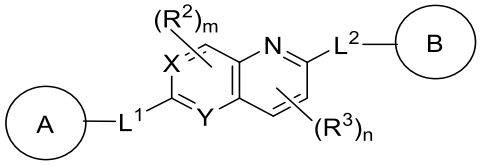
CLAIMS

1. A compound of Formula (I-a):



(I-a)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein:

A is heteroaryl, optionally substituted with one or more R^1;

B is heterocyclyl optionally substituted with one or more R^1;

L^1 and L^2 are each independently absent;

X and Y are each N or $C(R^6)$, wherein one of X and Y is independently N;

each R^1 is independently hydrogen, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, heteroaryl, aryl, C_1-C_6 alkylene-aryl, C_2-C_6 alkenylene-aryl, C_1-C_6 alkylene-heteroaryl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, or $–S(O)_xR^D$, wherein each alkyl, alkylene, alkenyl, alkenylene, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^7; or

two R^1 groups, together with the atoms to which they are attached, form a 3-7-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^7;

each R^2 and R^3 is independently C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, or $–S(O)_xR^D$;

each R^6 is independently hydrogen, halo, cyano, C_1-C_6-alkyl, C_1-C_6-haloalkyl, or $–OR^A$;

each R^7 is independently C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, or $–S(O)_xR^D$, wherein each of alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^8;

each R^A is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkylene-heteroaryl, –$C(O)R^D$, or –$S(O)_xR^D$, wherein each alkyl, alkylene, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^9;

each R^B and R^C is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_6 alkylene-cycloalkyl, C_1-C_6 alkylene-heterocyclyl, –OR^A, wherein each alkyl, alkylene, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^9; or

R^B and R^C together with the atom to which they are attached form a 3-7-membered heterocyclyl ring optionally substituted with one or more R^9;

each R^D is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, and haloalkyl is optionally substituted with one or more R^9;

each R^8 is independently C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, halo, cyano, oxo, or –OR^A;

each R^9 is C_1-C_6-alkyl, halo, cyano, oxo, or –OR^{A1};

each R^{A1} is hydrogen or C_1-C_6-alkyl;

n is 0, 1, or 2;

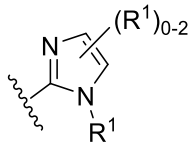
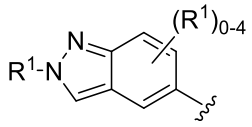
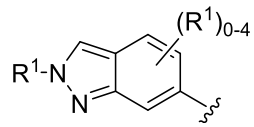
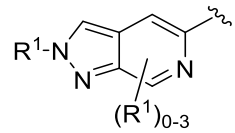
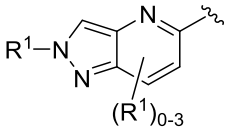
m is 0 or 1; and

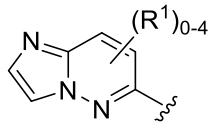
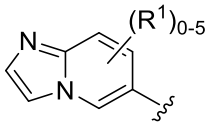
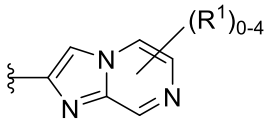
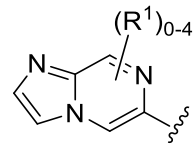
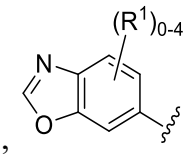
x is 0, 1, or 2.

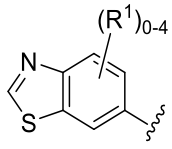
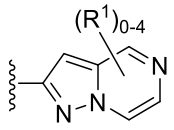
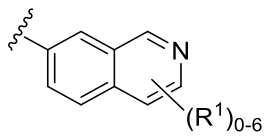
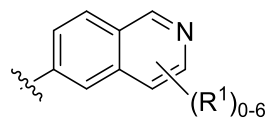
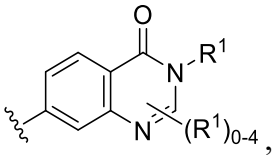
2. The compound of claim 1, wherein A is a monocyclic heteroaryl or bicyclic heteroaryl, each of which is optionally substituted with one or more R^1.

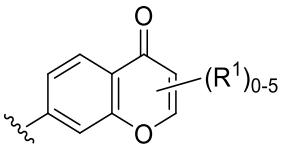
3. The compound of any one of the preceding claims, wherein A is a nitrogen-containing heteroaryl optionally substituted with one or more R^1.

4. The compound of any one of the preceding claims, wherein A is selected from

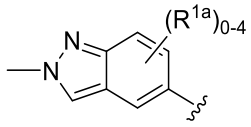
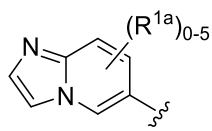
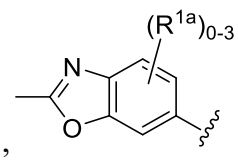
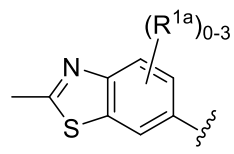
 ,  ,  ,  ,  ,

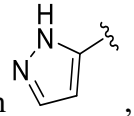
 ,  ,  ,  ,  ,

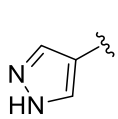
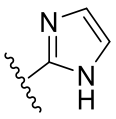
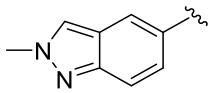
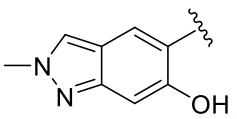
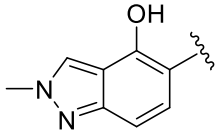
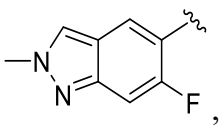
 ,  ,  ,  ,  ,

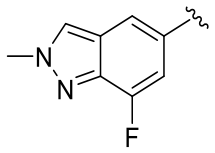
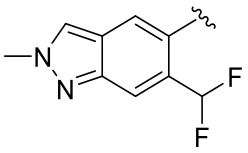
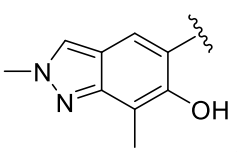
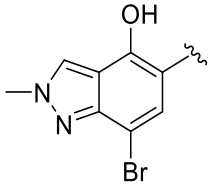
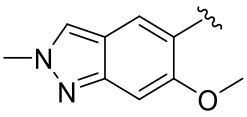
and  wherein R^1 is as described in claim 1.

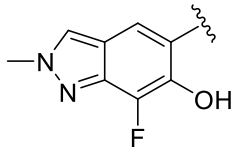
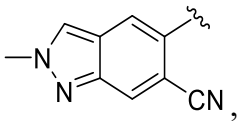
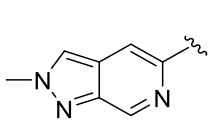
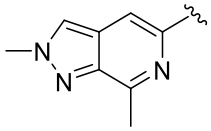
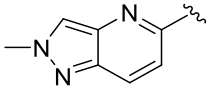
5. The compound of any one of the preceding claims, wherein A is selected from

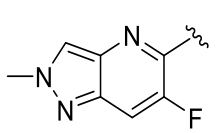
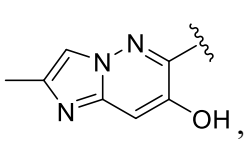
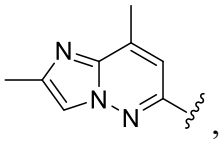
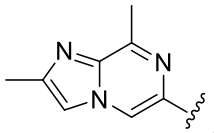
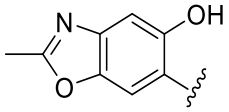
 ,  ,  and  , wherein each R^{1a} is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, or $–OR^A$, and each alkyl, heteroalkyl, and haloalkyl is optionally substituted with one or more R^7.

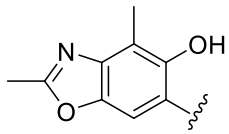
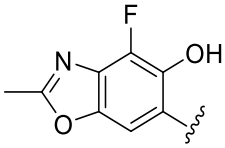
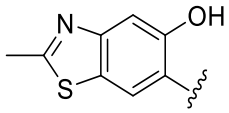
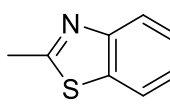
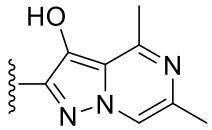
6. The compound of any one of the preceding claims, wherein A is selected from  ,

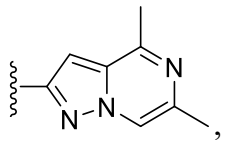
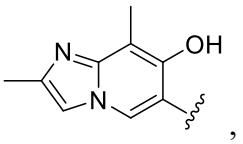
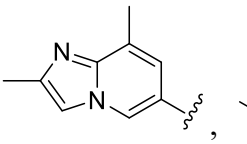
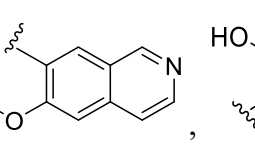
 ,  ,  ,  ,  ,  ,

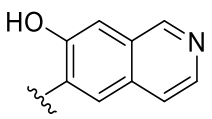
 ,  ,  ,  ,  ,

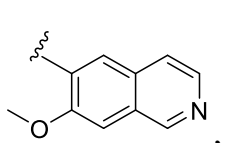
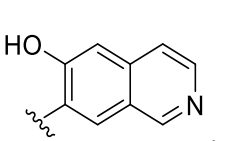
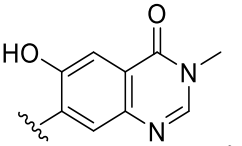
 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  ,  ,  , ,

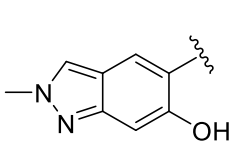
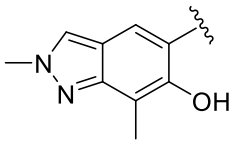
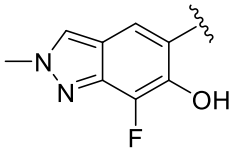
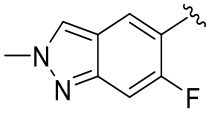
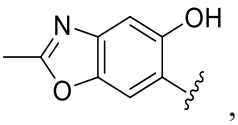
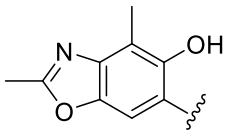
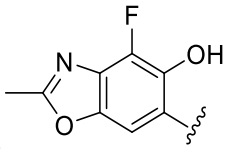
, , , ,  ,

 ,  ,  , , ,

, , , , and

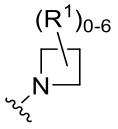
.

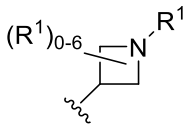
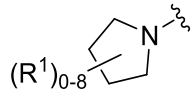
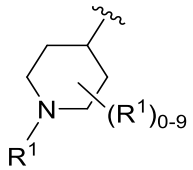
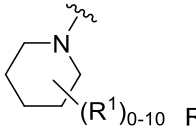
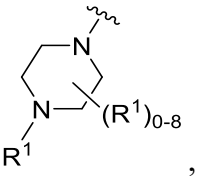
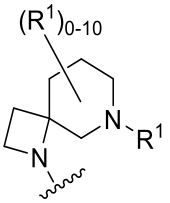
7. The compound of any one of the preceding claims, wherein A is selected from

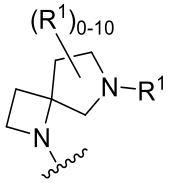
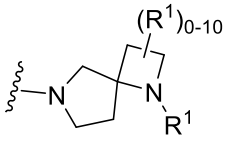
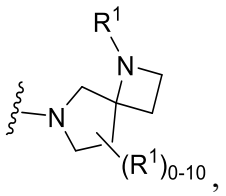
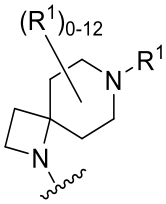
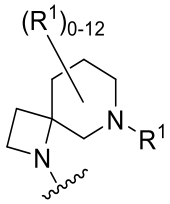
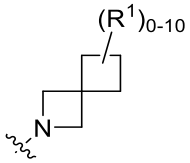
 ,  ,  ,  ,  ,  , and  .

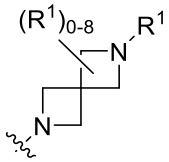
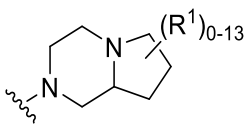
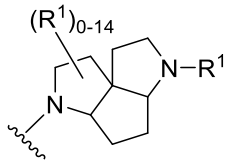
8. The compound of any one of the preceding claims, wherein B is a monocyclic heterocyclyl or bicyclic heterocyclyl, each of which is optionally substituted with one or more R^1.

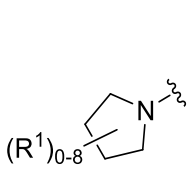
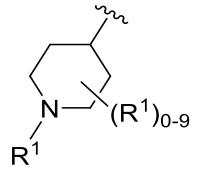
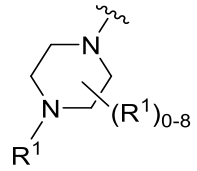
9. The compound of any one of the preceding claims, wherein B is a nitrogen-containing heterocyclyl optionally substituted with one or more R^1.

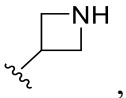
10. The compound of any one of the preceding claims, wherein B is selected from  ,

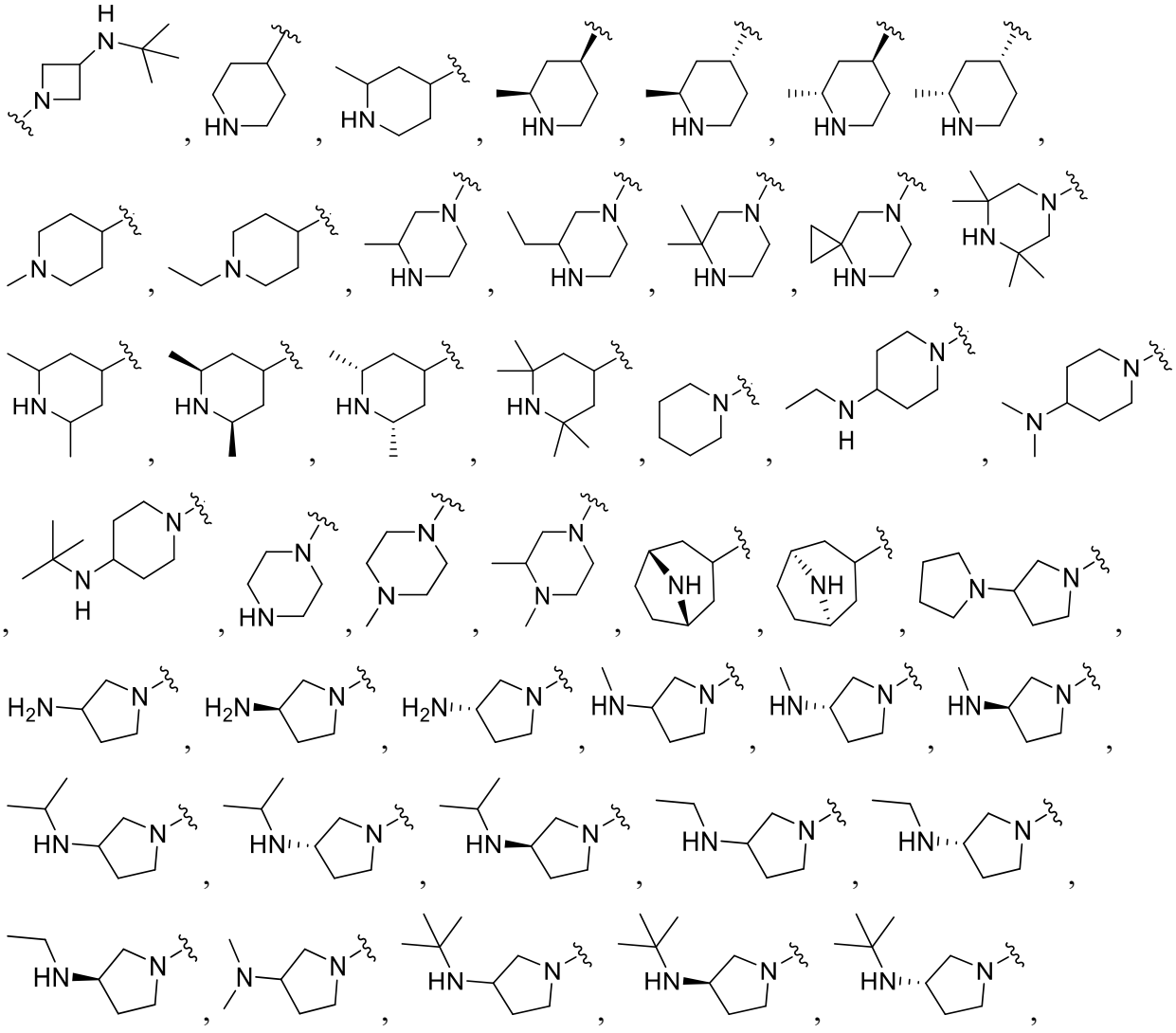
 ,  ,  ,  ,  ,  ,

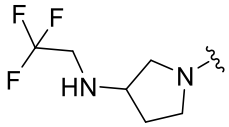
 ,  ,  ,  ,  ,  ,

 ,  , and  wherein R^1 is as described in claim 1.

11. The compound of any one of the preceding claims, wherein B is selected from  ,  , and  , wherein R^1 is as described in claim 1.

12. The compound of any one of the preceding claims, wherein B is selected from  ,

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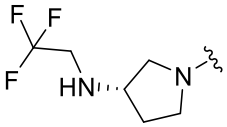
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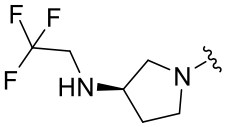
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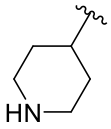
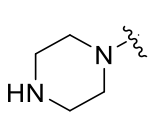
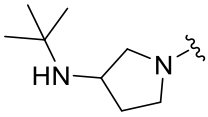
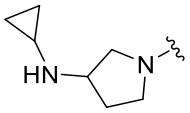
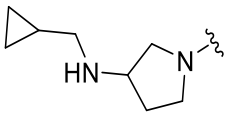
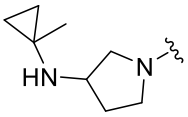
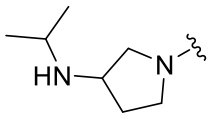
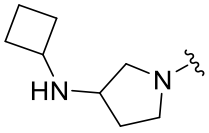
13. The compound of any one of the preceding claims, wherein B is selected from  ,

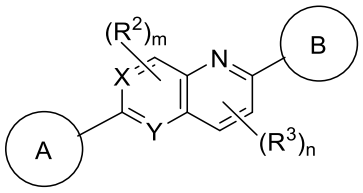
 ,  ,  ,  ,  ,

 , and  .

14. The compound of any one of claims 1-13, wherein each of X and Y is independently N.

15. The compound of any one of the preceding claims, wherein one of R^2 and R^3 is independently halo.

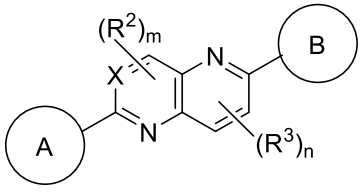
16. The compound of any one of the preceding claims, wherein the compound of Formula (I-a) is a compound of Formula (I-c):



(I-c)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, X, Y, R^2, R^3, m, n, and subvariables thereof are as defined in claim 1.

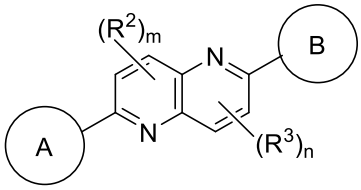
17. The compound of any one of the preceding claims, wherein the compound of Formula (I-a) is a compound of Formula (I-e):



(I-e),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, X, R^2, R^3, m, n, and subvariables thereof are as defined in claim 1.

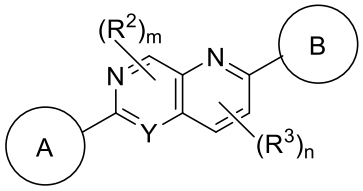
18. The compound of any one of the preceding claims, wherein the compound of Formula (I-a) is a compound of Formula (I-f):



(I-f),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein m is 0, 1 or 2; and A, B, R^2, R^3, m, n, and subvariables thereof are as defined in claim 1.

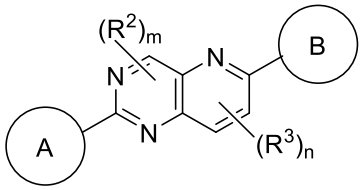
19. The compound of any one of claims 1-16, wherein the compound of Formula (I-a) is a compound of Formula (I-g):



(I-g),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, Y, R^2, R^3, m, n, and subvariables thereof are as defined in claim 1.

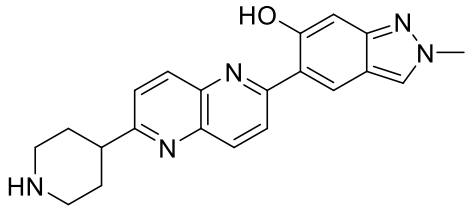
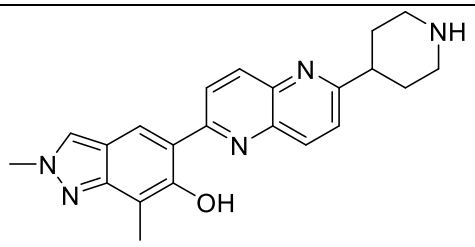
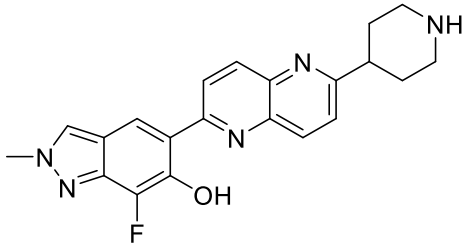
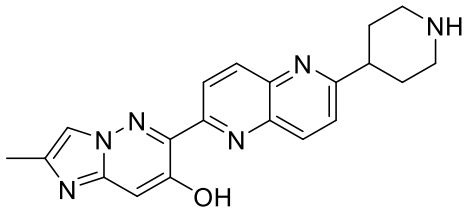
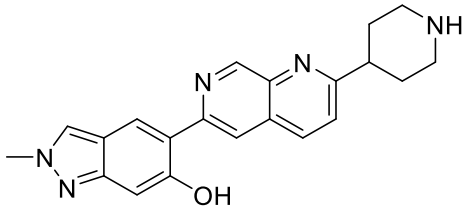
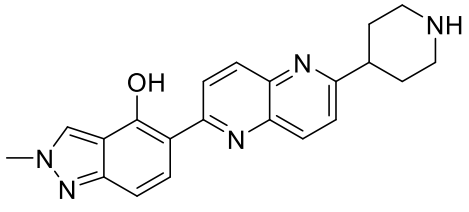
20. The compound of any one of the preceding claims, wherein the compound of Formula (I-a) is a compound of Formula (I-h):

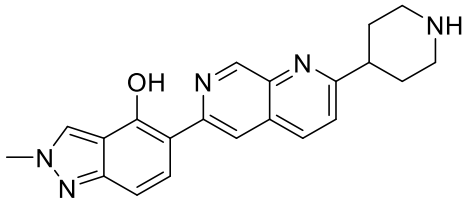
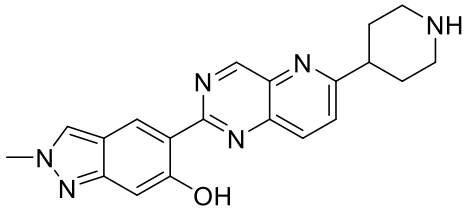
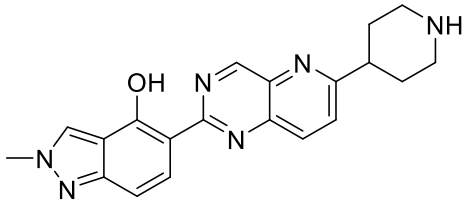
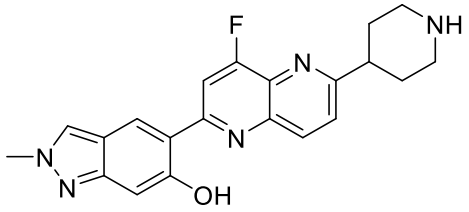
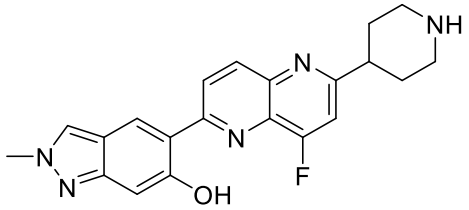
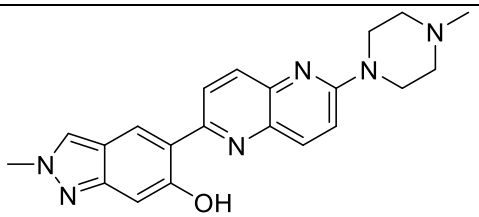
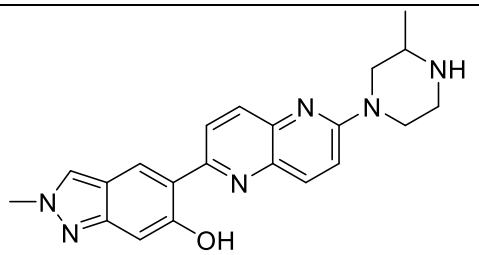


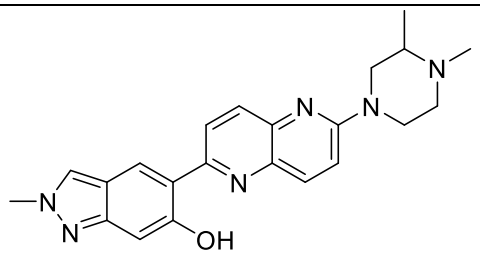
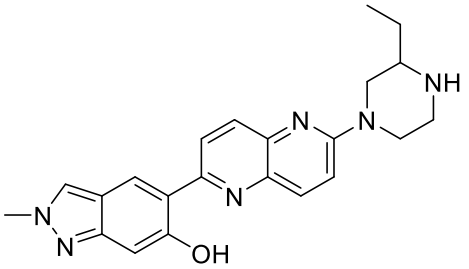
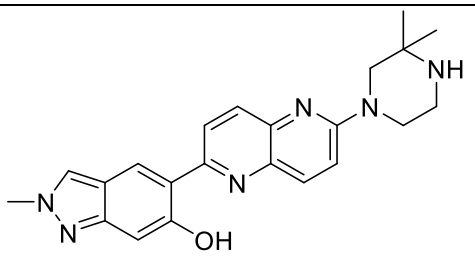
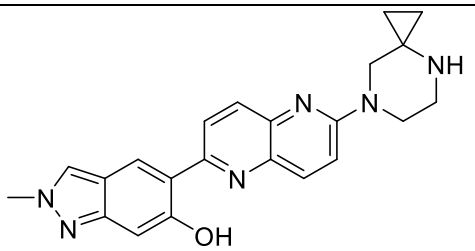
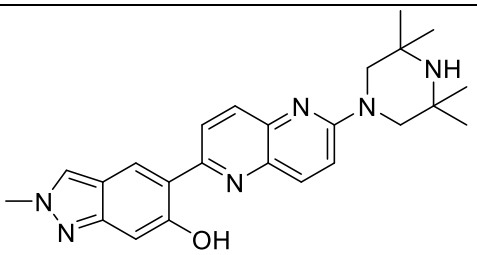
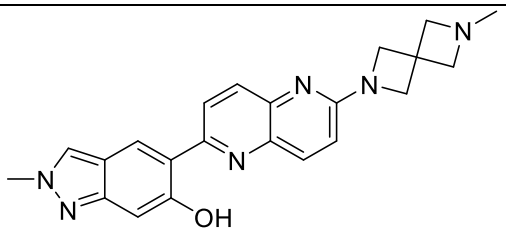
(I-h),

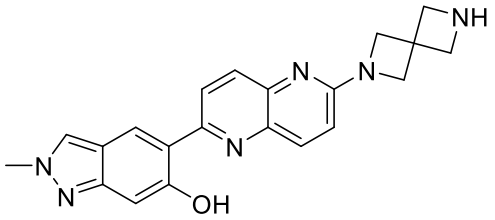
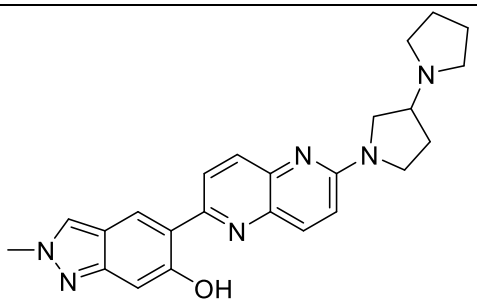
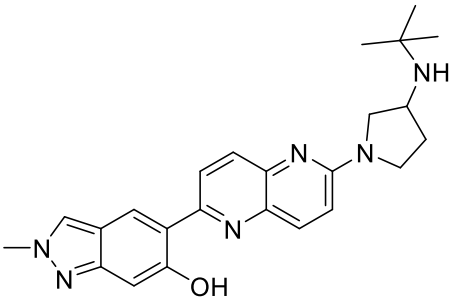
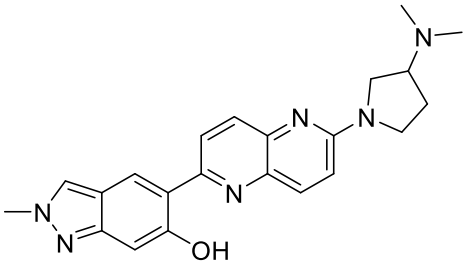
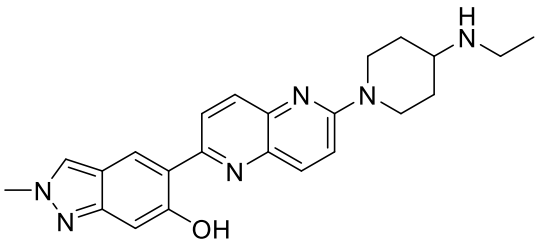
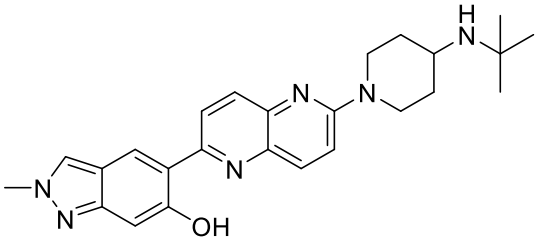
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, R^2, R^3, m, n, and subvariables thereof are as defined in claim 1.

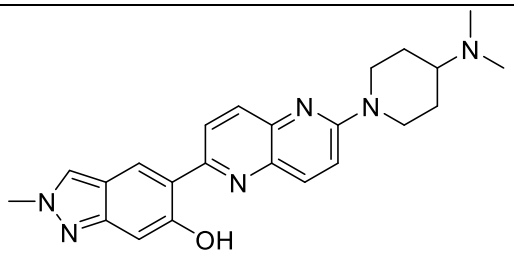
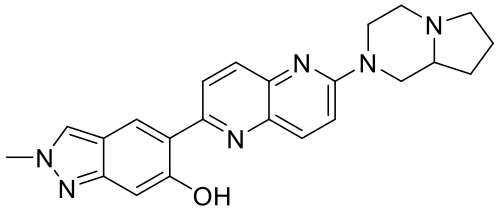
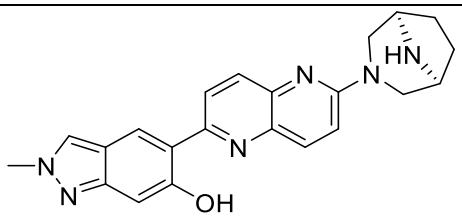
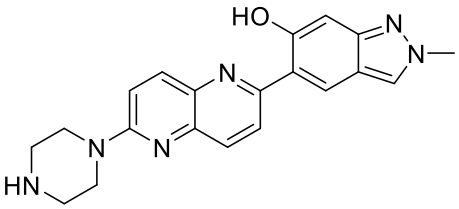
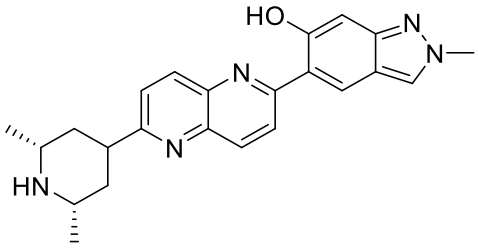
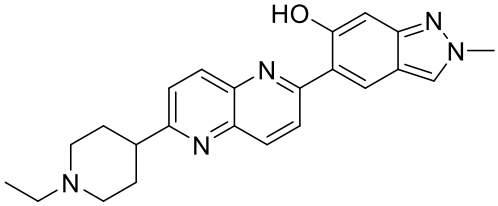
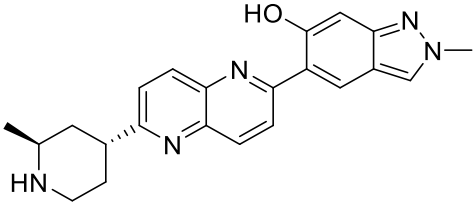
21. The compound of any one of the preceding claims, wherein the compound is selected from any one of the following compounds:

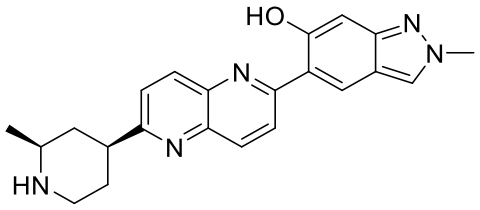
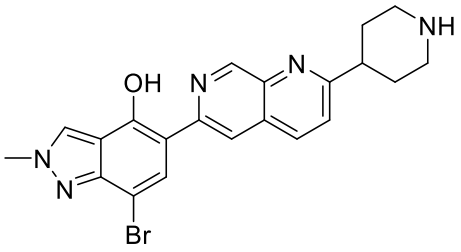
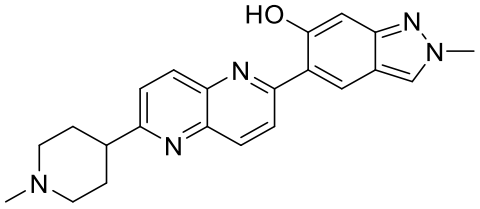
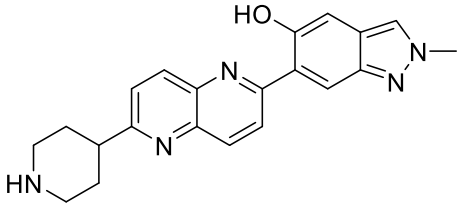
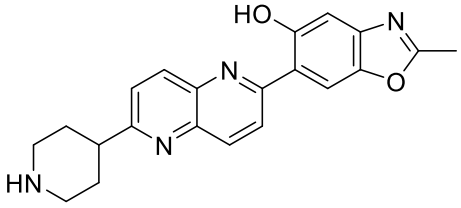
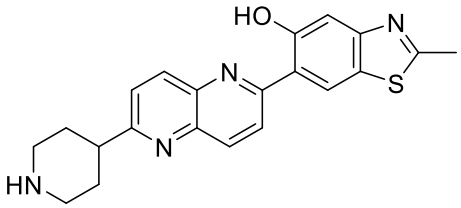
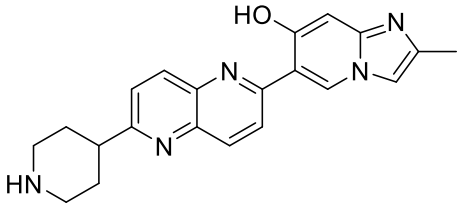
Compound No.	Structure
100	
101	
102	
103	
104	
105	

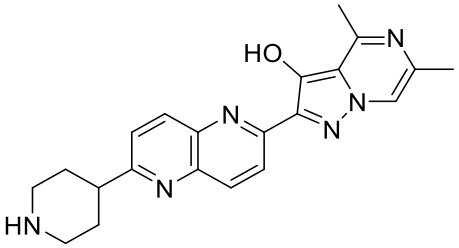
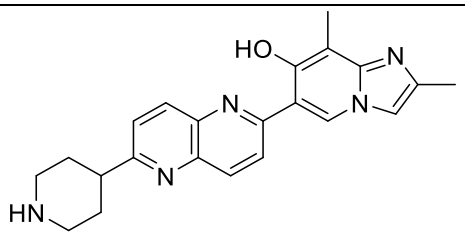
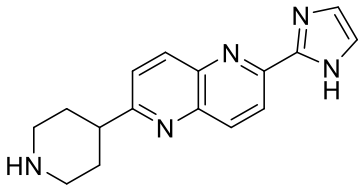
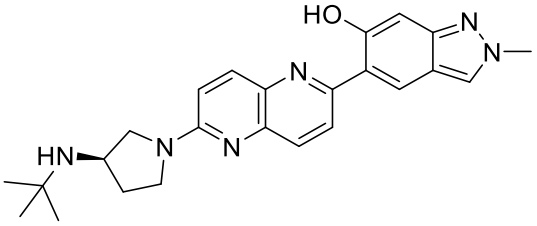
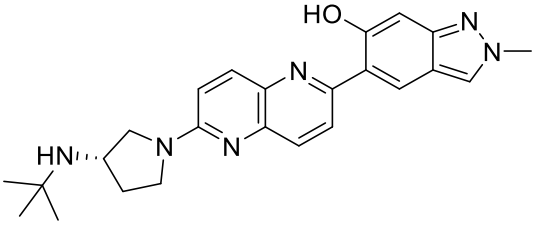
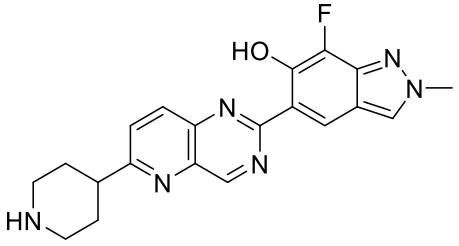
106	
107	
108	
113	
114	
116	
117	

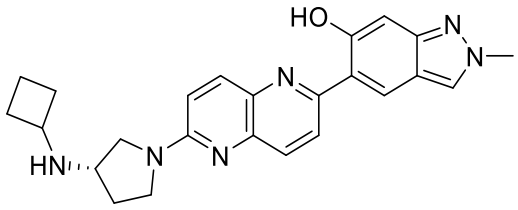
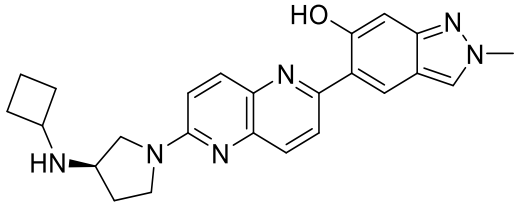
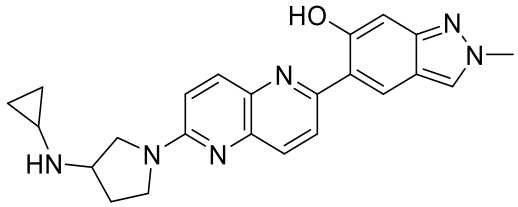
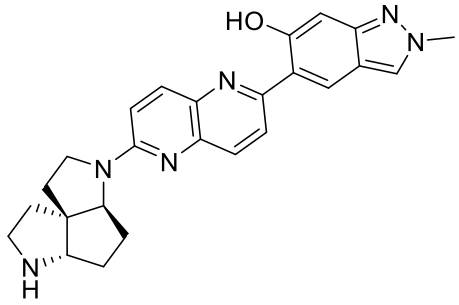
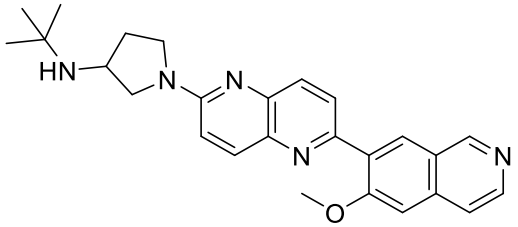
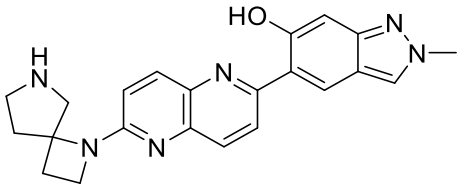
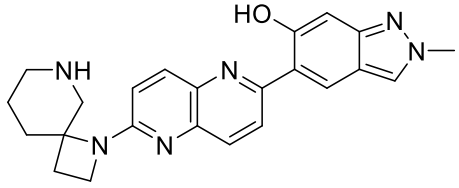
118	
119	
120	
121	
122	
123	

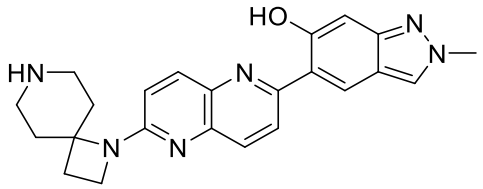
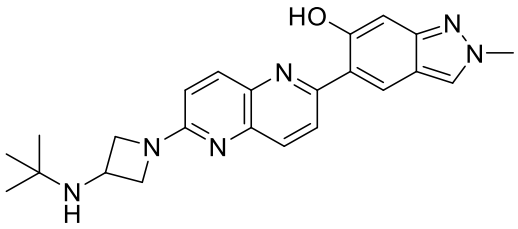
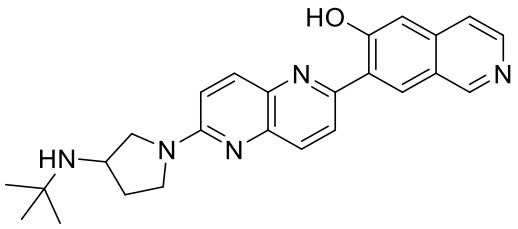
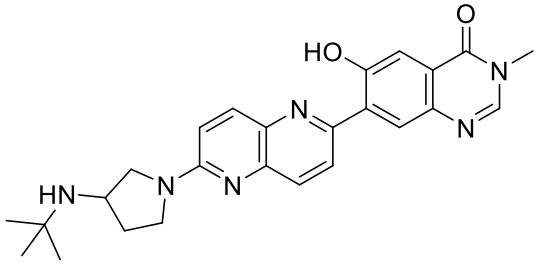
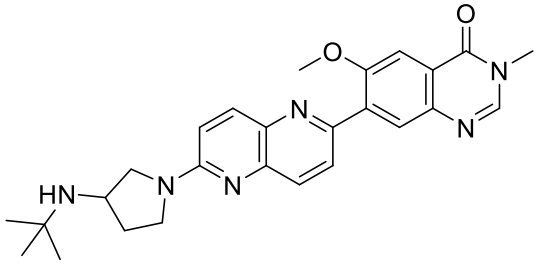
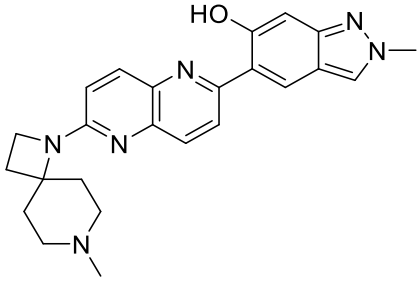
124	
125	
127	
129	
131	
132	

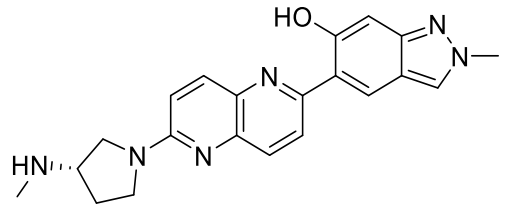
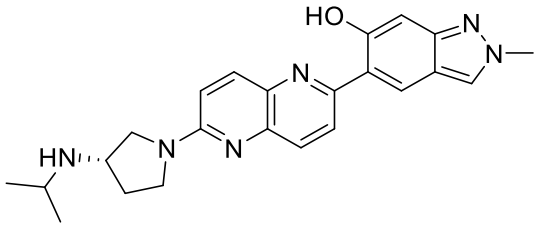
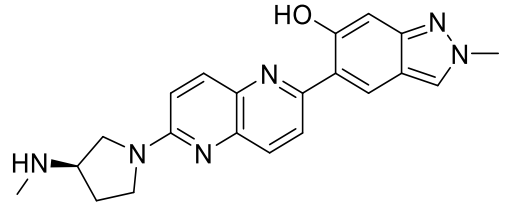
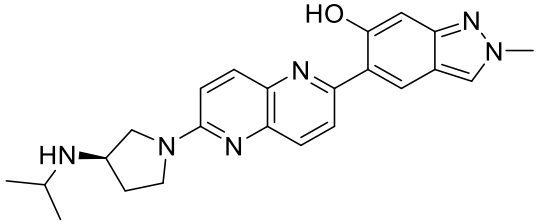
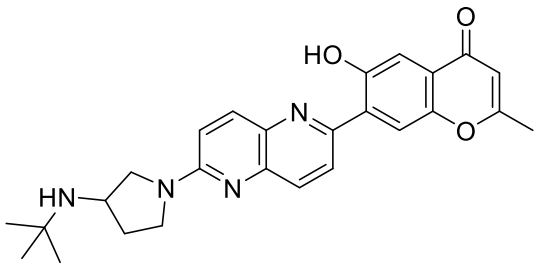
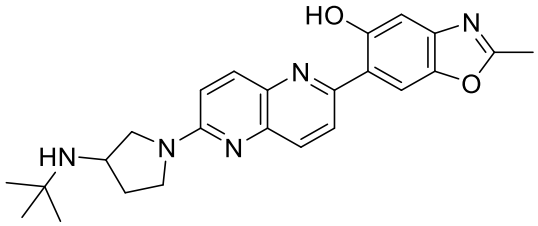
133	
134	
135	
136	
137	
138	
139	

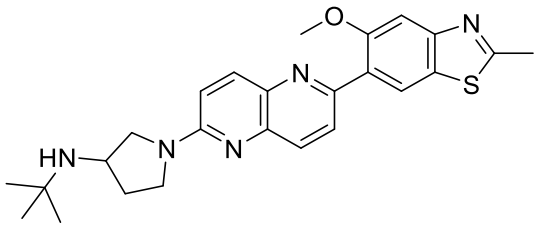
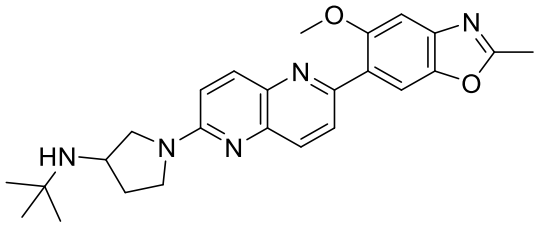
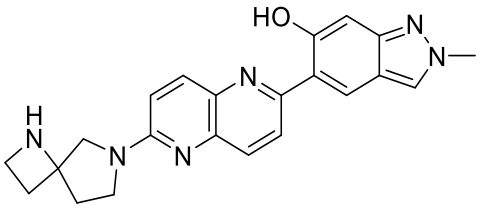
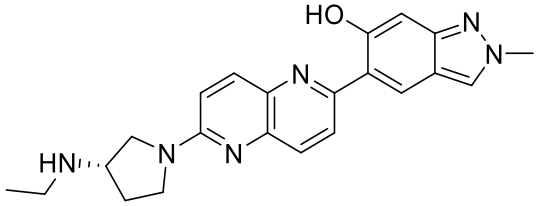
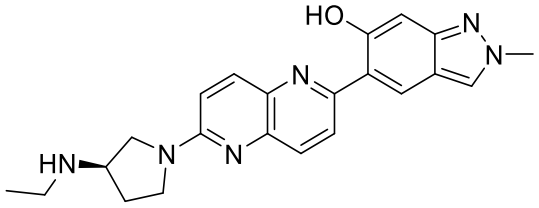
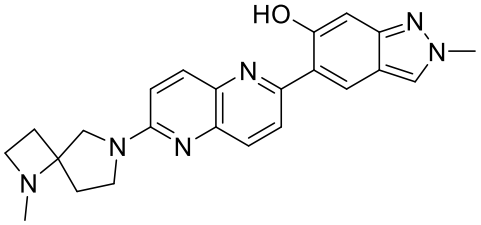
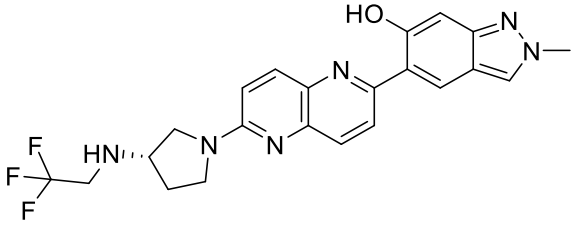
140	
141	
142	
146	
147	
148	
149	

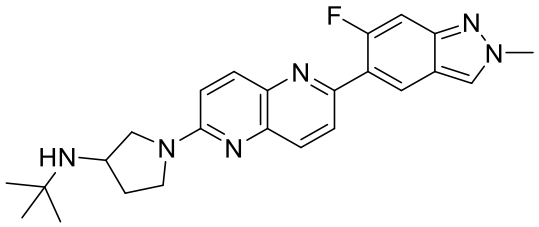
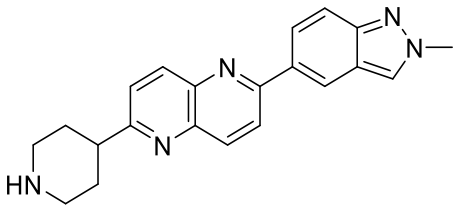
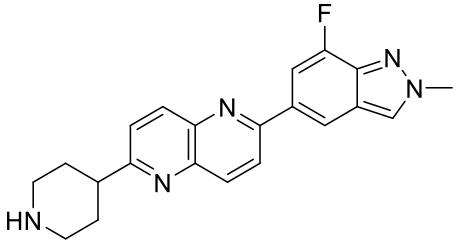
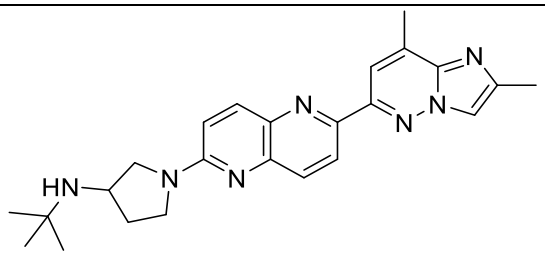
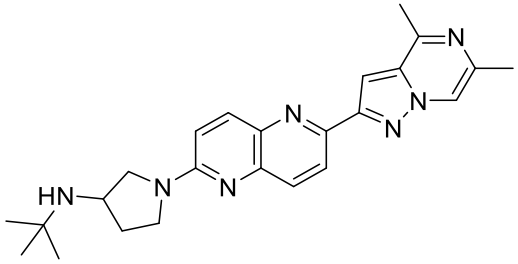
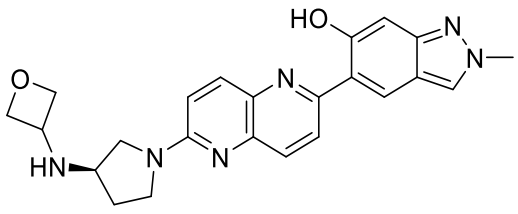
150	
151	
152	
153	
154	
155	

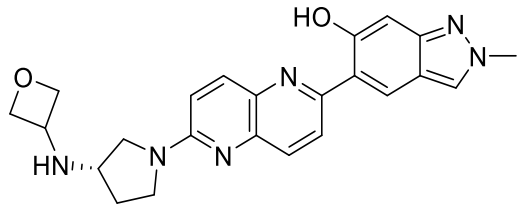
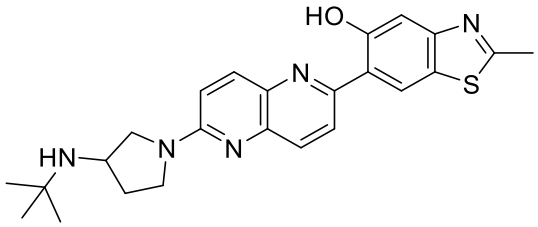
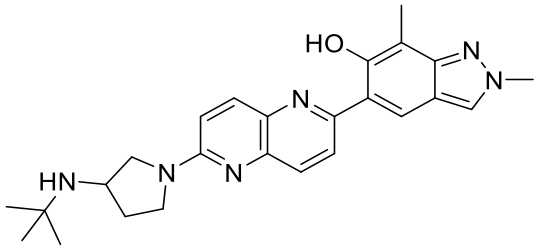
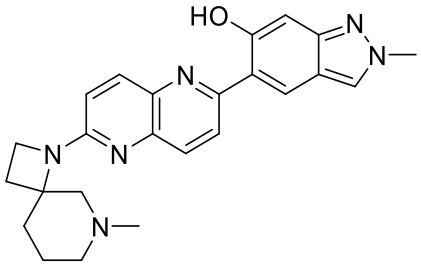
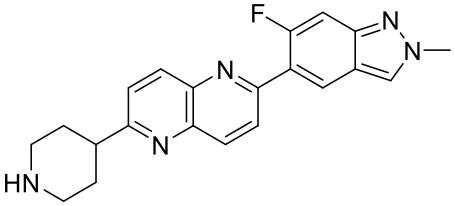
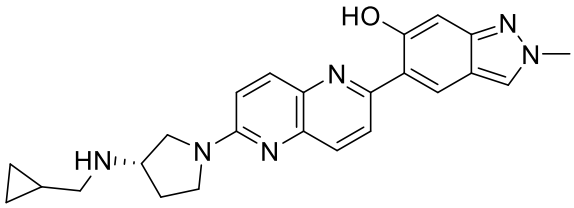
156	
157	
158	
160	
161	
162	
163	

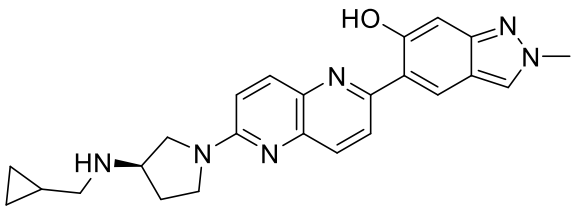
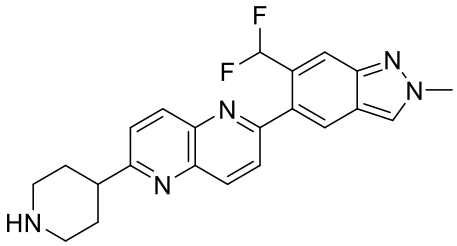
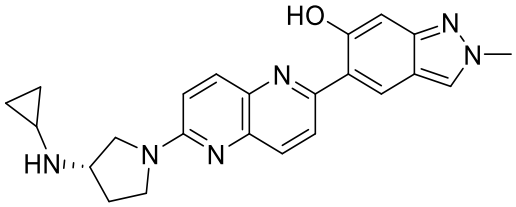
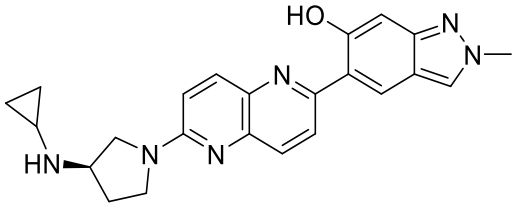
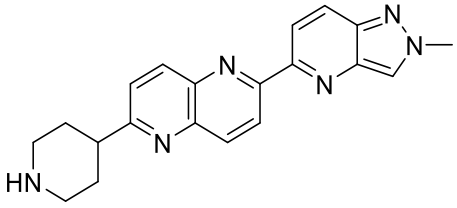
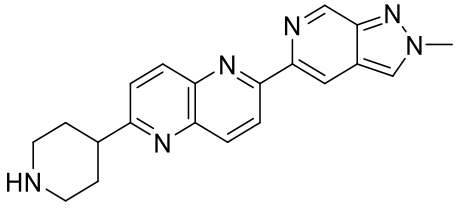
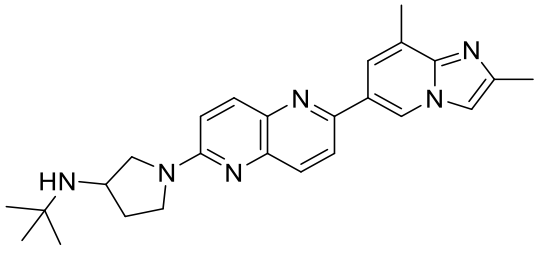
164	
165	
166	
167	
168	
169	

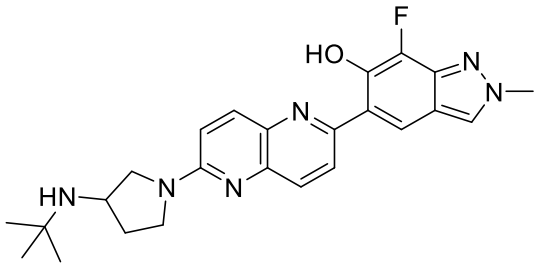
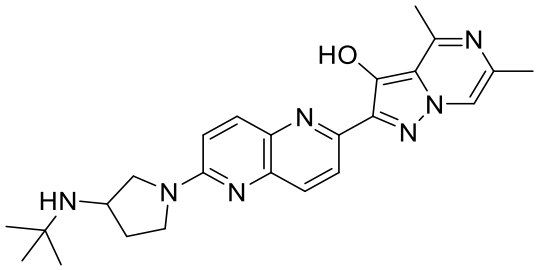
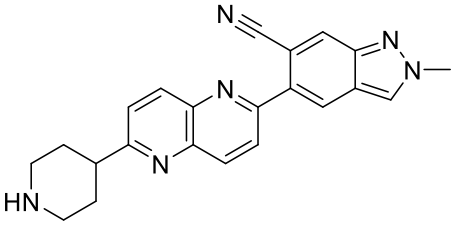
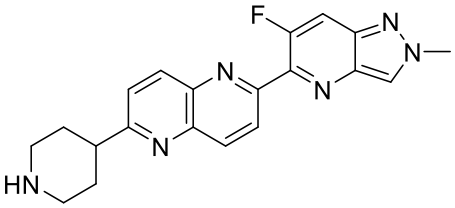
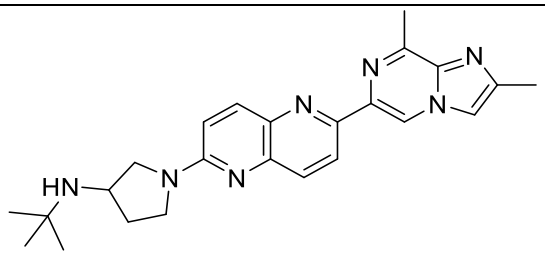
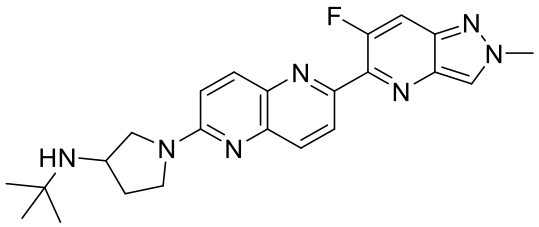
170	
171	
172	
173	
174	
175	

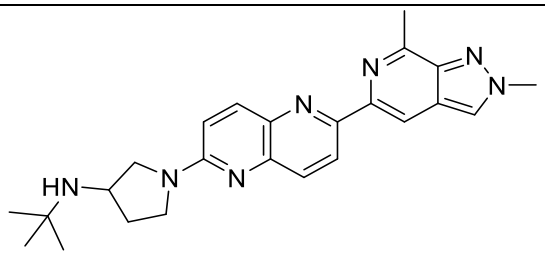
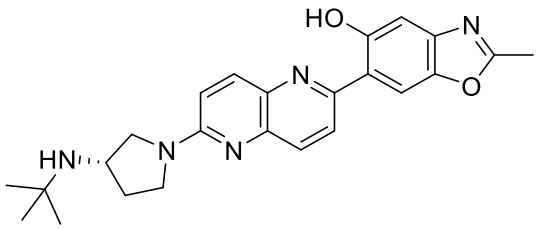
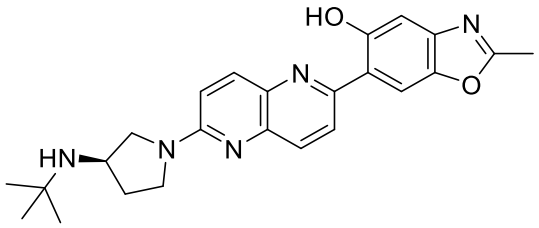
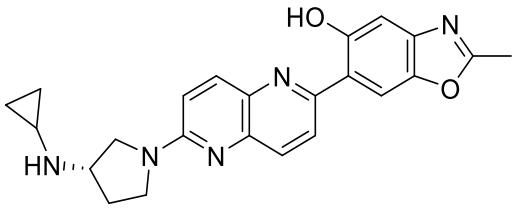
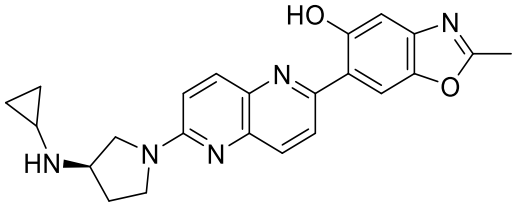
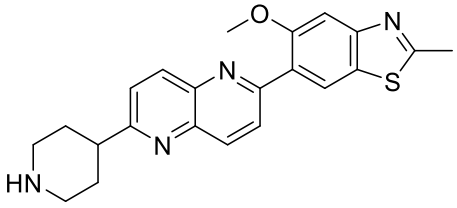
176	
177	
178	
179	
180	
181	
182	

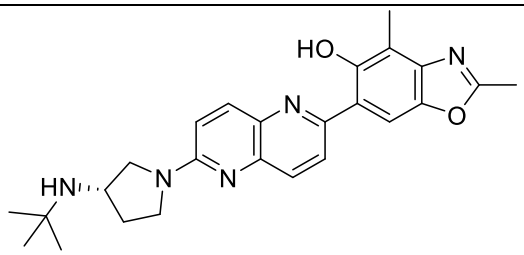
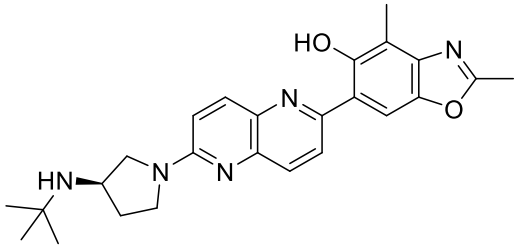
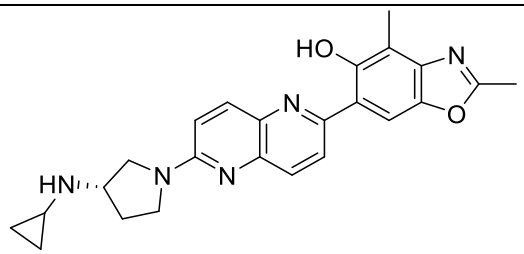
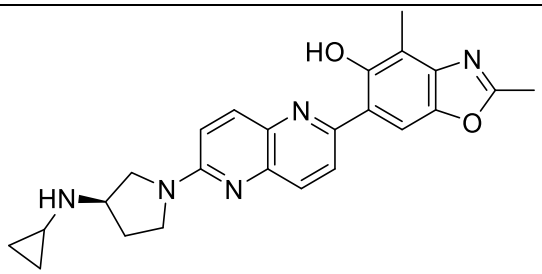
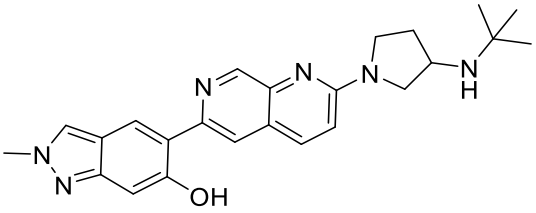
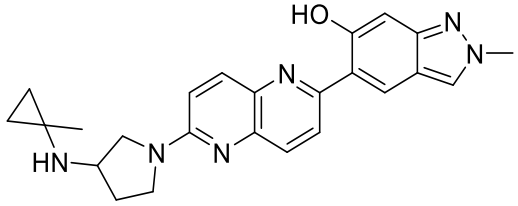
183	
184	
185	
186	
187	
188	

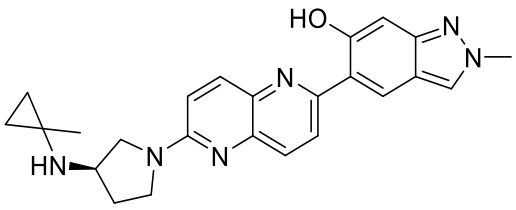
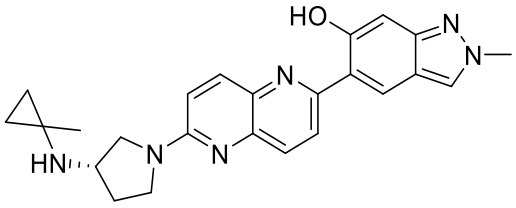
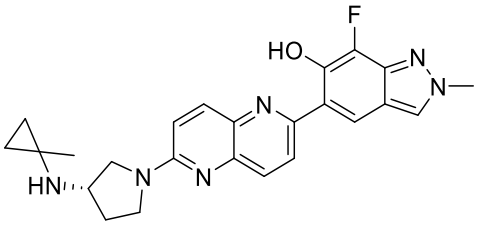
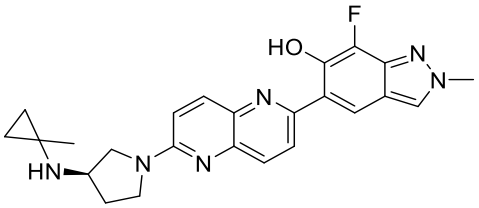
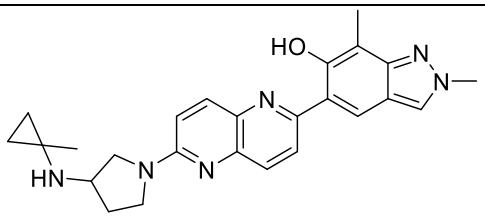
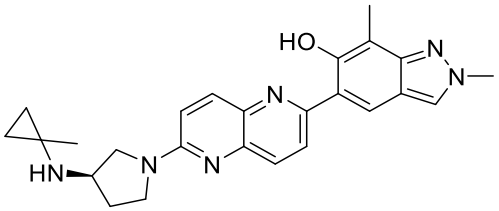
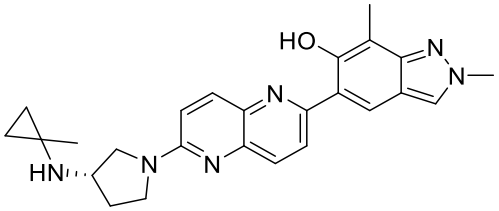
189	
190	
191	
192	
193	
194	

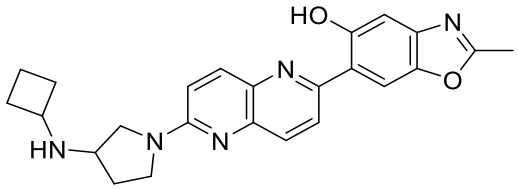
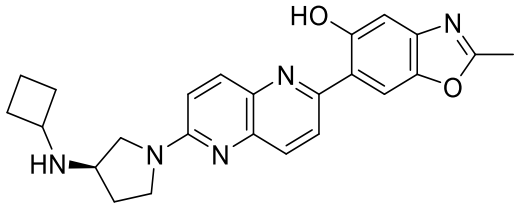
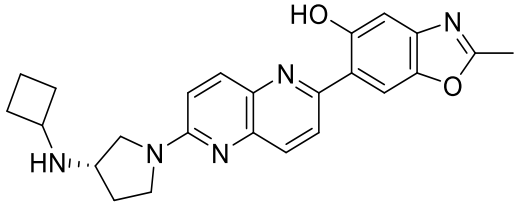
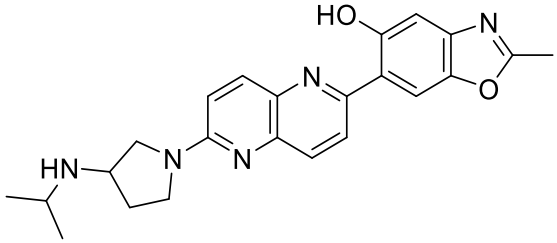
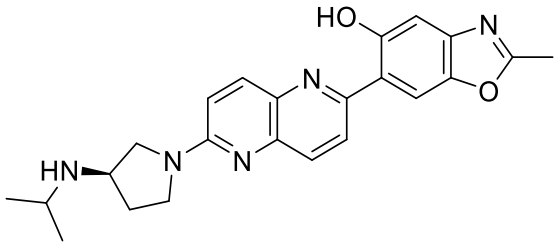
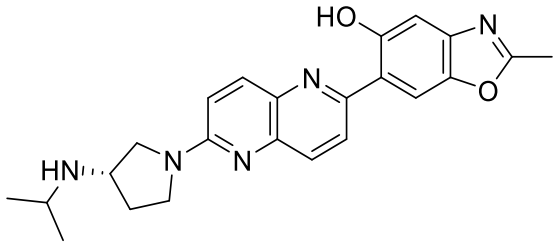
195	
196	
197	
198	
199	
200	
201	

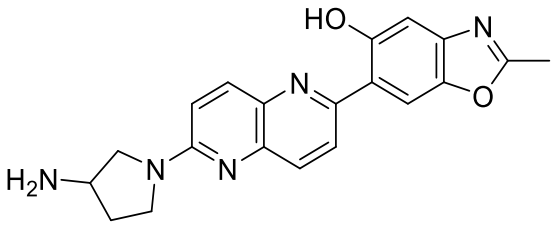
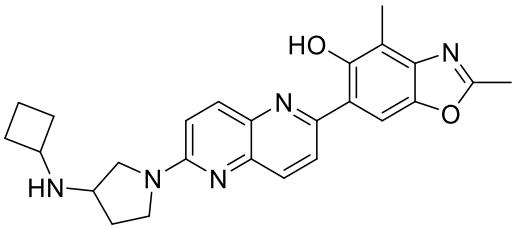
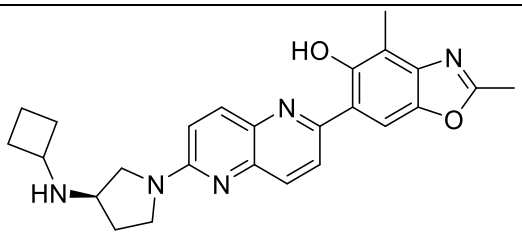
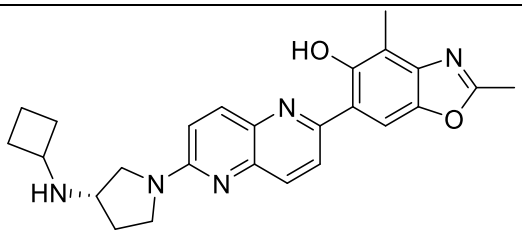
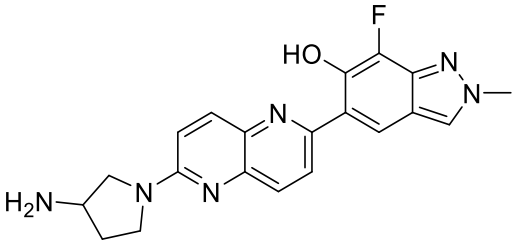
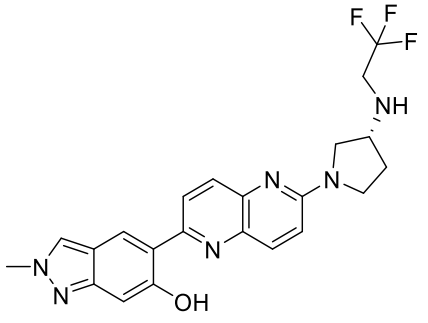
202	
203	
204	
205	
206	
207	

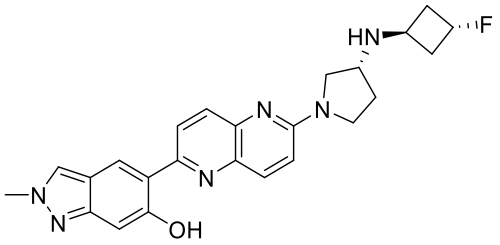
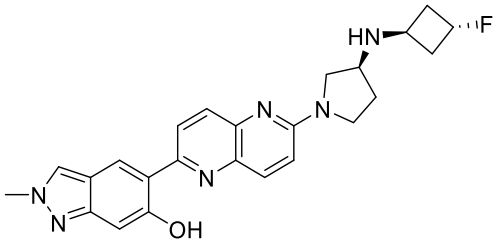
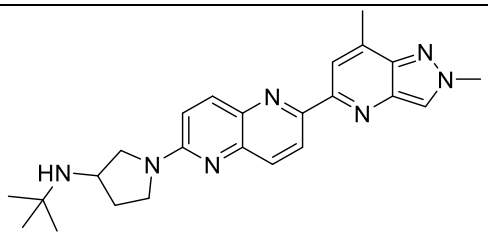
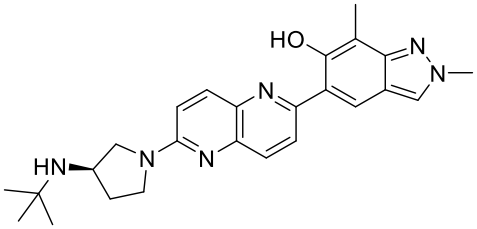
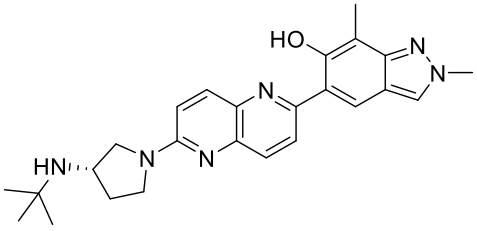
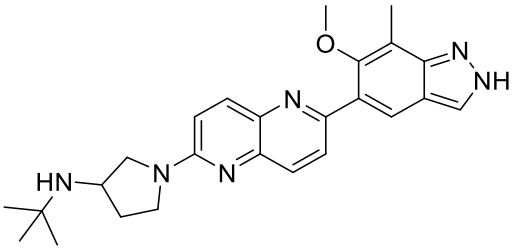
208	
209	
210	
211	
212	
213	

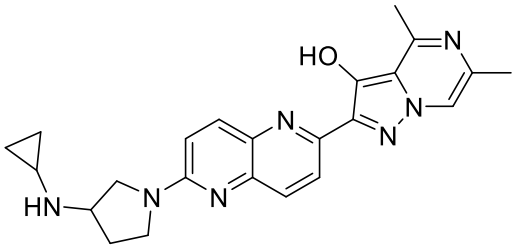
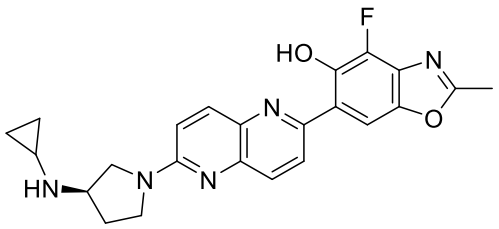
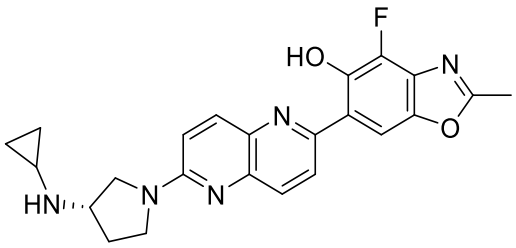
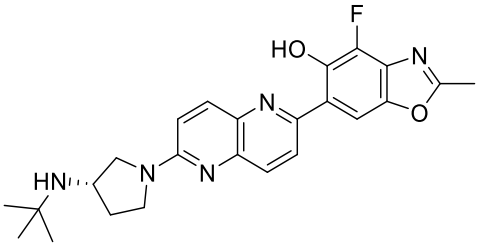
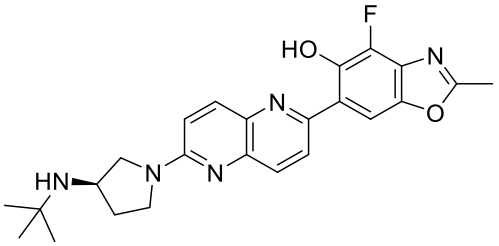
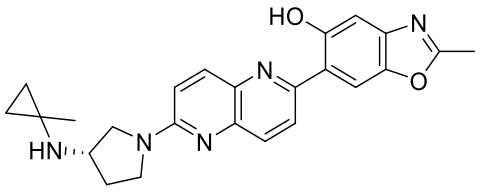
214	
215	
216	
217	
218	
219	

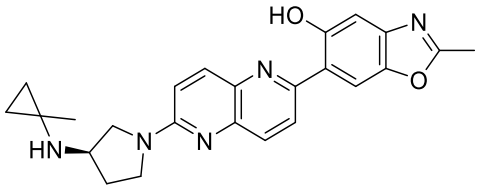
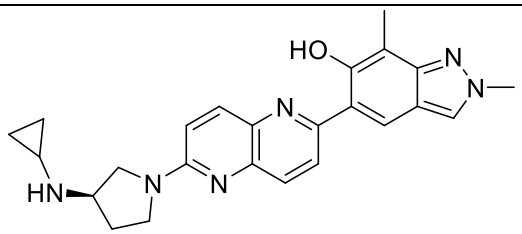
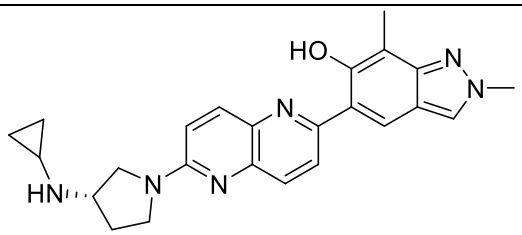
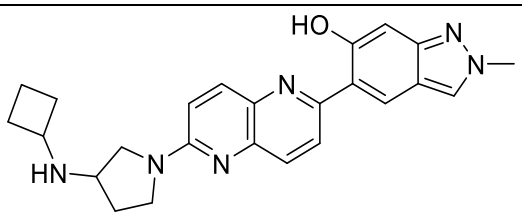
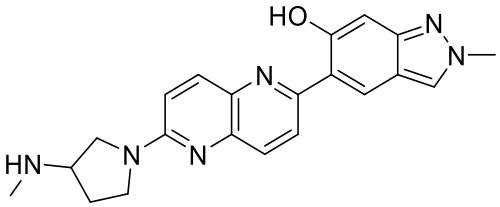
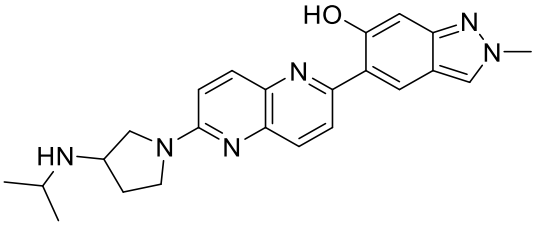
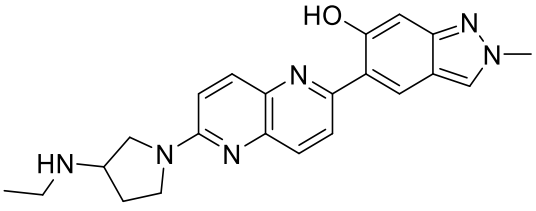
220	
221	
222	
223	
224	
225	
226	

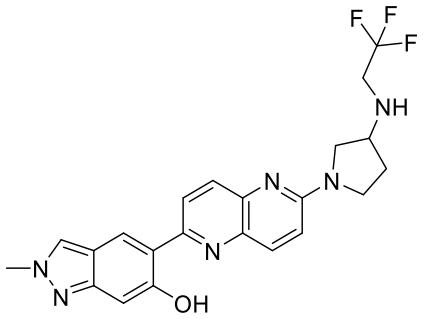
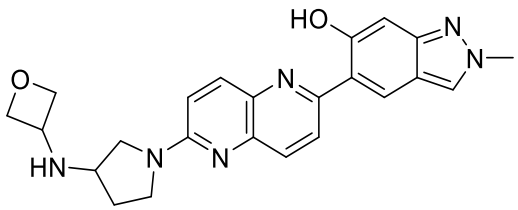
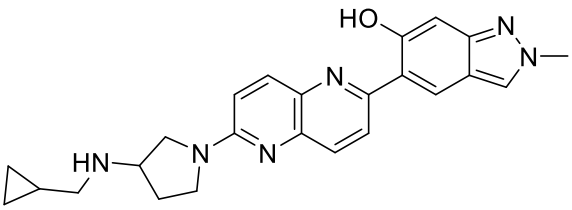
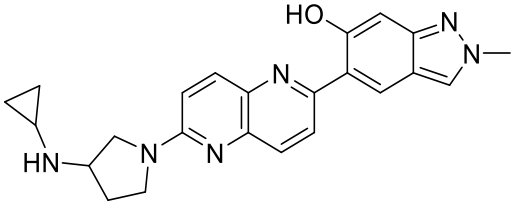
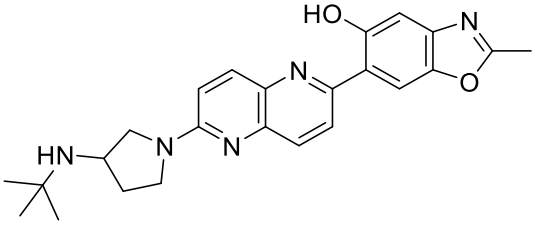
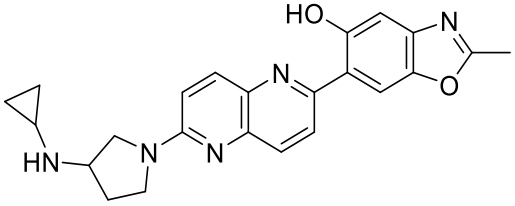
228	
229	
230	
231	
232	
233	

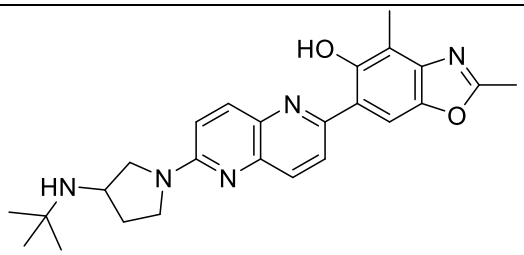
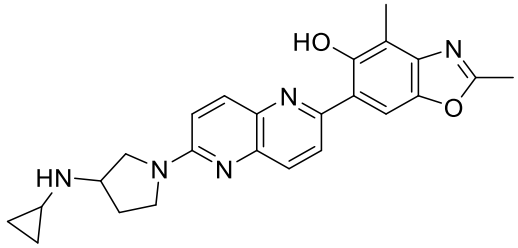
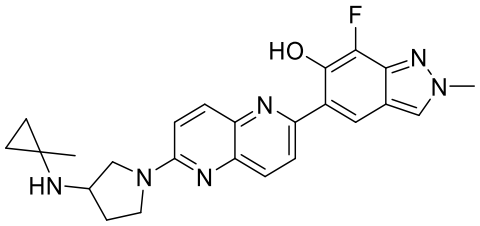
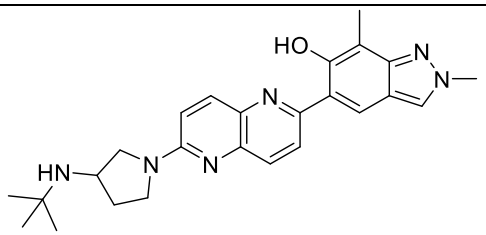
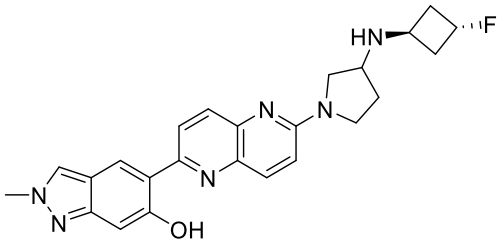
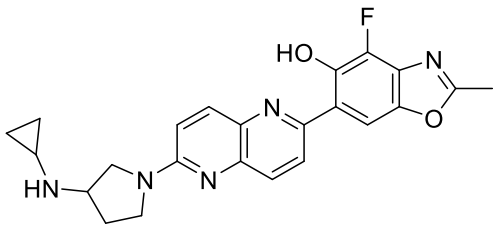
234	
235	
236	
237	
238	
245	

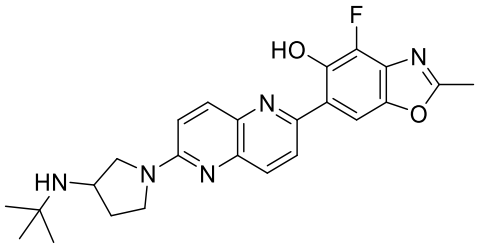
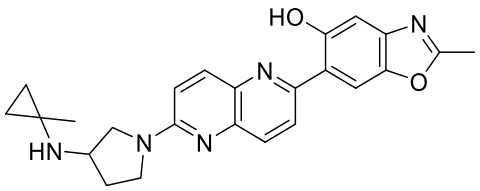
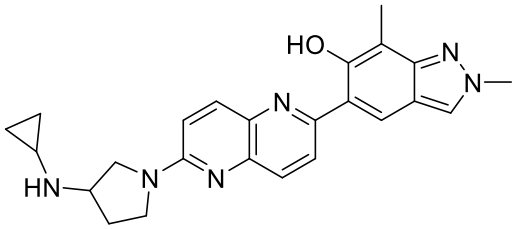
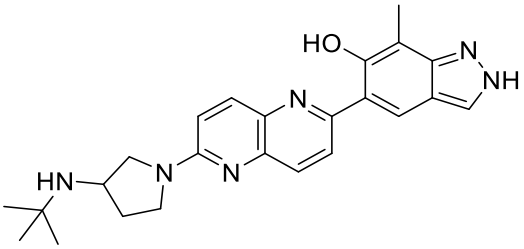
246	
247	
248	
249	
250	
251	

252	
253	
254	
255	
256	
257	

258	
259	
260	
262	
263	
264	
265	

266	
267	
268	
269	
270	
271	

272	
273	
274	
275	
277	
278	

279	
280	
281	
282	

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof.

22. A pharmaceutical composition comprising a compound of any one of claims 1-21 and a pharmaceutically acceptable excipient.

23. The compound of any one of claims 1-21 or the pharmaceutical composition of claim 22, wherein:

(i) the compound alters a target nucleic acid;

(ii) the compound binds to a target nucleic acid; and/or

(iii) the compound stabilizes a target nucleic acid.

24. The compound of any one of claims 1-21 or the pharmaceutical composition of claim 22, wherein:

(i) the compound increases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more; and/or

(ii) the compound decreases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more.

25. An *in vitro* method of modulating splicing of a nucleic acid comprising contacting the nucleic acid with a compound of Formula (I-a) as described in any one of claims 1-21 or a pharmaceutical composition of claim 22.

26. The *in vitro* method of claim 25, wherein:

(i) the compound increases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more; and/or

(ii) the compound decreases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more.

27. An *in vitro* method of forming a complex comprising a component of a spliceosome, a nucleic acid, and a compound of Formula (I-a):

comprising contacting the nucleic acid with a compound of Formula (I-a), according to any one of claims 1-21 or the pharmaceutical composition of claim 22.

28. The *in vitro* method of claim 27, wherein the component of a spliceosome is recruited to the nucleic acid in the presence of the compound of Formula (I-a).

29. An *in vitro* method of altering the conformation of a nucleic acid comprising contacting the nucleic acid with a compound of Formula (I-a), according to any one of claims 1-21 or the pharmaceutical composition of claim 22.

30. The *in vitro* method of claim 29, wherein:

(i) the altering comprises forming a bulge in the nucleic acid;

(ii) the altering comprises stabilizing a bulge in the nucleic acid; and/or

(iii) the altering comprises reducing a bulge in the nucleic acid.

31. The *in vitro* method of any one of claims 29-30, wherein the nucleic acid comprises a splice site.

32. A composition for use in treating a disease or disorder in a subject comprising a compound of Formula (I-a), according to any one of claims 1-21 or the pharmaceutical composition of claim 22.

33. Use of a compound of Formula (I-a), according to any one of claims 1-21 or the pharmaceutical composition of claim 22 in the manufacture of a medicament for treating a disease or disorder.

34. The use of claim 33, wherein the disease or disorder comprises a proliferative disease.

35. The use of claim 33, wherein the disease or disorder comprises a neurological disease or disorder, autoimmune disease or disorder, immunodeficiency disease or disorder, lysosomal storage disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, respiratory disease or disorder, renal disease or disorder, or infectious disease.