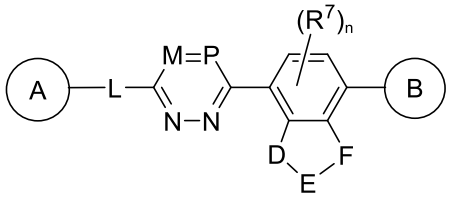
CLAIMS

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



(I-d)

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

A is nitrogen-containing heterocyclyl, optionally substituted with one or more R^1; and B is nitrogen-containing heterocyclyl or heteroaryl, optionally substituted with one or more R^1;

L is absent, -O-, or -N(R^3)-;

M and P are each independently C(R^2) or N, wherein M and P are not both N;

D, E, and F are each independently C(R^{5d}), C(R^{5d})(R^{5e}), N, N(R^{5f}), S, or O, wherein the bonds between the atoms in the ring comprising D, E, and F may be a single bonds or double bonds as valency permits;

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, aryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkenylene-aryl, C_1-C_6 alkylene-heteroaryl, heteroaryl, halo, cyano, oxo, –OR^A, –NR^BR^C, –$NR^BC(O)R^D$, –NO_2, –$C(O)NR^BR^C$, –$C(O)R^D$, –$C(O)OR^D$, –SR^E, 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^8; 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^8;

each R^2 is independently hydrogen, halo, cyano, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, or –OR^A;

each R^3 is independently hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl or heterocyclyl; wherein each alkyl, heteroalkyl, haloalkyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more R^{12};

R^{5d} and R^{5e} are each independently hydrogen, halo, or C_1-C_6 alkyl; or

R^{5d} and R^{5e} are taken together to form an oxo group;

R^{5f} is hydrogen, halo, or C_1-C_6 alkyl;

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, halo, oxo, cyano, $NR^BC(O)R^D$, $–C(O)NR^BR^C$, $–C(O)R^D$, or $–SR^E$, wherein alkyl, alkenyl, alkynyl, heteroalkyl, and haloalkyl are optionally substituted with one or more R^9;

R^8 and R^9 are each 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, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, $–SR^E$, 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^{11};

each R^A is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, aryl, heteroaryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkylene-heteroaryl, $–C(O)R^D$, or $–S(O)_xR^D$;

each of R^B and R^C is independently hydrogen, C_1-C_6 alkyl, C_1-C_6-heteroalkyl, cycloalkyl, heterocyclyl, $–OR^A$; 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^{10};

each R^D and R^E 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, aryl, heteroaryl, C_1-C_6 alkylene-aryl, or C_1-C_6 alkylene-heteroaryl;

each R^{10} is independently C_1-C_6-alkyl or halo;

each R^{11} is independently C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, or $–OR^A$;

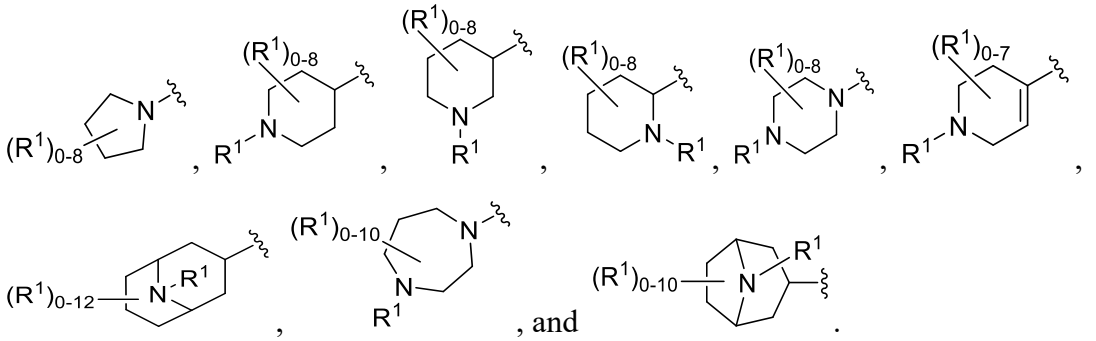
each R^{12} is independently deuterium, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, or $–OR^A$;

n is 0, 1, 2, 3, or 4; and

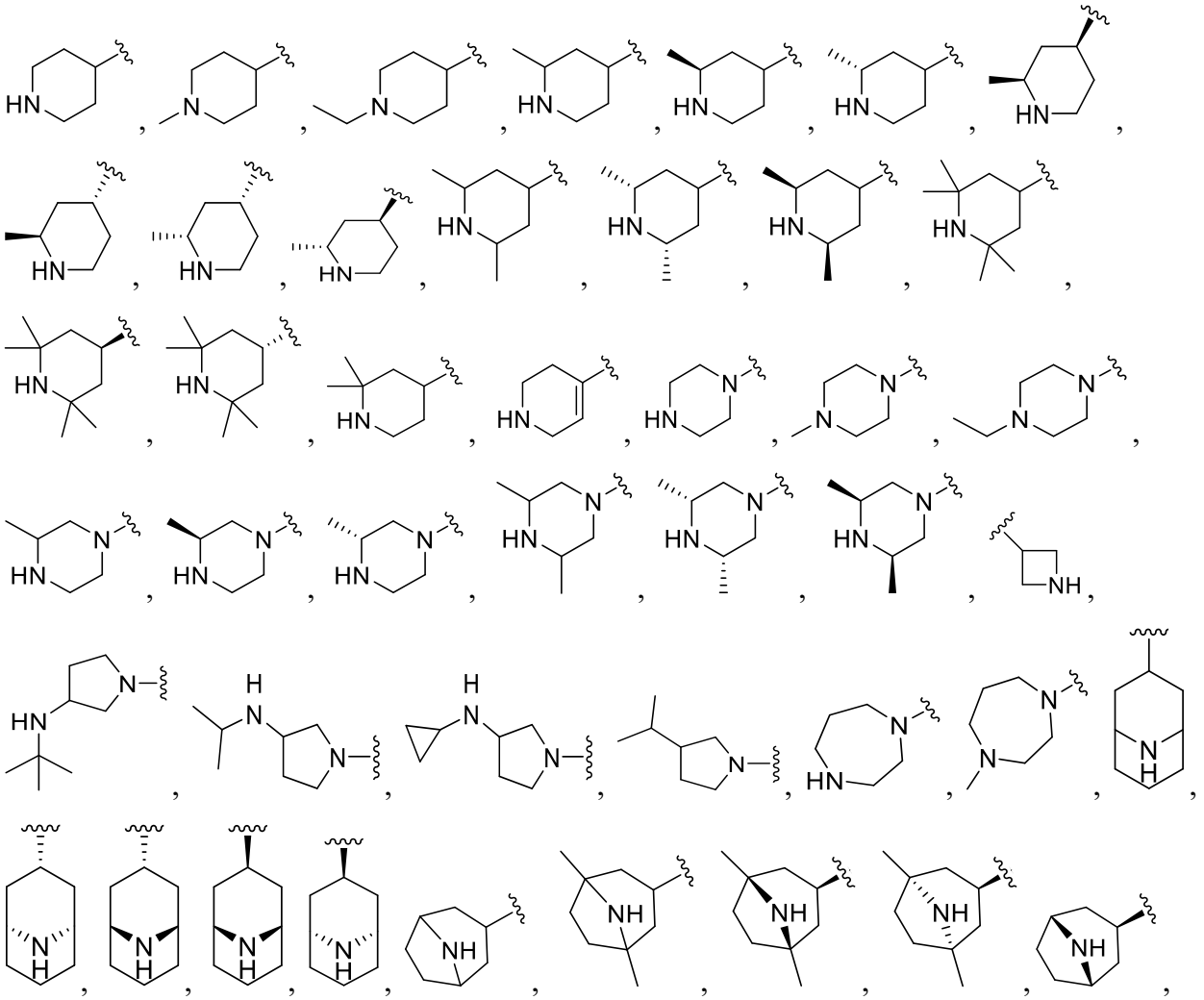
x is 0, 1, or 2.

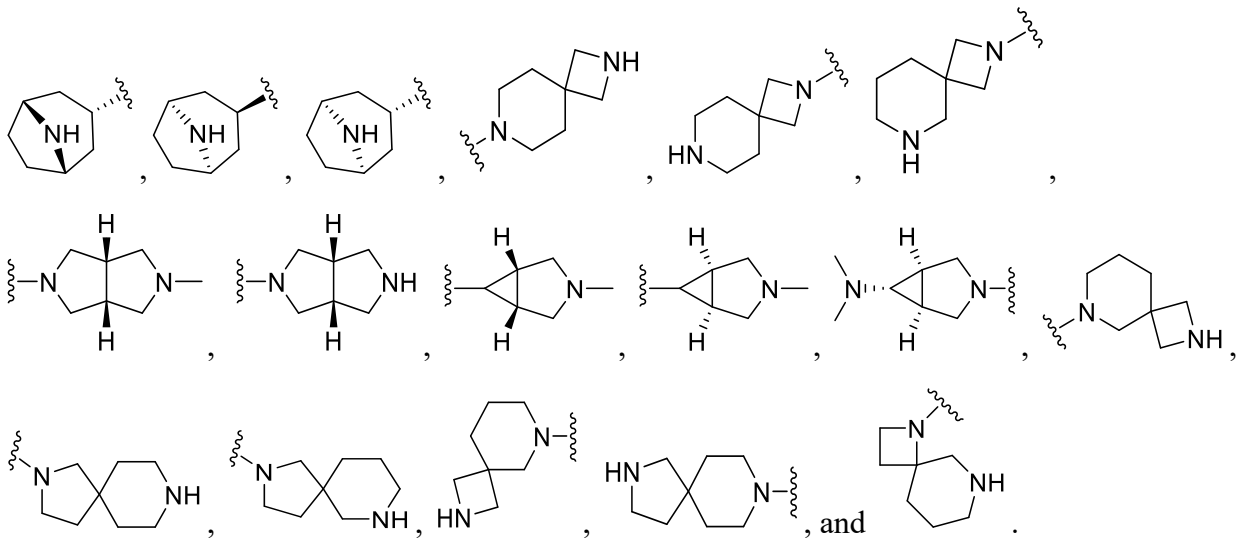
2. The compound of claim 1, wherein A is a monocyclic or bicyclic heterocyclyl.

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

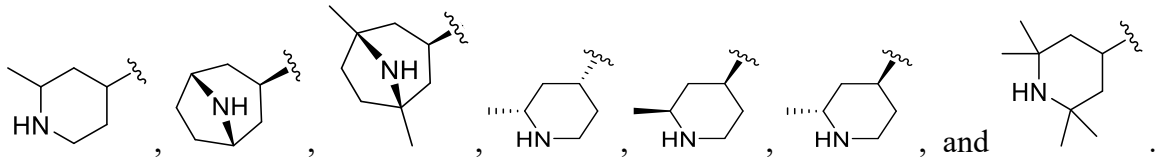


4. The compound of any one of the preceding claims, wherein A is selected from

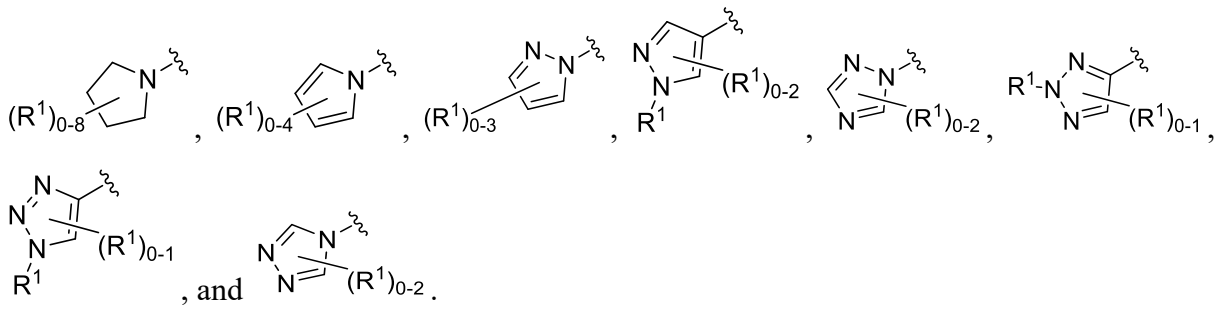




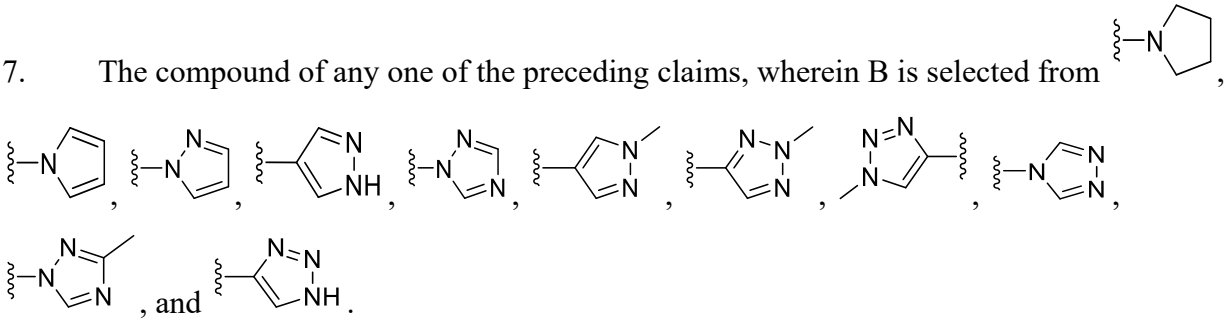
5. The compound of any one of the preceding claims, wherein A is selected from

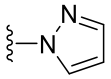
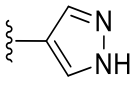


6. The compound of any one of the preceding claims, wherein B is selected from



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



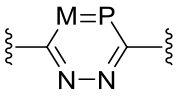
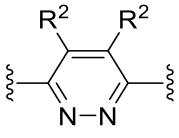
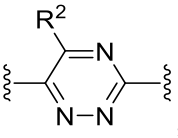
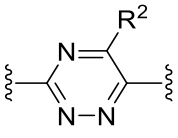
8. The compound of any one of the preceding claims, wherein B is selected from  and .

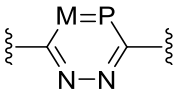
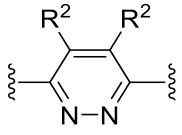
9. The compound of any one of the preceding claims, wherein L is -O- or -N(R^3)-.

10. The compound of any one of the preceding claims, wherein L is -N(R^3)- and R^3 is hydrogen, C_1-C_6-alkyl, or cycloalkyl, wherein each alkyl and heteroalkyl are each optionally substituted with one or more R^{12}.

11. The compound of any one of the preceding claims, wherein L is -N(CH_3)- or -N(H)-.

12. The compound of any one of the preceding claims, wherein L is -N(CH_3)-.

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

14. The compound of any one of the preceding claims, wherein  is .

15. The compound of any one of the preceding claims, wherein each of M and P is independently C(R^2).

16. The compound of any one of claims 1-13, wherein one of M and P is independently $C(R^2)$ and the other of M and P is independently N.

17. The compound of any one of claims 1-13 and 16, wherein M is CH and P is N.

18. The compound of any one of the preceding claims, wherein one of D, E, and F is independently N or $N(R^{5f})$.

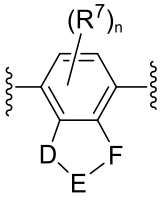
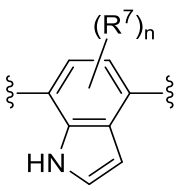
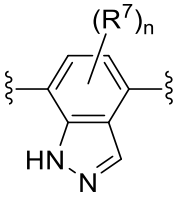
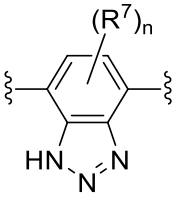
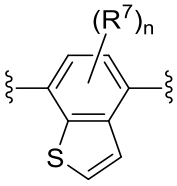
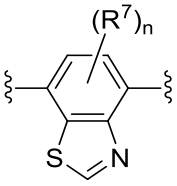
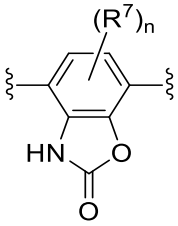
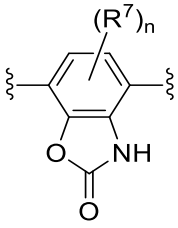
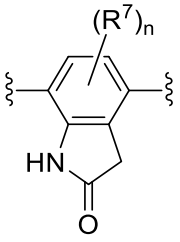
19. The compound of any one of the preceding claims, wherein two of D, E, and F is independently N or $N(R^{5f})$.

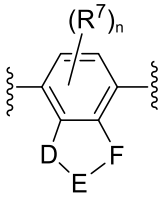
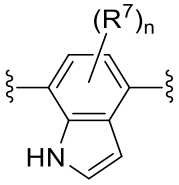
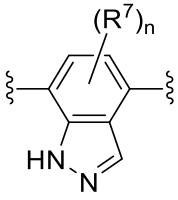
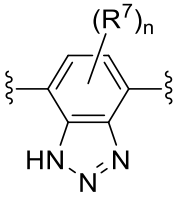
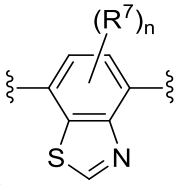
20. The compound of any one of claims 1-17, wherein D is N, $N(R^{5f})$, or S.

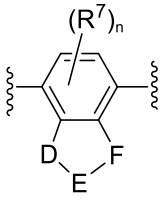
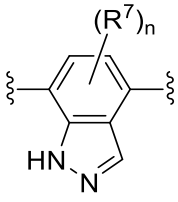
21. The compound of any one of the preceding claims, wherein D is N or $N(R^{5f})$.

22. The compound of any one of the preceding claims, wherein each of D and E is independently N or $N(R^{5f})$.

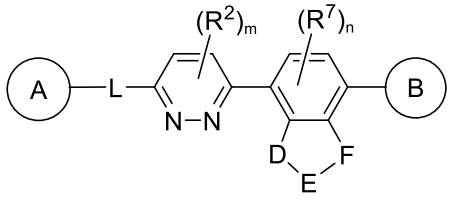
23. The compound of any one of the preceding claims, wherein F is $C(R^{5d})$ or $C(R^{5d})(R^{5e})$.

24. The compound of any one of claims 1-17, wherein  is selected from , , , , , , , and .

25. The compound of claim 24, wherein  is selected from , , , and .

26. The compound of claim 25, wherein  is .

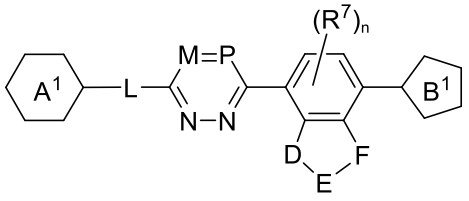
27. The compound of claim 1, wherein the compound is a compound of Formula (I-e):



(I-e),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein m is 2; and wherein A, B, L, D, E, F, R^2, R^7, n, and subvariables thereof are as described in claim 1.

28. The compound of claim 1, wherein the compound is a compound of Formula (I-f):



(I-f),

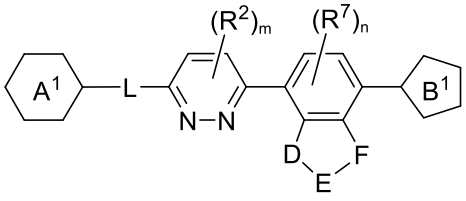
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein:

A^1 is 6-membered heterocyclyl, optionally substituted with one or more R^1;

B^1 is 5-membered heterocyclyl, or heteroaryl, each of which is optionally substituted with one or more R^1; and

L, M, P, D, E, F, R^1, R^7, n, and subvariables thereof are as described in claim 1.

29. The compound of claim 1, wherein the compound is a compound of Formula (I-g):



(I-g),

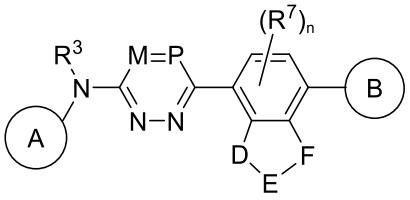
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein:

A^1 is 6-membered heterocyclyl, optionally substituted with one or more R^1;

B^1 is 5-membered heterocyclyl, or heteroaryl, each of which is optionally substituted with one or more R^1; m is 2; and

L, D, E, F, R^1, R^2, R^7, n, and subvariables thereof are as described in claim 1.

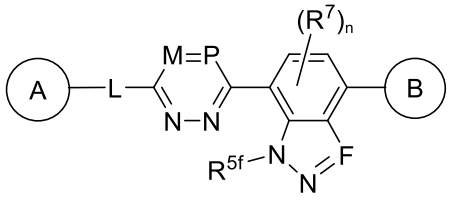
30. The compound of claim 1, wherein the compound is a compound of Formula (I-h):



(I-h),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, M, P, D, E, F, R^3, R^7, n, and subvariables thereof are as described in claim 1.

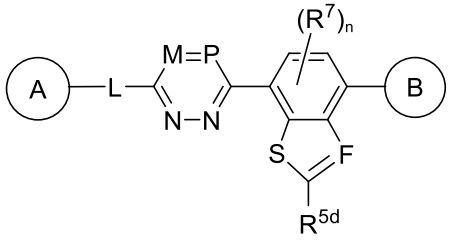
31. The compound of claim 1, wherein the compound is a compound of Formula (I-k):



(I-k),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, M, P, L, F, R^{5f}, R^7, n, and subvariables thereof are as described in claim 1.

32. The compound of claim 1, wherein the compound is a compound of Formula (I-n):



(I-n),

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, M, P, L, F, R^{5d}, R^7, n, and subvariables thereof are as described in claim 1.

33. The compound of claim 1, wherein:

A is a monocyclic, bicyclic, or tricyclic heterocyclyl;

B is a monocyclic heterocyclyl or heteroaryl;

L is absent, -N(R^3)-, or -O-;

M is CH;

P is CH or N;

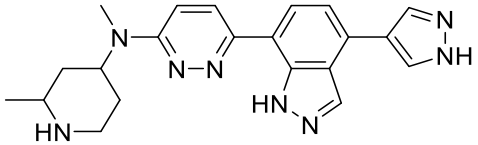
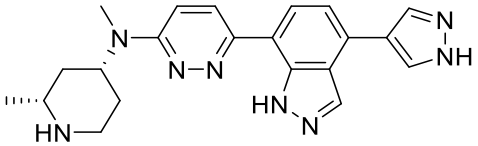
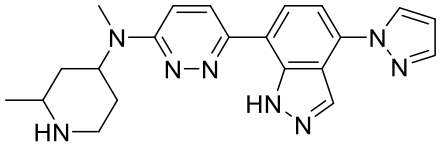
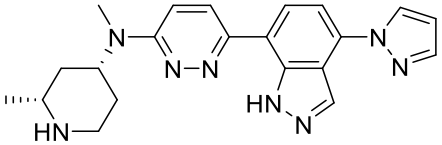
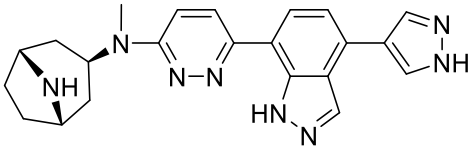
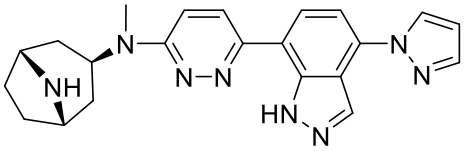
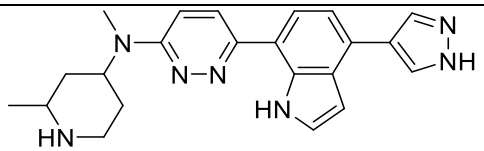
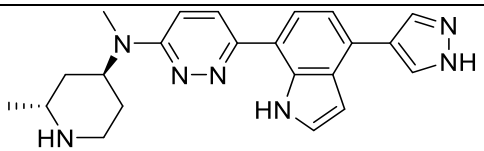
D is N(R^{5f}), C(R^{5d}), or S;

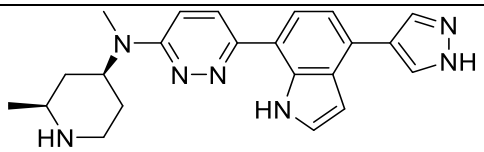
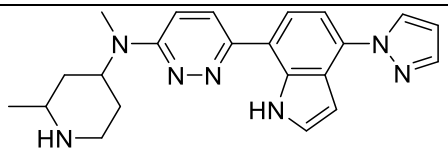
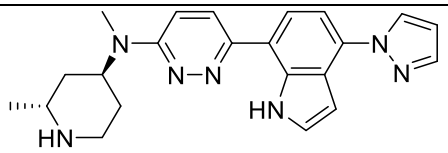
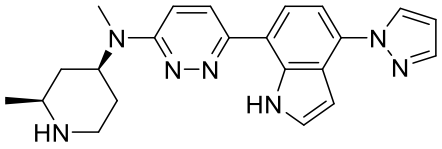
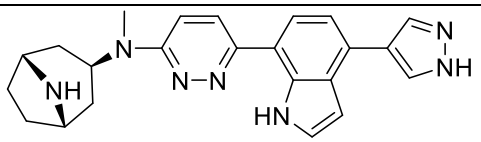
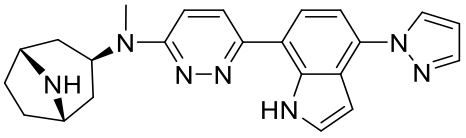
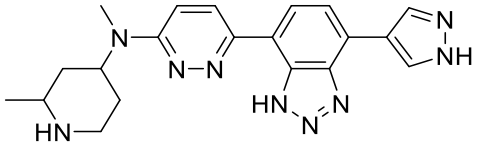
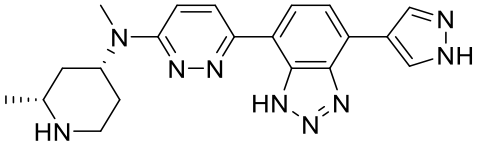
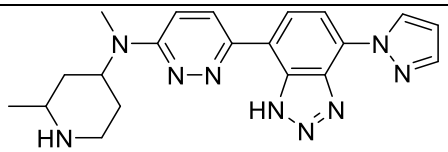
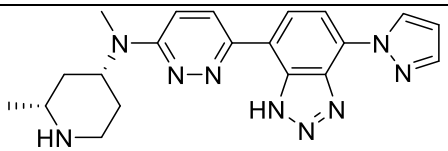
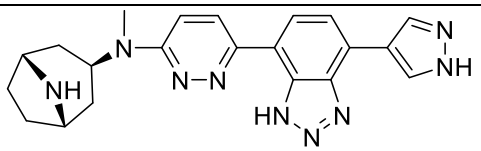
E and F is each independently N, NH, C(R^{5d}), C(R^{5d})(R^{5e});

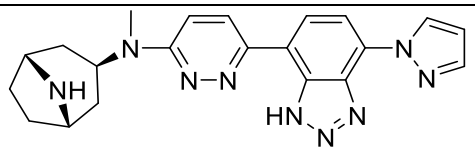
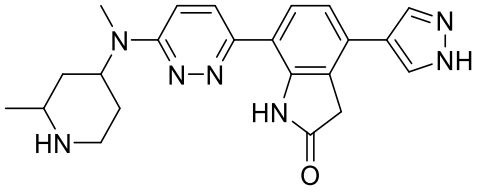
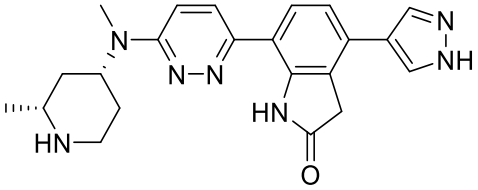
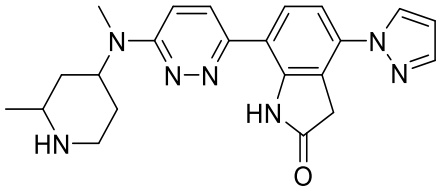
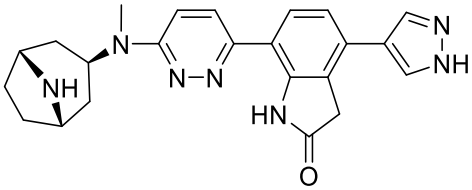
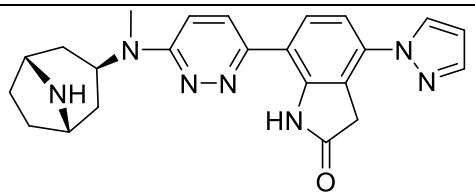
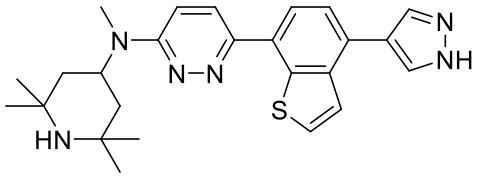
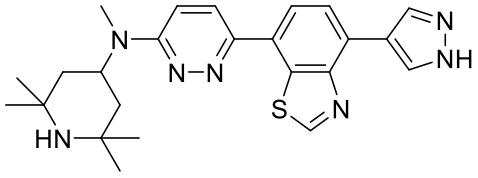
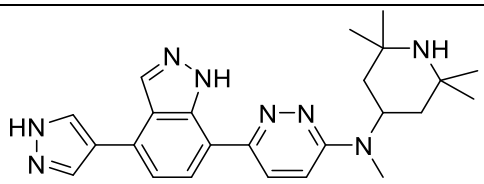
R^7 is halo; and

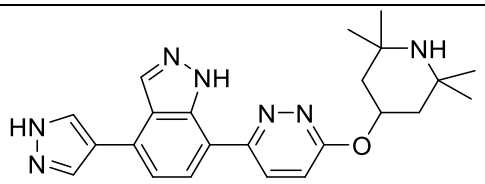
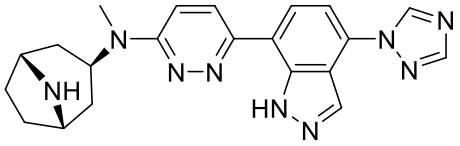
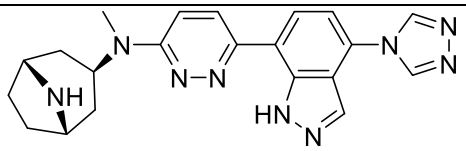
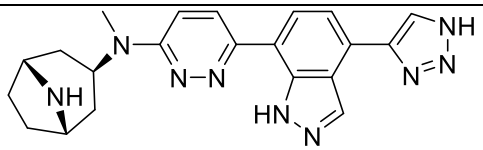
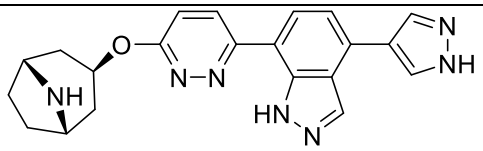
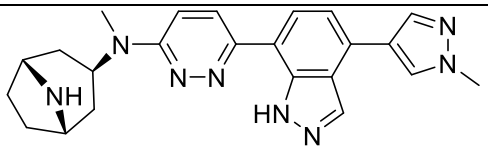
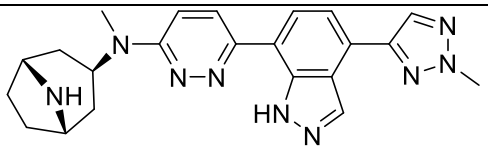
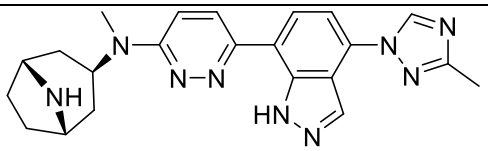
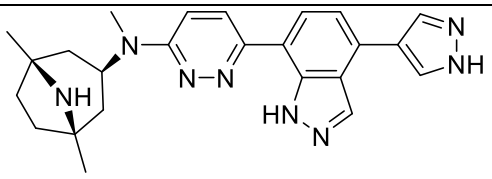
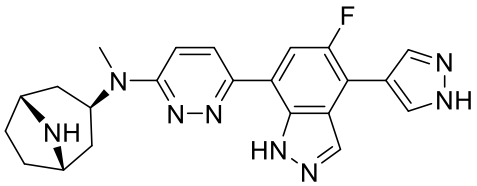
m is 0 or 1.

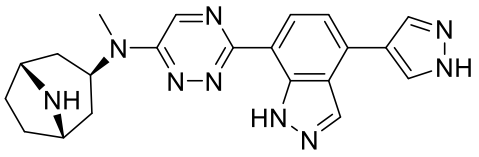
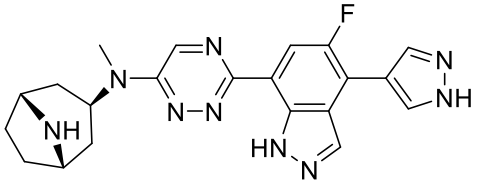
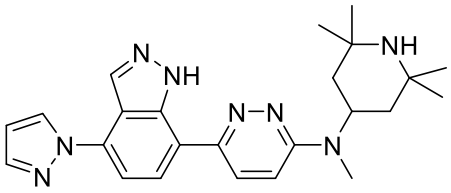
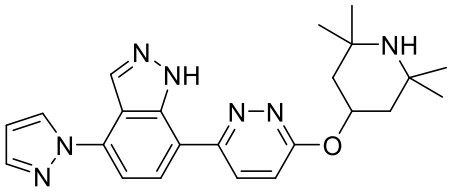
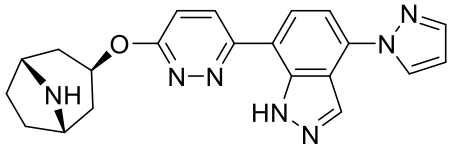
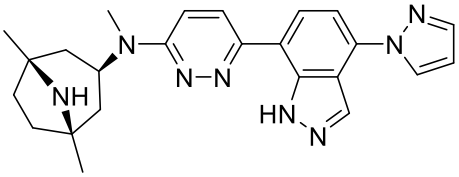
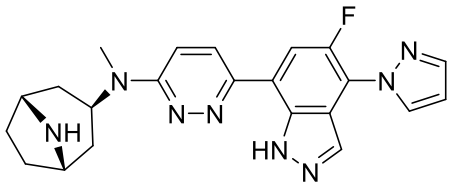
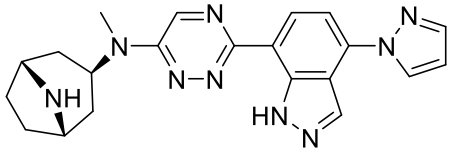
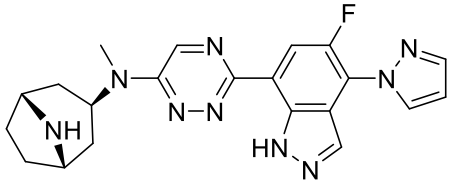
34. The compound of claim 1, wherein the compound is selected from any one of the following compounds:

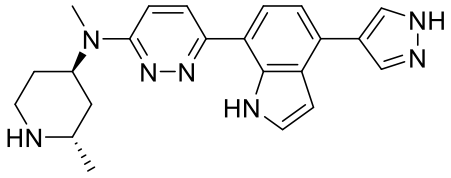
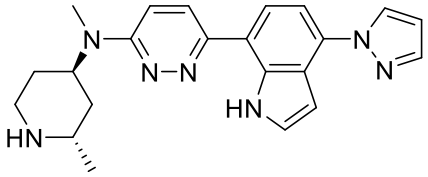
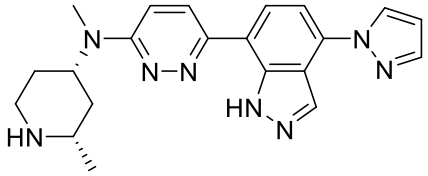
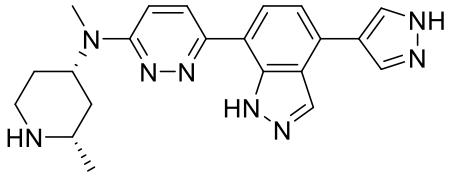
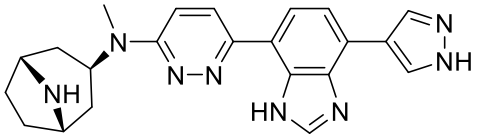
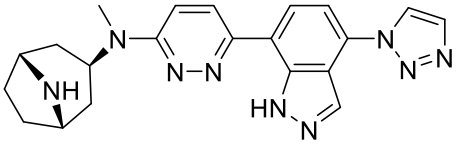
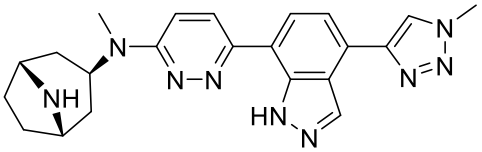
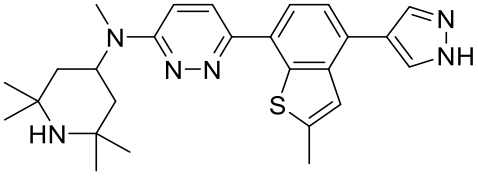
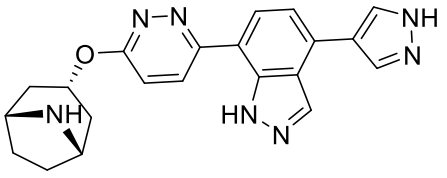
Compound No.	Structure
100	
101	
102	
103	
104	
105	
106	
107	

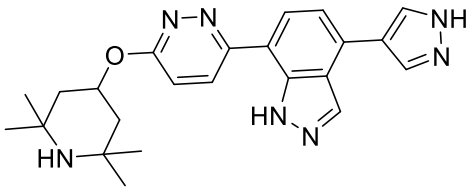
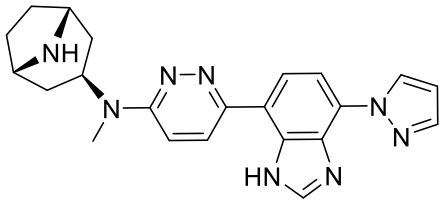
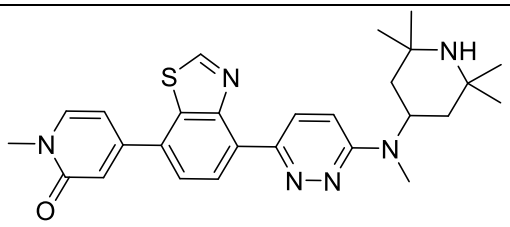
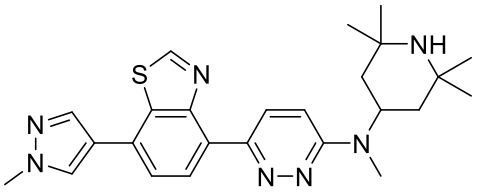
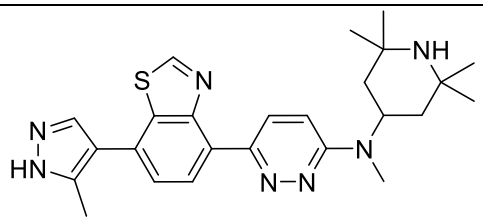
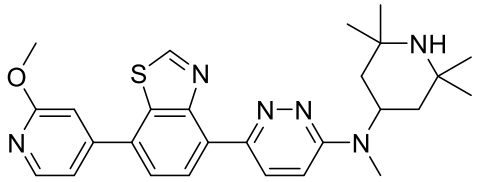
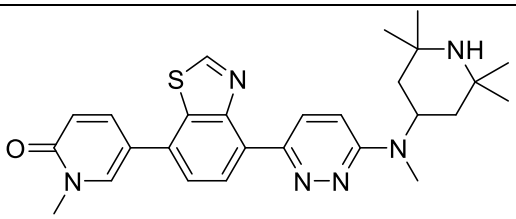
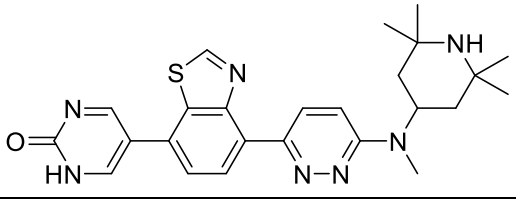
108	
109	
110	
111	
112	
113	
114	
115	
116	
117	
118	

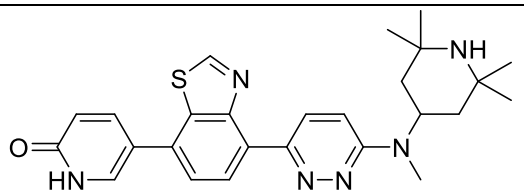
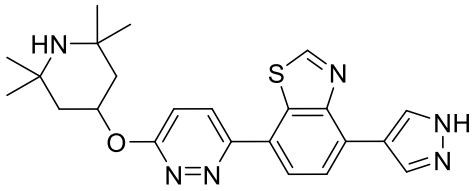
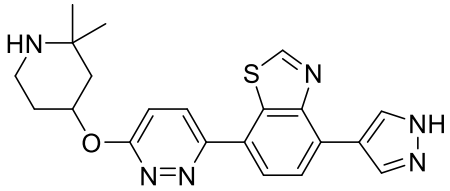
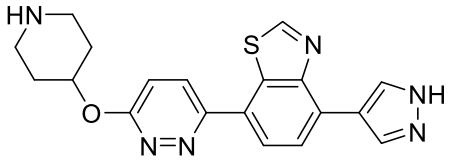
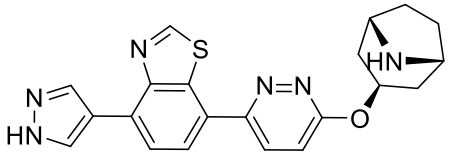
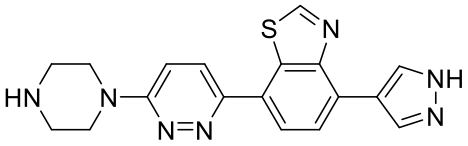
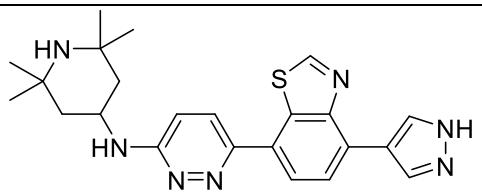
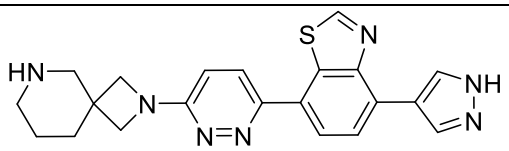
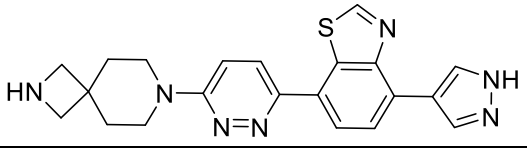
119	
120	
121	
122	
123	
124	
131	
132	
137	

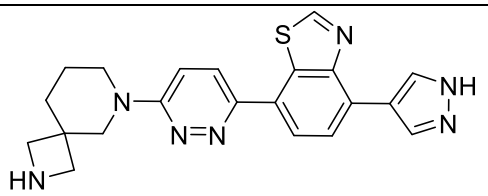
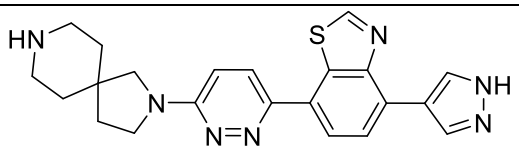
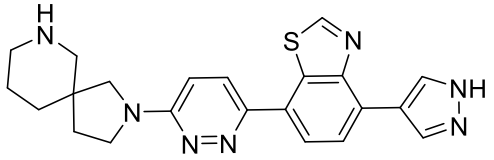
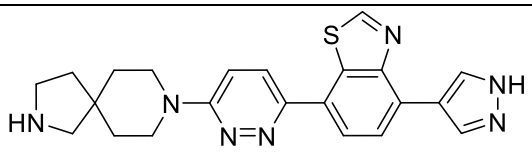
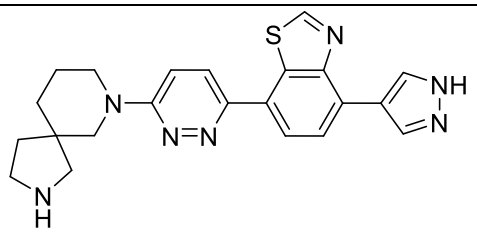
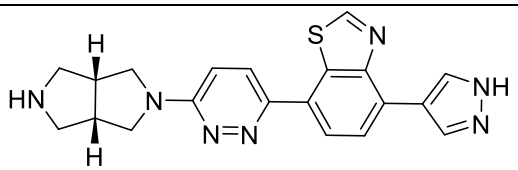
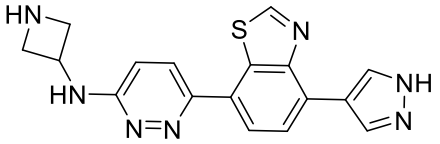
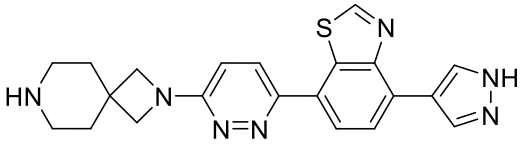
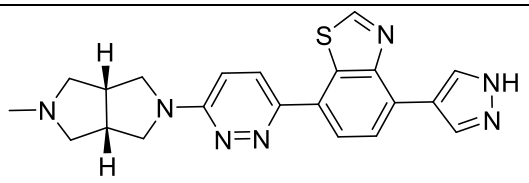
138	
139	
140	
141	
142	
143	
144	
145	
146	
147	

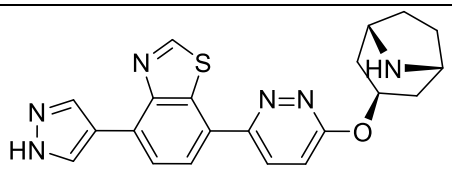
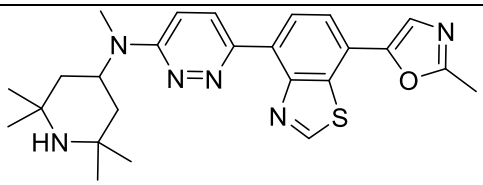
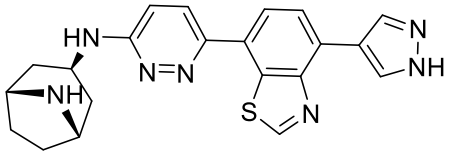
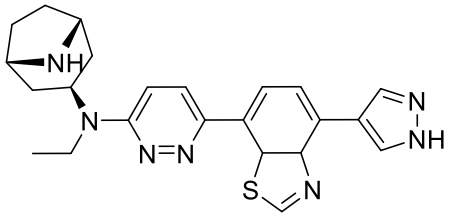
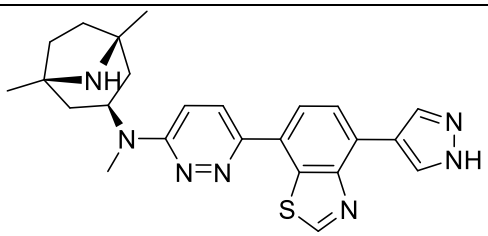
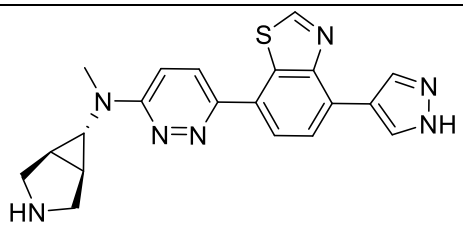
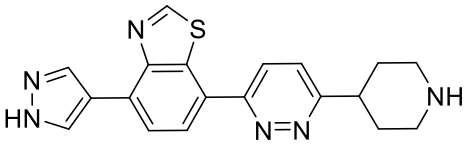
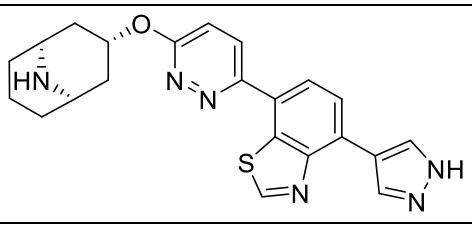
148	
149	
150	
151	
152	
153	
154	
155	
156	

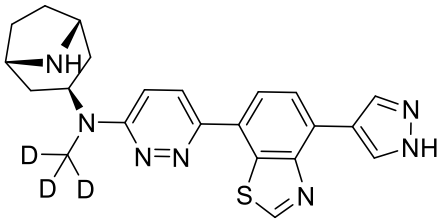
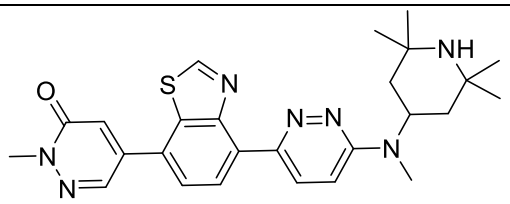
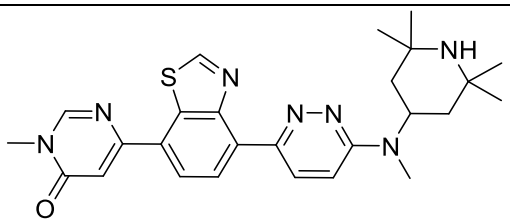
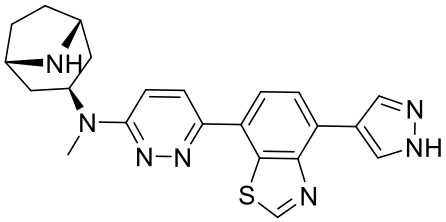
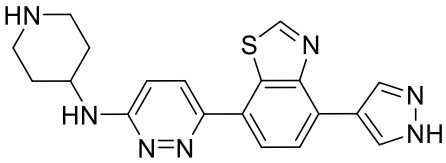
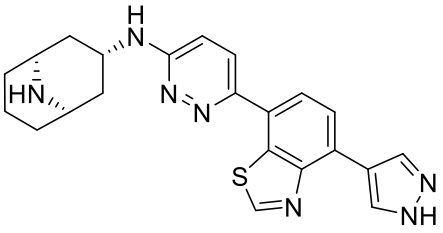
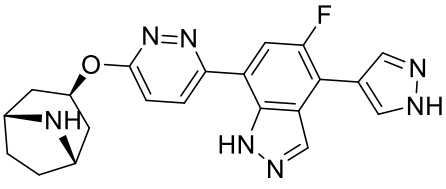
157	
158	
159	
160	
163	
164	
165	
166	
168	

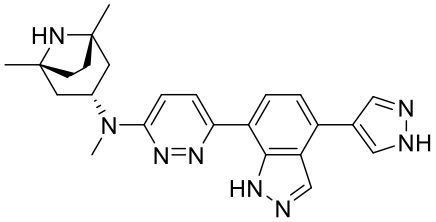
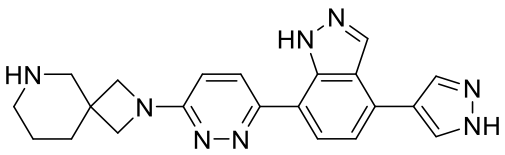
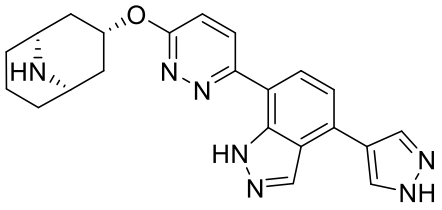
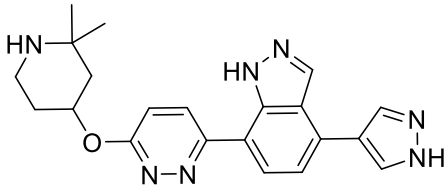
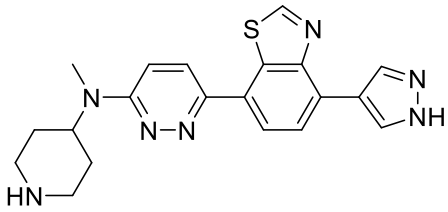
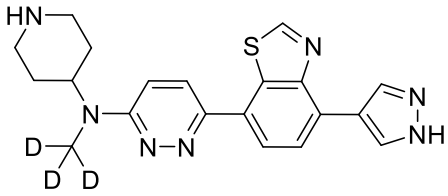
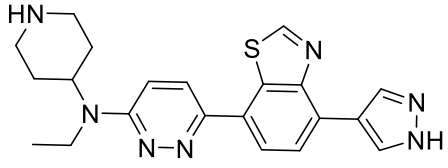
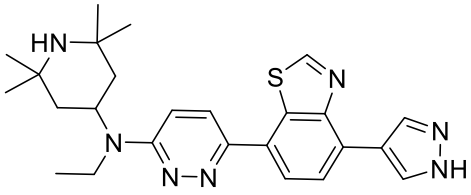
169	
170	
174	
175	
176	
177	
178	
179	

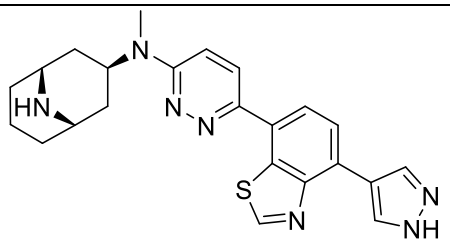
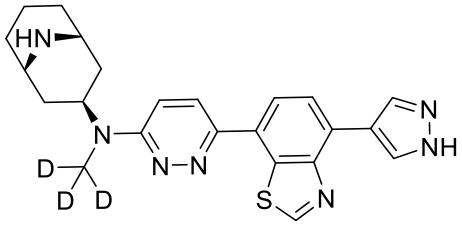
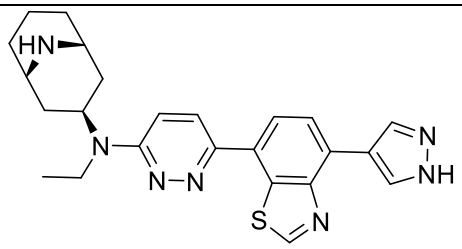
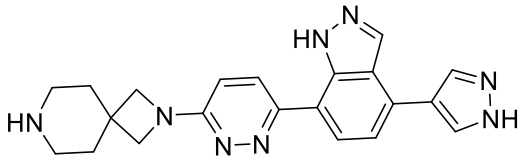
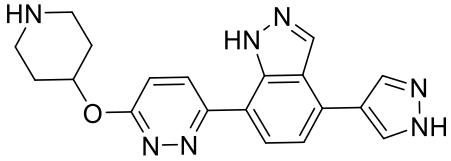
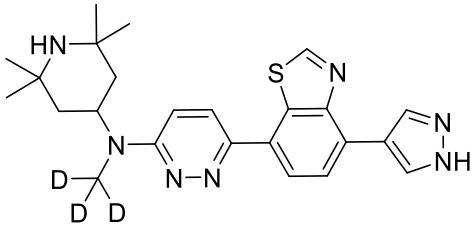
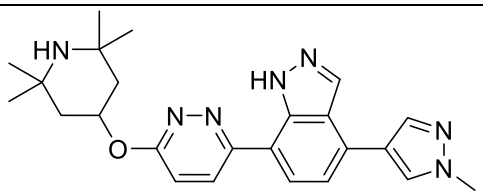
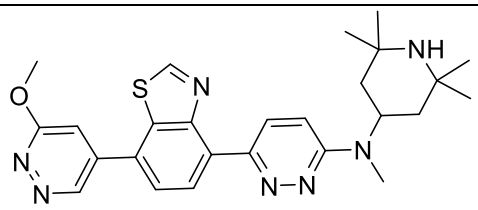
180	
181	
182	
183	
184	
185	
186	
187	
188	

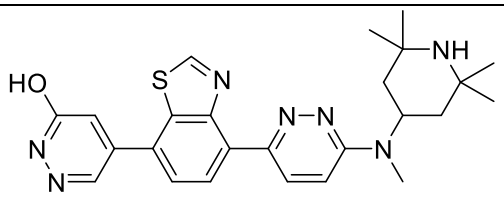
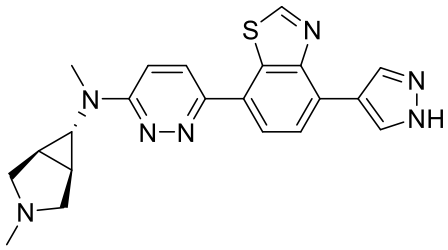
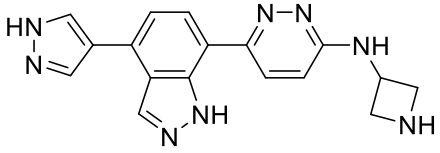
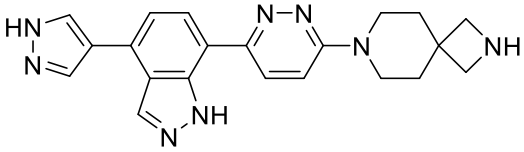
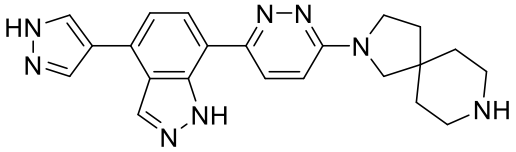
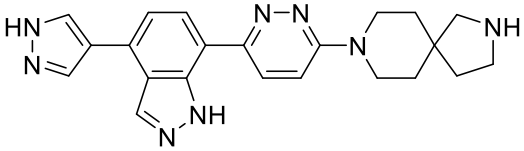
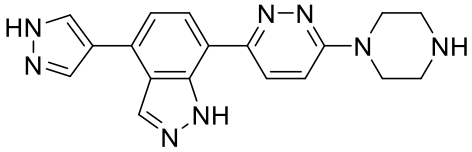
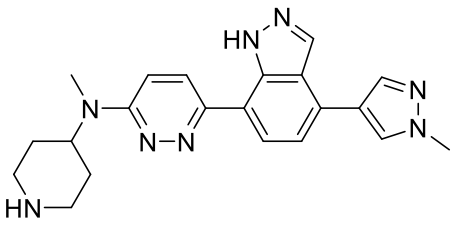
189	
190	
191	
192	
193	
194	
196	
197	
198	

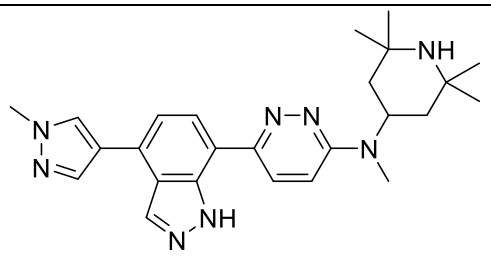
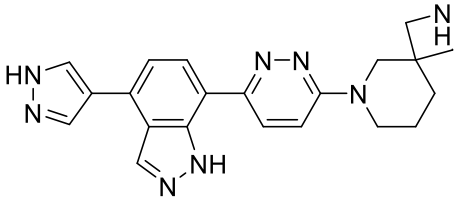
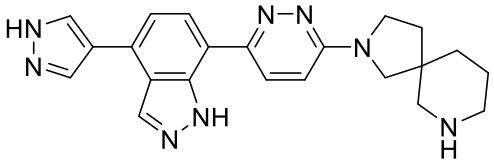
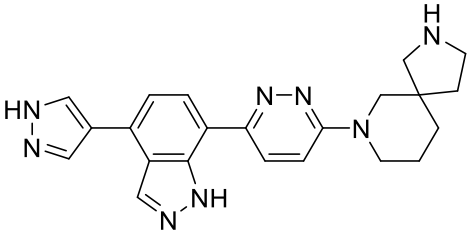
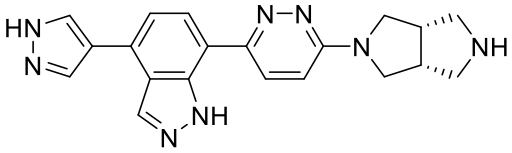
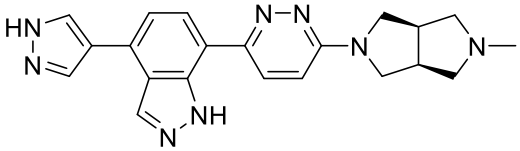
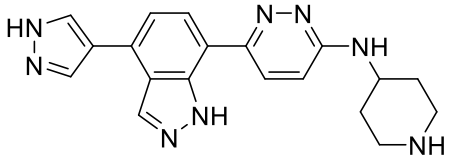
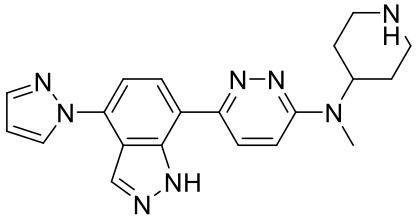
199	
201	
202	
203	
204	
205	
206	
209	

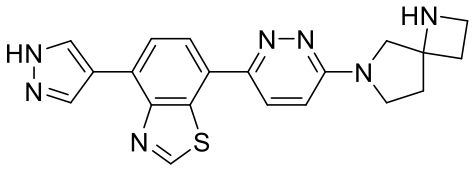
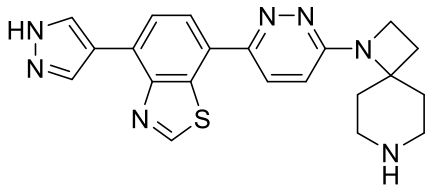
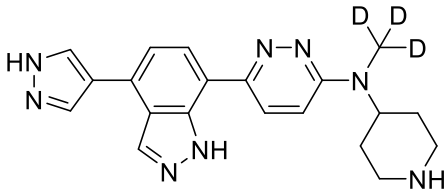
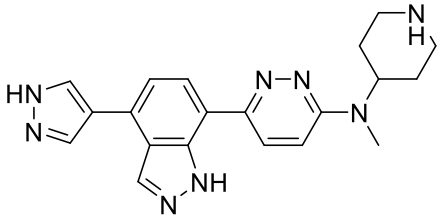
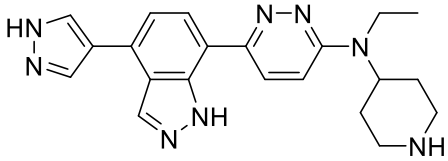
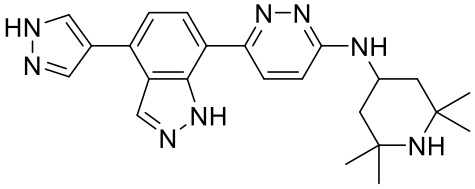
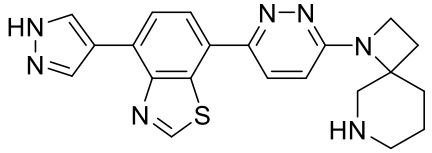
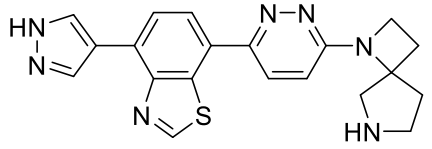
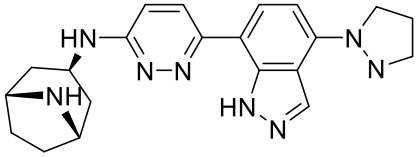
210	
211	
212	
213	
214	
215	
216	

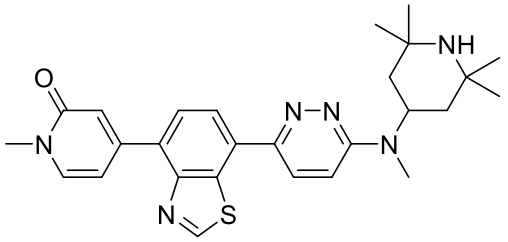
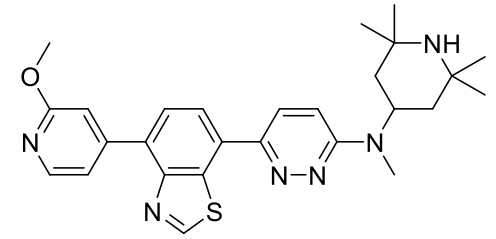
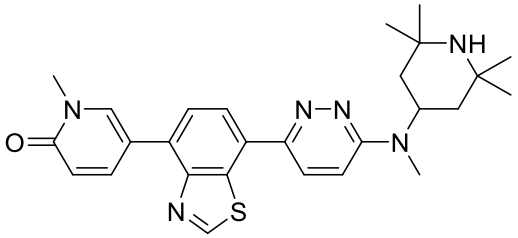
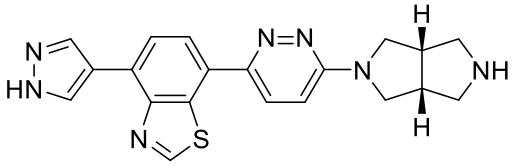
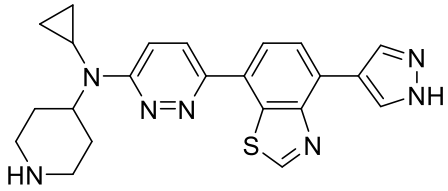
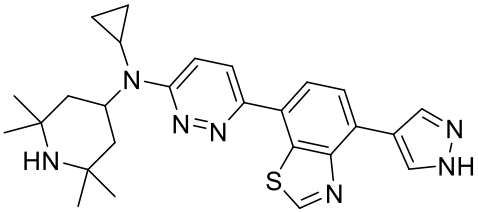
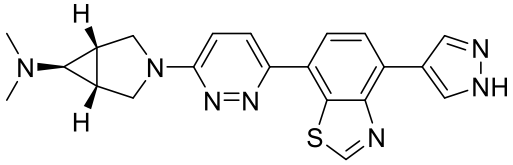
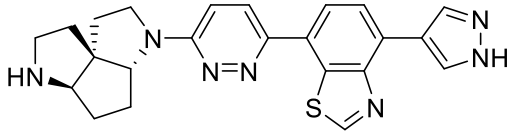
217	
218	
219	
220	
222	
223	
224	
225	

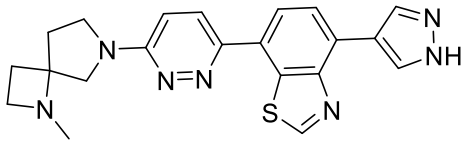
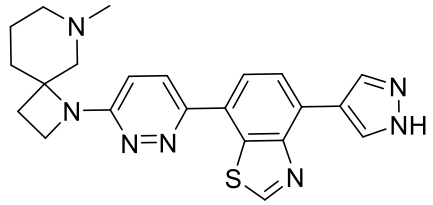
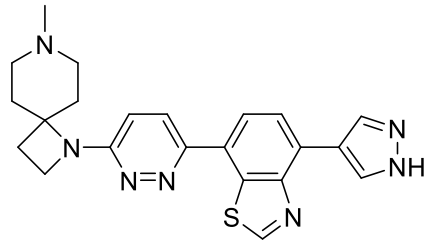
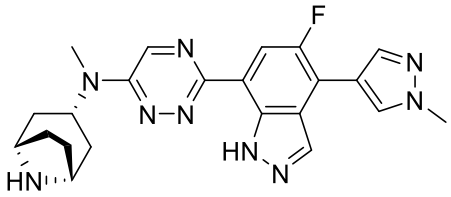
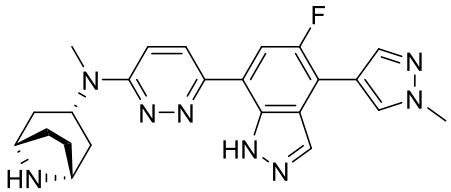
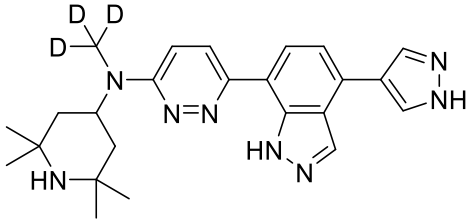
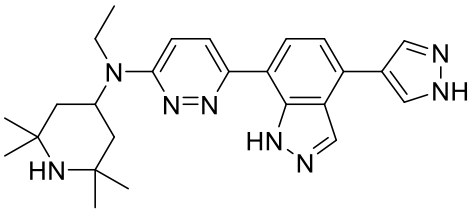
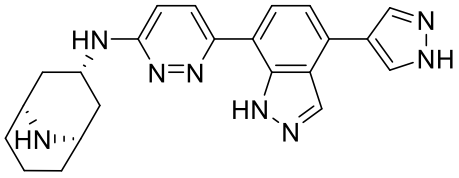
226	
227	
228	
229	
230	
231	
232	
233	

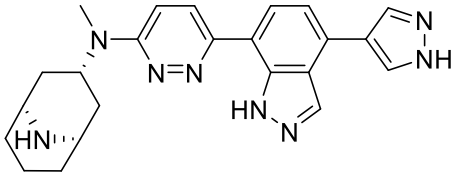
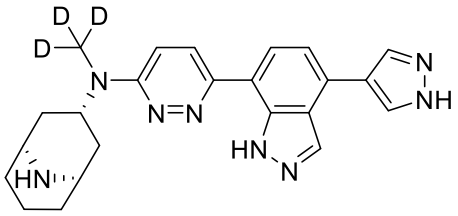
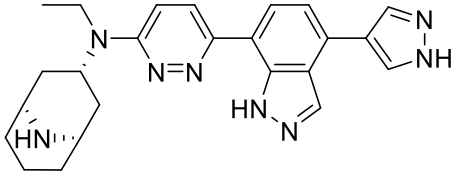
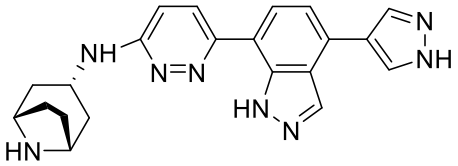
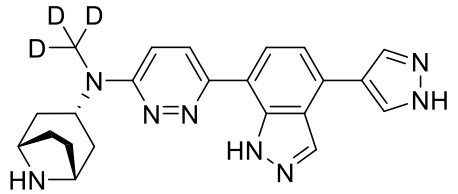
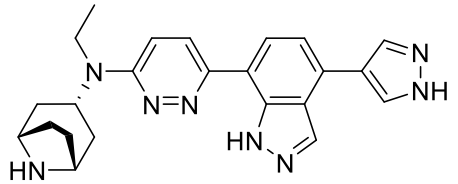
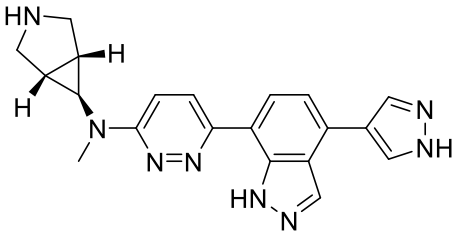
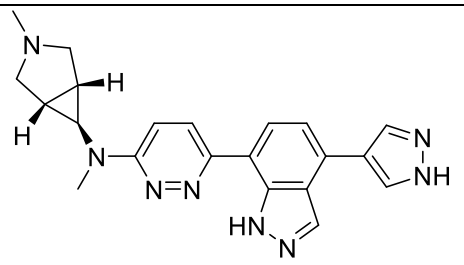
234	
235	
237	
238	
239	
240	
241	
242	

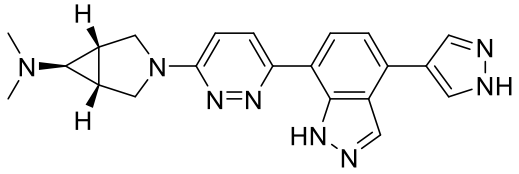
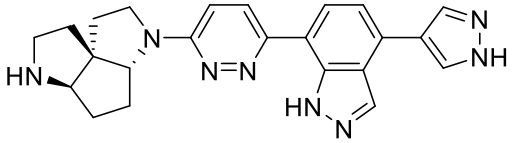
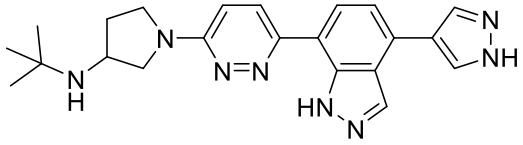
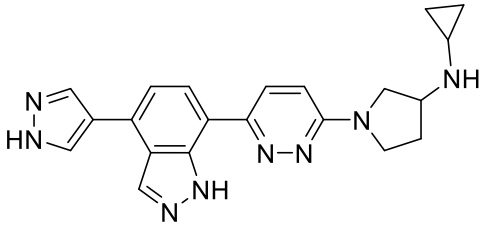
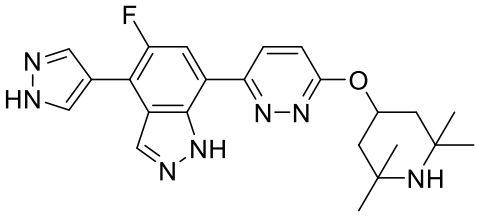
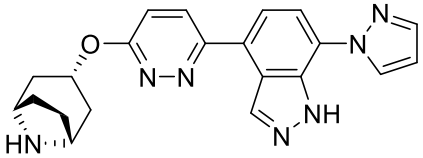
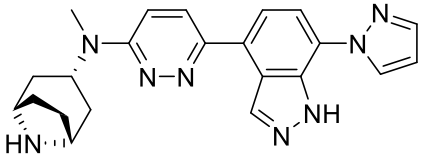
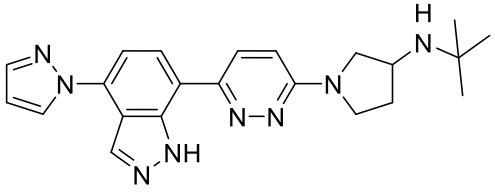
243	
251	
252	
253	
254	
255	
263	
264	

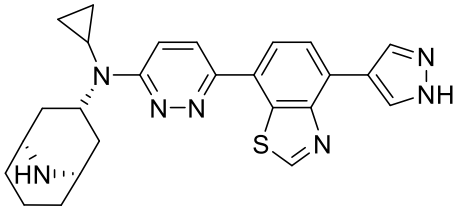
265	
266	
267	
273	
274	
275	
276	
277	
278	

279	
280	
281	
282	
283	
284	
285	
286	

287	
288	
289	
290	
291	
292	
293	
294	

295	
296	
297	
298	
299	
300	
301	
302	

303	
304	
305	
306	
307	
308	
309	
310	

311	

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

35. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable excipient.

36. The compound of any one of claims 1-34, or the pharmaceutical composition of claim 35, wherein the compound:

(i) alters a target nucleic acid

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

(iii) stabilizes a target nucleic acid.

37. The compound of any one of claims 1-34, or the pharmaceutical composition of claim 35, wherein the compound

(i) 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; or

(ii) 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.

38. A method of forming a complex comprising a component of a spliceosome (, a nucleic acid, and a compound of Formula (I-d) according to any one of claims 1-34, comprising contacting the nucleic acid with a compound of Formula (I-d).

39. The method of claim 38, wherein the component of a spliceosome is recruited to the nucleic acid in the presence of the compound of Formula (I-d).

40. A method of altering the conformation of a nucleic acid comprising contacting the nucleic acid with a compound of Formula (I-d) according to any one of claims 1-34 or the pharmaceutical composition of claim 35.

41. The method of claim 40, wherein the altering comprises:
(i) forming a bulge in the nucleic acid;
(ii) stabilizing a bulge in the nucleic acid; and/or
(iii) reducing a bulge in the nucleic acid.

42. The method of any one of claims 40-41, wherein the nucleic acid comprises a splice site.

43. Use of a compound of Formula (I-d) according to any one of claims 1-34 or the pharmaceutical composition of claim 35 in the manufacture of a medicament for the treatment of a disease or disorder in a subject, wherein the disease or disorder comprises a proliferative disease, or 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.

44. The use of claim 43, wherein the disease or disorder comprises neurological disease or disorder.

45. The use of claim 43, wherein the disease or disorder comprises Huntington's disease.

46. A compound of Formula (I-d) according to any one of claims 1-34 or the pharmaceutical composition of claim 35 for use in therapy.