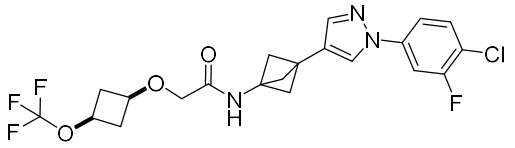
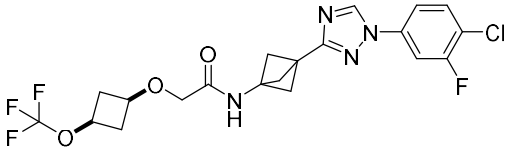
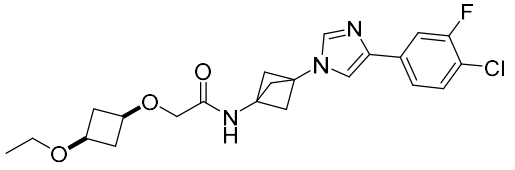
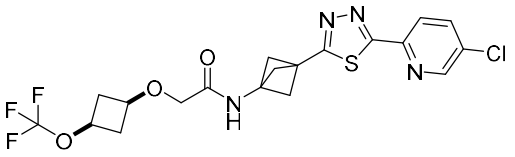
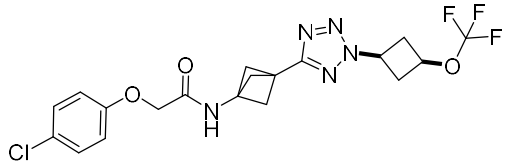
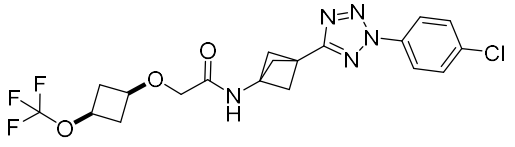
Ex.	Compound
130	
134	
135	
136	
137	
138	
139	
140	

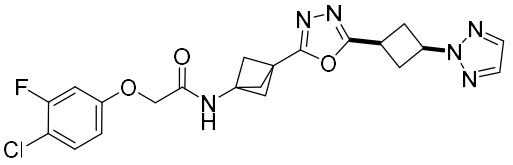
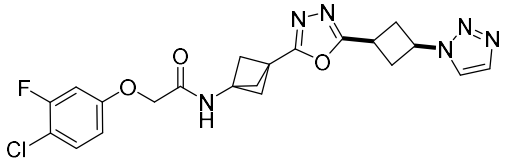
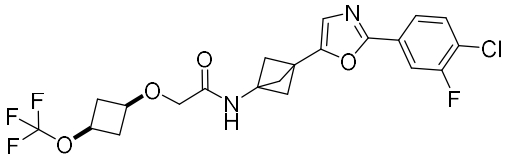
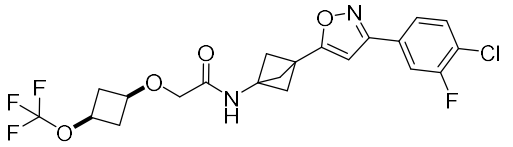
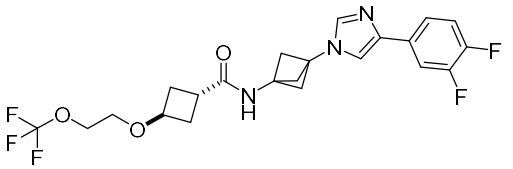
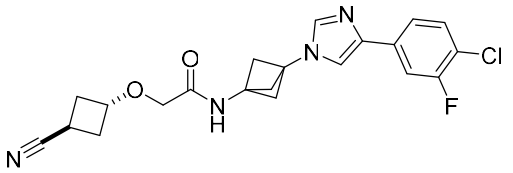
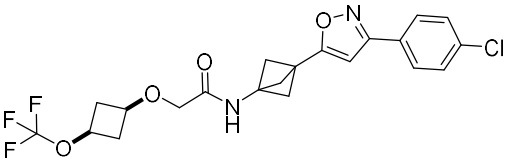
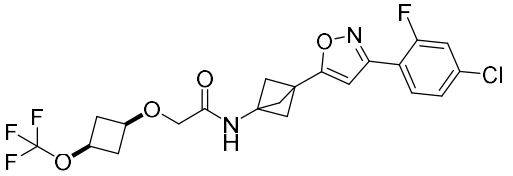
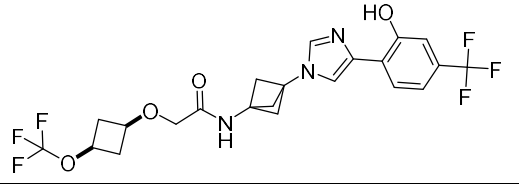
Ex.	Compound
141	
142	
143	
144	
145	
146	
147	
148	
149	

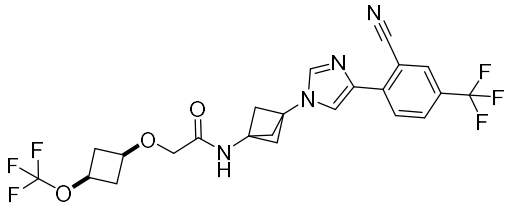
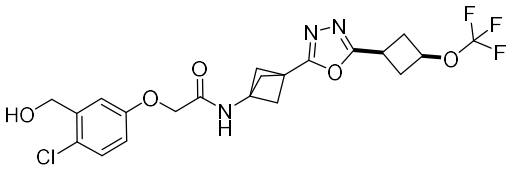
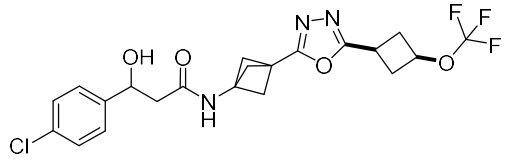
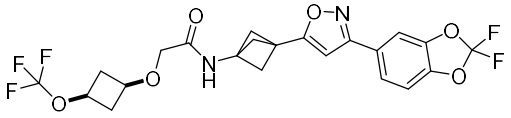
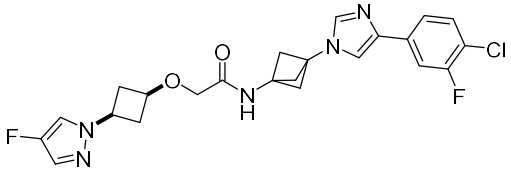
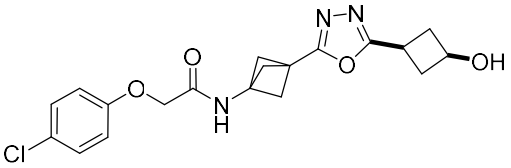
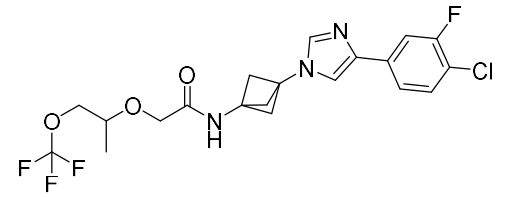
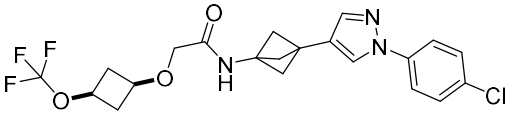
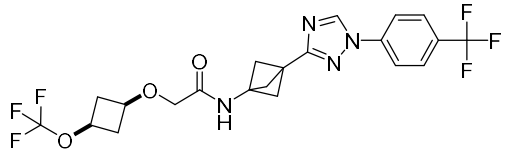
Ex.	Compound
150	
151	
152	
153	
154	
155	
156	
157	 first eluting enantiomer
158	 second eluting enantiomer
159	 first eluting enantiomer

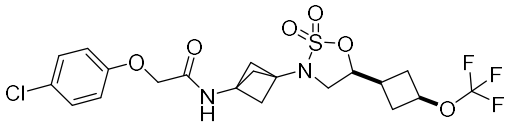
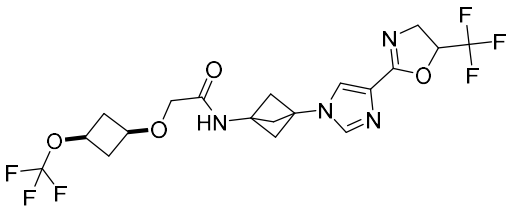
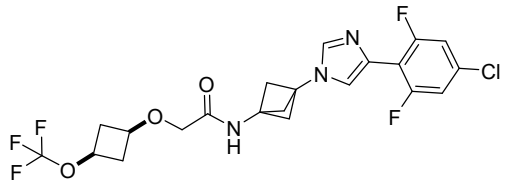
Ex.	Compound
160	 Second eluting enantiomer
161	
162	
163	
172	
173	
174	
199	
201	

Ex.	Compound
202	
203	
204	
205	
219	
226	
227	
228	
229	
230	

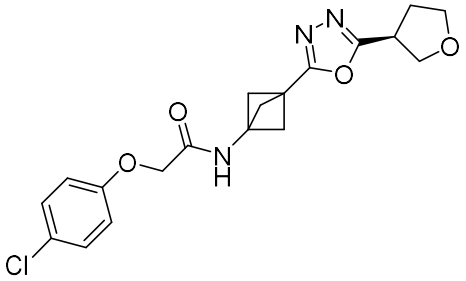
Ex.	Compound
231	
232	
235	
236	
239	
240	
241	
242	
243	

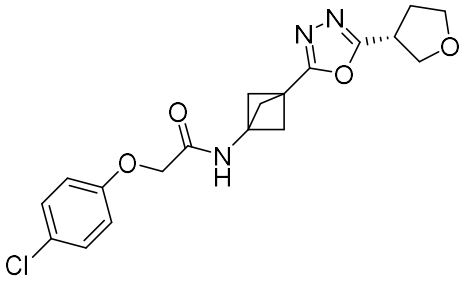
Ex.	Compound
244	
245	
247	
248	
249	
250	
251	
252	
254	

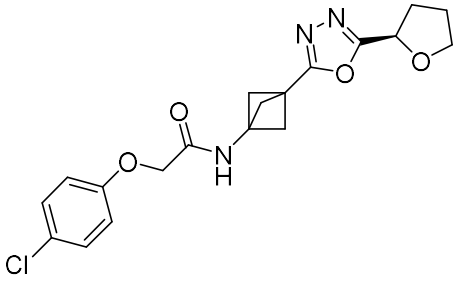
Ex.	Compound
255	
256	
257	
258	
259	
261	
262	
263	
265	

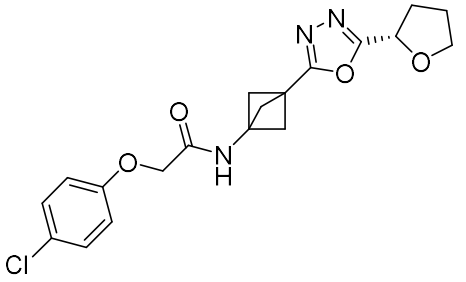
Ex.	Compound
266	
267	
269	

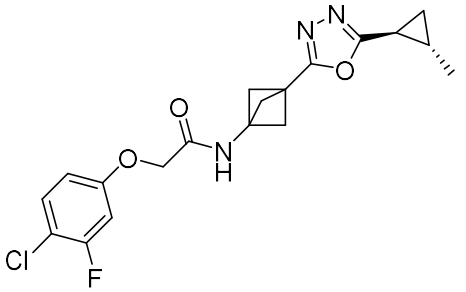
31. A compound or a pharmaceutically acceptable salt, isotopically enriched analog, stereoisomer, mixture of stereoisomers or prodrug thereof selected from :

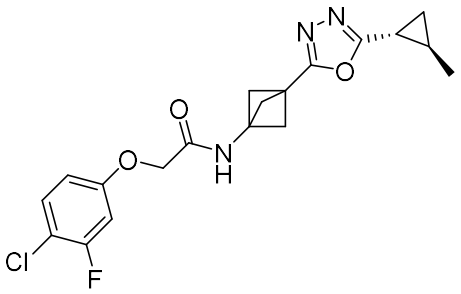


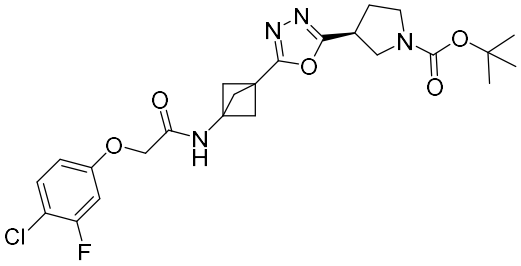


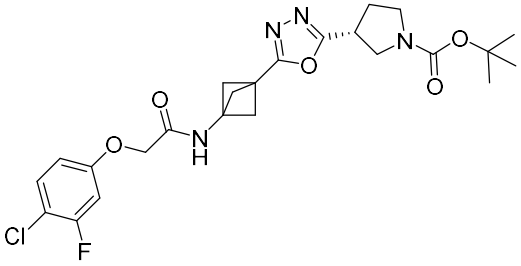


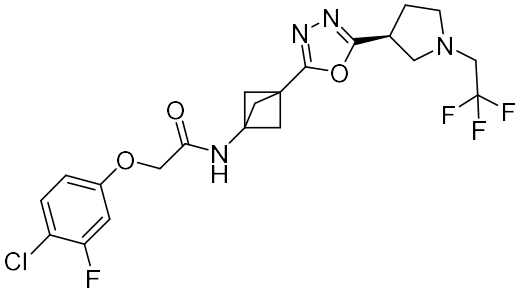


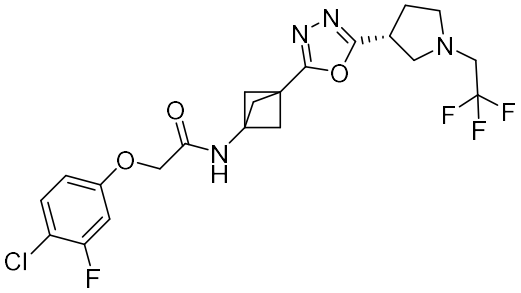


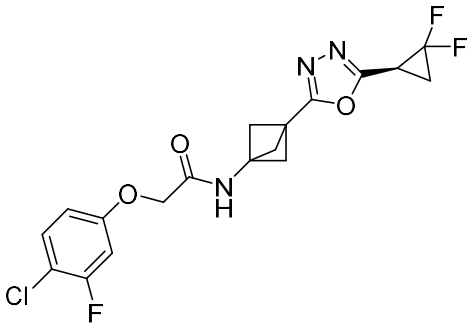


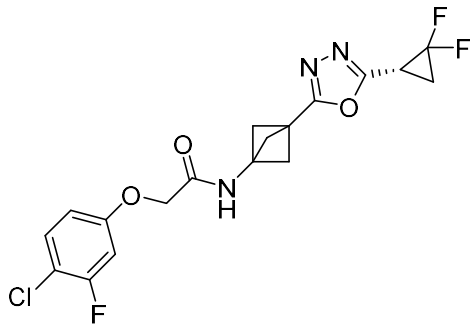


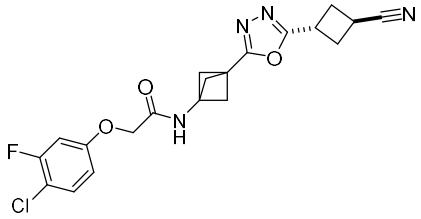


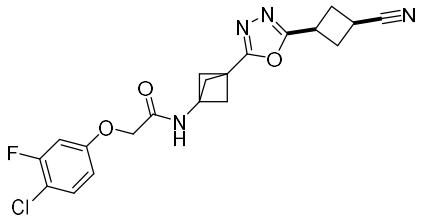


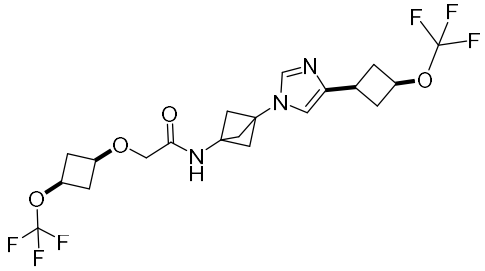


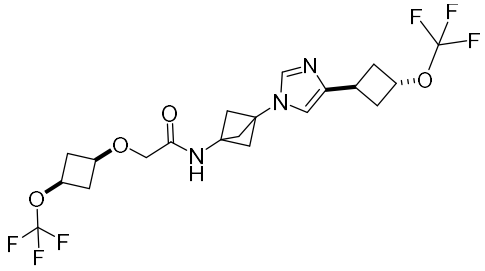


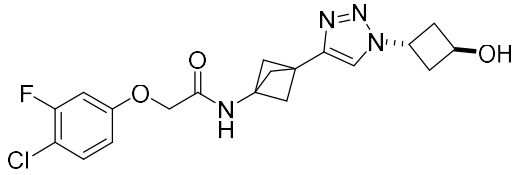


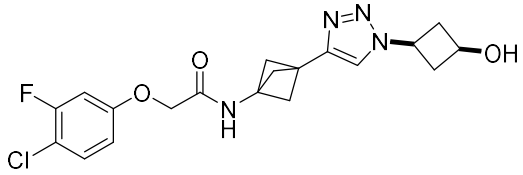


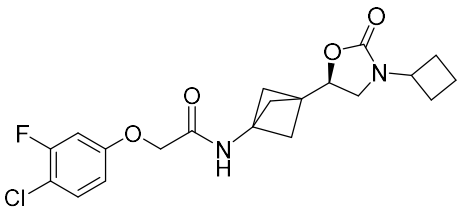


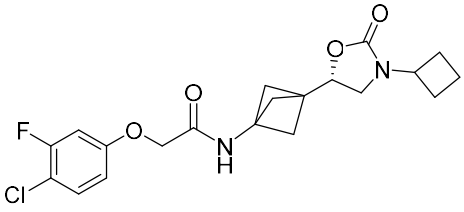


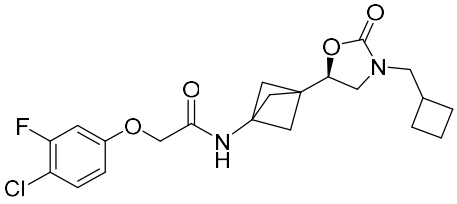


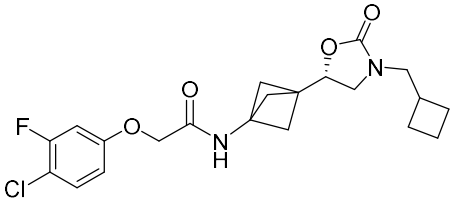


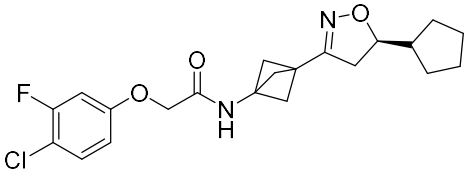


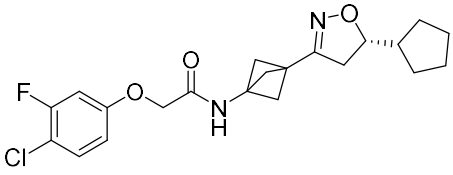


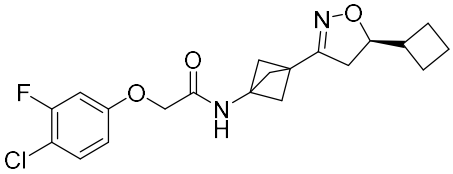


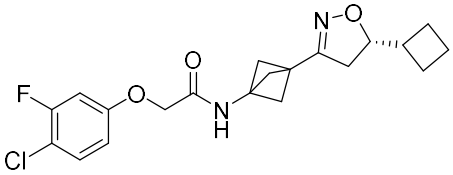


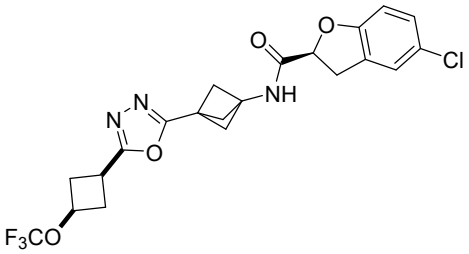


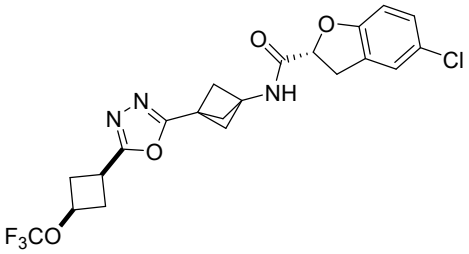


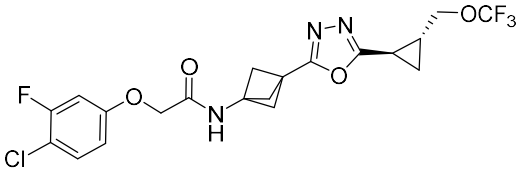


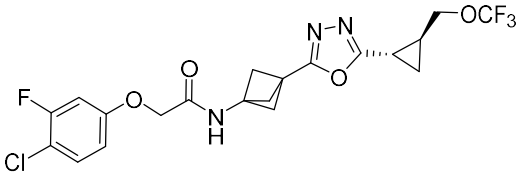


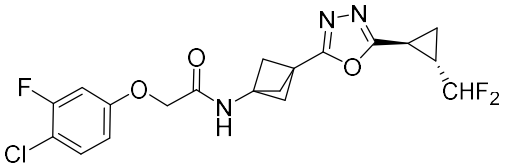


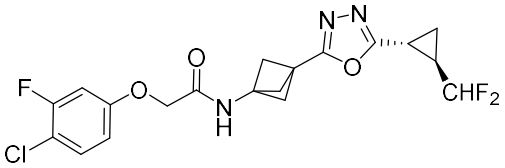


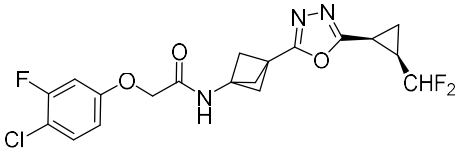


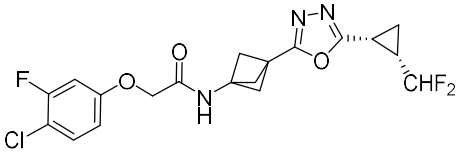


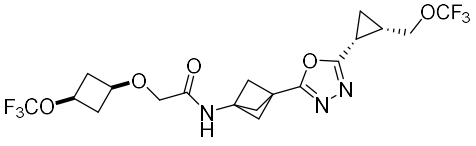


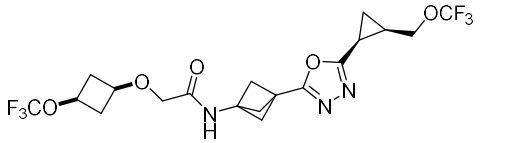


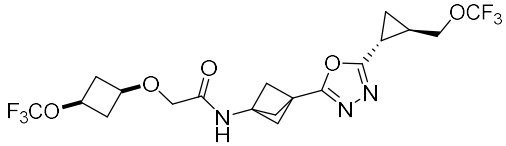


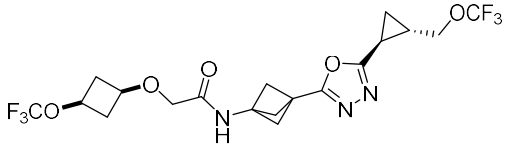


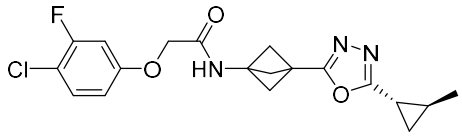


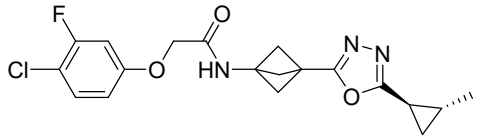


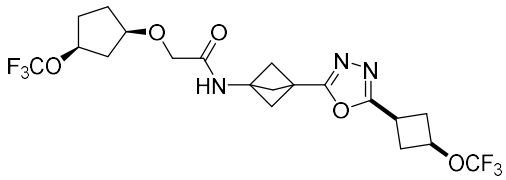


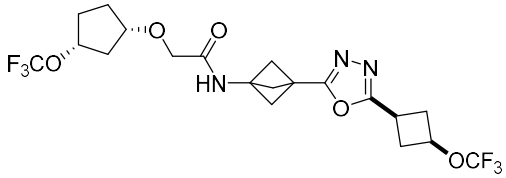


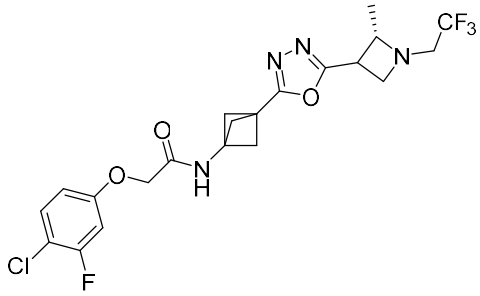


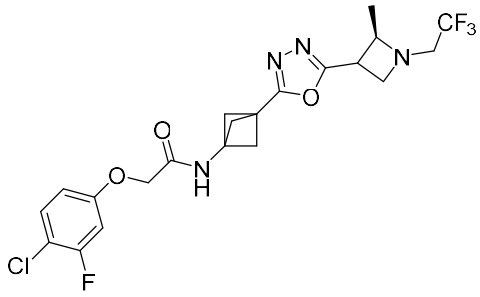


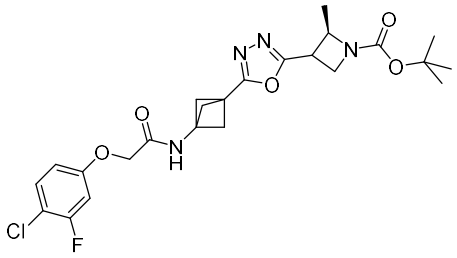


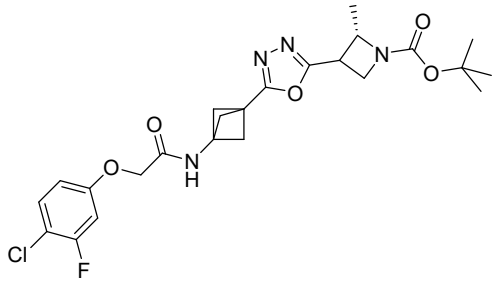


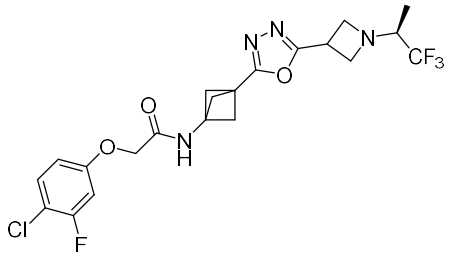


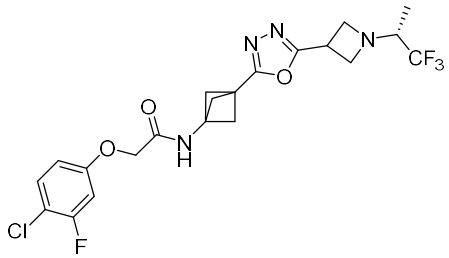


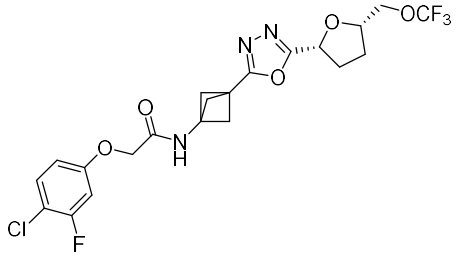


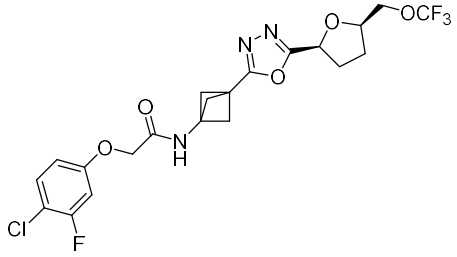


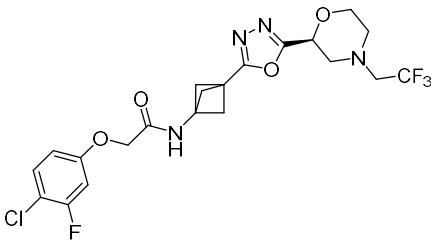


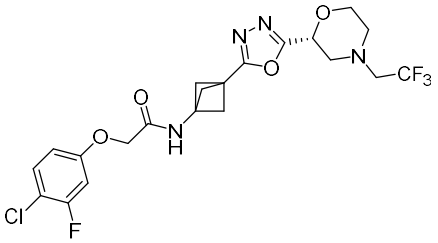


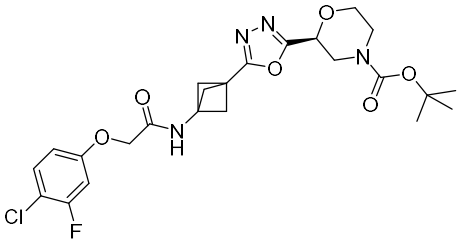


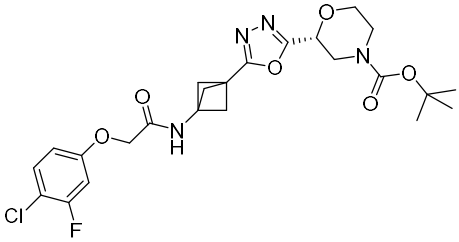


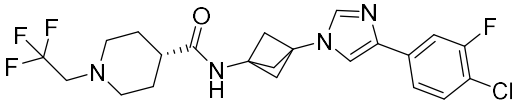


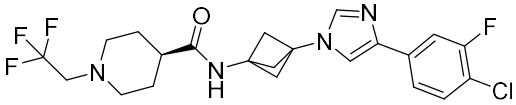


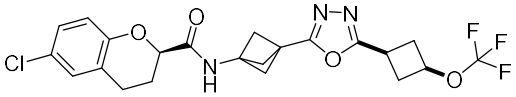


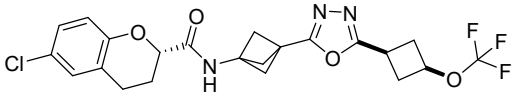


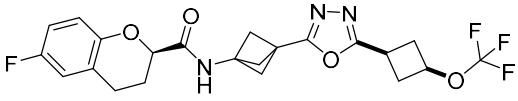


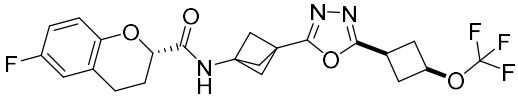


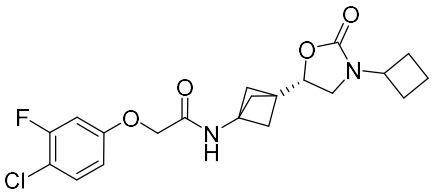


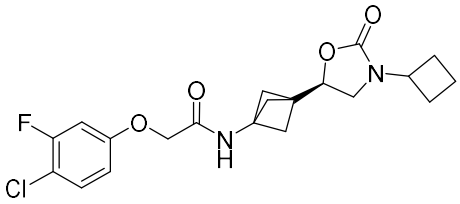


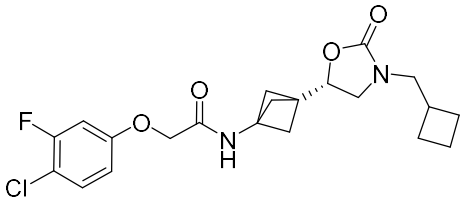


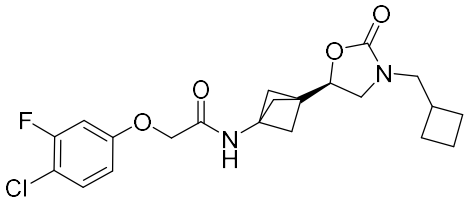


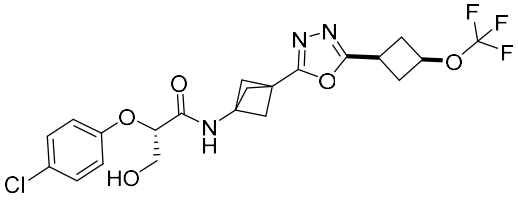


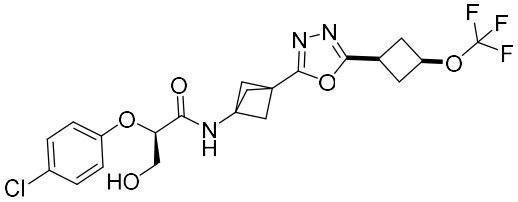


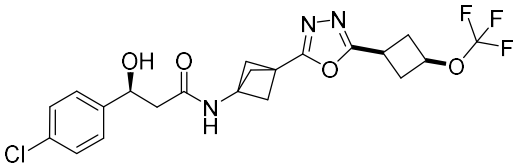


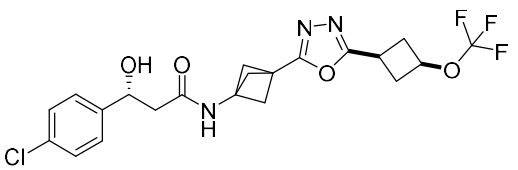


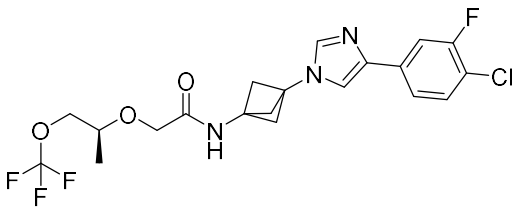


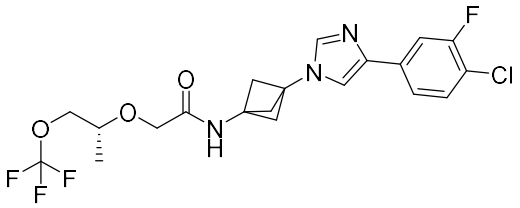


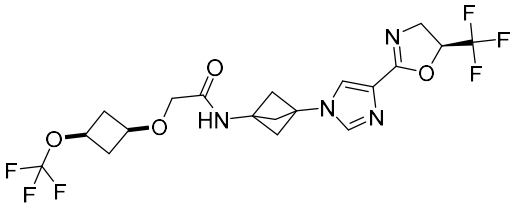


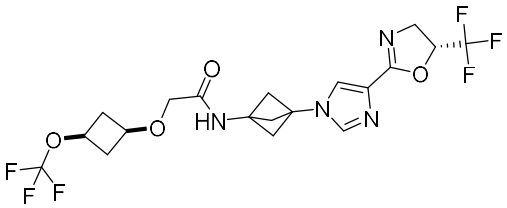


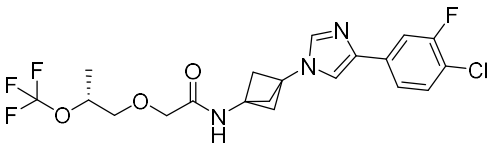


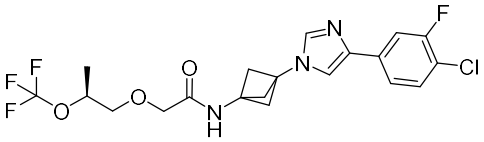






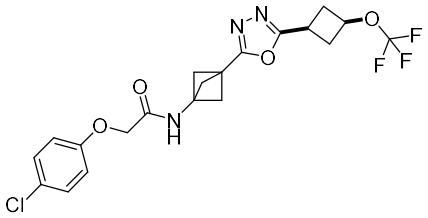






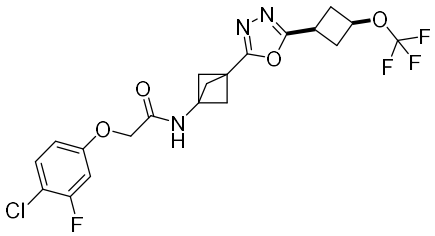
.

32. A compound having the structure:

3 

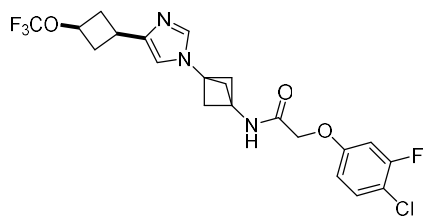
or a pharmaceutically acceptable salt thereof.

33. A compound having the structure:

6 

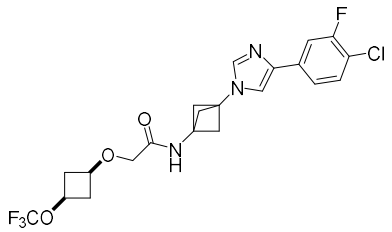
or a pharmaceutically acceptable salt thereof.

34. A compound having the structure:

61 

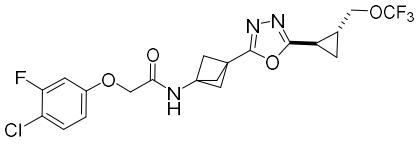
or a pharmaceutically acceptable salt thereof.

35. A compound having the structure:

70 

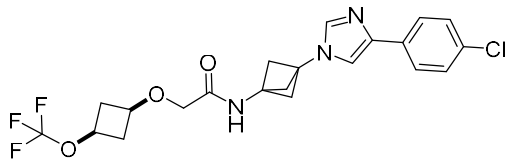
or a pharmaceutically acceptable salt thereof.

36. A compound having the structure:

81 

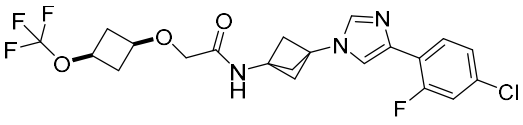
or a pharmaceutically acceptable salt thereof.

37. A compound having the structure:

139 

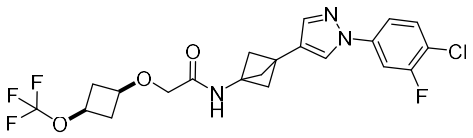
or a pharmaceutically acceptable salt thereof.

38. A compound having the structure:

146 

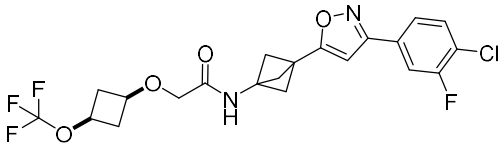
or a pharmaceutically acceptable salt thereof.

39. A compound having the structure:

236 

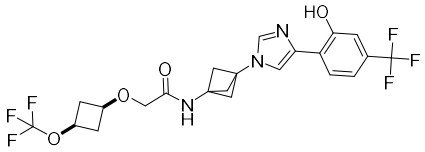
or a pharmaceutically acceptable salt thereof.

40. A compound having the structure:

248 

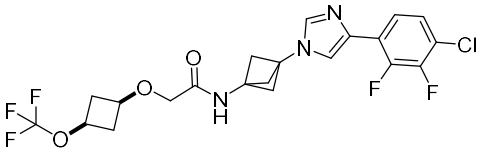
or a pharmaceutically acceptable salt thereof.

41. A compound having the structure:

254 

or a pharmaceutically acceptable salt thereof.

42. A compound having the structure:

270 

or a pharmaceutically acceptable salt thereof.

43. A pharmaceutical composition comprising a compound of any one of claims 1-42, or a pharmaceutically acceptable salt, stereoisomer, mixture of stereoisomers or prodrug thereof, and a pharmaceutically acceptable carrier.

44. Use of a compound of any one of claims 1 to 42 for the manufacture of a medicament for treating a neurodegenerative disease.

45. The use of claim 44, wherein the disease is Alexander's disease, Alper's disease, Alzheimer's disease, Amyotrophic lateral sclerosis, Ataxia telangiectasia, Batten disease (also known as Spielmeyer-Vogt-Sjogren-Batten disease), Bovine spongiform encephalopathy (BSE), Canavan disease, Cockayne syndrome, Corticobasal degeneration, Creutzfeldt- Jakob disease, frontotemporal dementia, Gerstmann-Straussler-Scheinker syndrome, Huntington's disease, HIV-associated dementia, Kennedy's disease, Krabbe's disease, kuru, Lewy body dementia, Machado-Joseph disease

(Spinocerebellar ataxia type 3), Multiple sclerosis, Multiple System Atrophy, Narcolepsy, Neuroborreliosis, Parkinson's disease, Pelizaeus-Merzbacher Disease, Pick's disease, Primary lateral sclerosis, Prion diseases, Refsum's disease, Sandhoffs disease, Schilder's disease, Subacute combined degeneration of spinal cord secondary to Pernicious Anaemia, Schizophrenia, Spinocerebellar ataxia (multiple types with varying characteristics), Spinal muscular atrophy, Steele-Richardson-Olszewski disease, insulin resistance, vanishing white matter disease or Tabes dorsalis.

46. Use of a compound of any one of claims 1 to 42 for the manufacture of a medicament for treating Alzheimer's disease, ALS, Parkinson's disease, vanishing white matter disease or dementia.