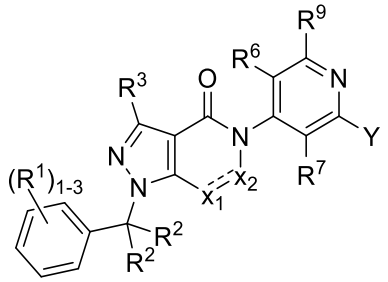
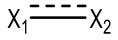
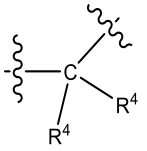
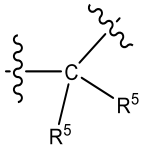
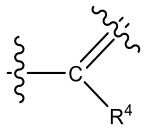
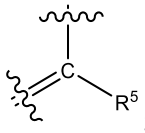
CLAIMS

1. A compound of Formula I:



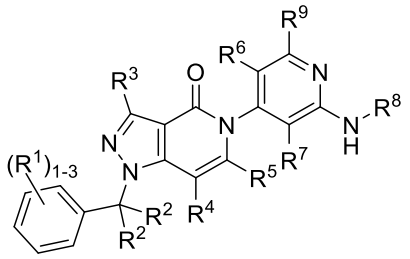
(Formula I),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, or a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

-  is a single bond or a double bond, wherein when a single bond is present, **x1** is  and **x2** is  and when a double bond is present, **x1** is  and **x2** is ;
- each **R1** is independently selected from hydrogen, C_1-C_3 alkyl (substituted with 0-2 groups selected from oxo, hydroxyl, and amino), C_1-C_3 alkoxy, halogen, and cyano;
- each **R2** is independently selected from hydrogen and C_1-C_3 alkyl;
- **R3** is selected from hydrogen, C_1-C_3 alkyl, halogen, and cyano;
- each **R4** and **R5** are independently selected from hydrogen, C_1-C_3 alkyl, and halogen;
- **R6** and **R9** are independently selected from hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, and cyano;
- **R7** is selected from hydrogen, C_1-C_3 alkyl, and halogen; and
- **R8** is selected from:
    - hydrogen,
    - C_1-C_8 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl,
        - oxo,
        - amino,

        - cyano,
        - halogen,
        - C_1-C_3 alkoxy (substituted with 0-1 oxo group),
        - C_3-C_6 cycloalkyl (substituted with 0-2 groups independently selected from hydroxyl, halogen, C_1-C_3 alkyl),
        - 3- to 7-membered heterocyclyl (substituted with 0-3 groups independently selected from halogen, hydroxyl, oxo, and C_1-C_3 alkyl (substituted with 0-1 hydroxyl group)), and
        - 5- to 6-membered heteroaryl (substituted with 0-3 groups independently selected from oxo, C_1-C_3 alkyl, and C_3-C_6 cycloalkyl);
    - C_3-C_7 cycloalkyl substituted with 0-3 groups independently selected from:
        - hydroxyl,
        - halogen,
        - C_1-C_3 alkyl (substituted with 0-3 groups independently selected from hydroxyl and halogen), and
        - C_1-C_3 alkoxy; and
    - 5- to 9-membered heterocyclyl substituted with 0-3 groups independently selected from:
        - oxo,
        - halogen,
        - hydroxyl, and
        - C_1-C_3 alkyl (substituted with 0-1 hydroxyl group); and
- **Y** is selected from
    - OR^8,
    - $N(R^8)_2$, and
    - 3- to 10-membered heterocyclyl or 3- to 10-membered heteroaryl, each of which is substituted with 0-2 groups independently selected from:
        - $N(R^8)_2$,
        - hydroxyl,
        - oxo,
        - C_1-C_3 alkoxy, and
        - C_1-C_3 alkyl (substituted with 0-2 groups selected from amino, hydroxyl, C_3-C_4 alkyl, oxo, and C_1-C_3 alkoxy).

2. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, selected from a compound of Formula Ia:



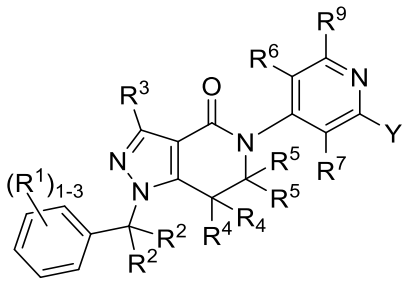
(Formula Ia),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

- each **R^1** is independently selected from hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, and cyano;
- each **R^2** is independently selected from hydrogen and C_1-C_3 alkyl;
- **R^3** is selected from hydrogen, C_1-C_3 alkyl, halogen, and cyano;
- **R^4** and **R^5** are independently selected from hydrogen, C_1-C_3 alkyl, and halogen;
- **R^6** and **R^9** are independently selected from hydrogen, C_1-C_3 alkyl, halogen, and cyano;
- **R^7** is selected from hydrogen, C_1-C_3 alkyl, and halogen; and
- **R^8** is selected from:
    - hydrogen,
    - C_1-C_8 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl,
        - oxo,
        - amino,
        - cyano,
        - halogen,
        - C_1-C_3 alkoxy (substituted with 0-1 oxo group),
        - C_3-C_6 cycloalkyl (substituted with 0-2 groups independently selected from hydroxyl, halogen, C_1-C_3 alkyl),

        - 3- to 6-membered heterocyclyl (substituted with 0-3 groups independently selected from halogen, hydroxyl, oxo, and C_1-C_3 alkyl (substituted with 0-1 hydroxyl group)), and
        - 5- to 6-membered heteroaryl (substituted with 0-3 groups independently selected from oxo, C_1-C_3 alkyl, and C_3-C_6 cycloalkyl);
    - C_3-C_7 cycloalkyl substituted with 0-3 groups independently selected from:
        - hydroxyl,
        - halogen,
        - C_1-C_3 alkyl (substituted with 0-3 groups independently selected from hydroxyl and halogen), and
        - C_1-C_3 alkoxy; and
    - 5- to 9-membered heterocyclyl substituted with 0-2 groups independently selected from:
        - oxo,
        - hydroxyl, and
        - C_1-C_3 alkyl (substituted with 0-1 hydroxyl group).

3. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, selected from a compound of Formula Ib:



(Formula Ib),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

- each **R^1** is independently selected from hydrogen, C_1-C_3 alkyl (substituted with 0-2 groups selected from oxo, hydroxyl, and amino), C_1-C_3 alkoxy, halogen, and cyano;
- each **R^2** is independently selected from hydrogen and C_1-C_3 alkyl;
- **R^3** is selected from hydrogen, C_1-C_3 alkyl, halogen, and cyano;
- each **R^4** and **R^5** are independently selected from hydrogen, C_1-C_3 alkyl, and halogen;

- **R^6** and **R^9** are independently selected from hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, and cyano;
- **R^7** is selected from hydrogen, C_1-C_3 alkyl, and halogen; and
- **R^8** is selected from:
    - hydrogen,
    - C_1-C_8 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl,
        - oxo,
        - amino,
        - cyano,
        - halogen,
        - C_1-C_3 alkoxy (substituted with 0-1 oxo group),
        - C_3-C_6 cycloalkyl (substituted with 0-2 groups independently selected from hydroxyl, halogen, and C_1-C_3 alkyl),
        - 3- to 6-membered heterocyclyl (substituted with 0-3 groups independently selected from halogen, hydroxyl, oxo, and C_1-C_3 alkyl (substituted with 0-1 hydroxyl group)), and
        - 5- to 6-membered heteroaryl (substituted with 0-3 groups independently selected from oxo, C_1-C_3 alkyl, and C_3-C_6 cycloalkyl);
    - C_3-C_7 cycloalkyl substituted with 0-3 groups independently selected from:
        - hydroxyl,
        - halogen,
        - C_1-C_3 alkyl (substituted with 0-3 groups independently selected from hydroxyl and halogen), and
        - C_1-C_3 alkoxy; and
    - 5- to 9-membered heterocyclyl substituted with 0-2 groups independently selected from:
        - oxo,
        - hydroxyl, and
        - C_1-C_3 alkyl (substituted with 0-1 hydroxyl group); and
- **Y** is selected from
    - $N(R^8)_2$, and
    - 3- to 10-membered heterocyclyl or 3- to 10-membered heteroaryl, each of which is substituted with 0-2 groups independently selected from:

- hydroxyl,
- oxo,
- C_1-C_3 alkoxy, and
- C_1-C_3 alkyl (substituted with 0-2 groups selected from amino, hydroxyl, C_3-C_4 alkyl, oxo, and C_1-C_3 alkoxy).

4. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 3, wherein each $\mathbf{R^1}$ is independently selected from hydrogen, methyl, methoxy, fluoro, chloro, and cyano.

5. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 4, wherein $\mathbf{R^2}$ is independently selected from hydrogen and methyl.

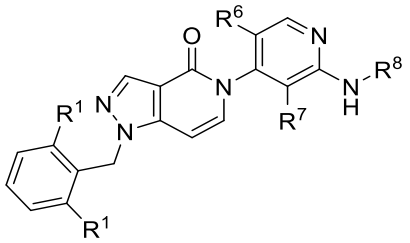
6. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 5, wherein $\mathbf{R^3}$ is selected from hydrogen, methyl, and cyano.

7. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 6, wherein $\mathbf{R^4}$ and $\mathbf{R^5}$ are independently selected from hydrogen and methyl.

8. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 7, wherein $\mathbf{R^6}$ is selected from hydrogen, methyl, ethyl, fluoro, chloro, bromo, and cyano.

9. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 8, wherein $\mathbf{R^7}$ is selected from hydrogen and fluoro.

10. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, selected from a compound of Formula II:



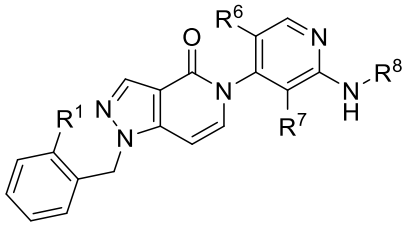
(Formula II),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

- each **R^1** is independently selected from hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, and cyano;
- **R^6** is selected from C_1-C_3 alkyl, halogen, and cyano;
- **R^7** is selected from hydrogen, C_1-C_3 alkyl, and halogen; and
- **R^8** is selected from:
    - hydrogen,
    - C_1-C_8 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl,
        - oxo,
        - amino,
        - cyano,
        - halogen,
        - C_1-C_3 alkoxy (substituted with 0-1 oxo group),
        - C_3-C_6 cycloalkyl (substituted with 0-2 groups independently selected from hydroxyl, halogen, and C_1-C_3 alkyl),
        - 3- to 6-membered heterocyclyl (substituted with 0-3 groups independently selected from halogen, hydroxyl, oxo, and C_1-C_3 alkyl (substituted with 0-1 hydroxyl group)), and
        - 5- to 6-membered heteroaryl (substituted with 0-3 groups independently selected from oxo, C_1-C_3 alkyl, and C_3-C_6 cycloalkyl);
    - C_3-C_7 cycloalkyl substituted with 0-3 groups independently selected from:
        - hydroxyl,

        - halogen,
        - C_1-C_3 alkyl (substituted with 0-3 groups independently selected from hydroxyl and halogen), and
        - C_1-C_3 alkoxy; and
    - 5- to 9-membered heterocyclyl substituted with 0-2 groups independently selected from:
        - oxo,
        - hydroxyl, and
        - C_1-C_3 alkyl (substituted with 0-1 hydroxyl group).

11. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, selected from a compound of Formula IIa:



(Formula IIa),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

- **R^1** is selected from hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, and cyano;
- **R^6** is selected from C_1-C_3 alkyl, halogen, and cyano;
- **R^7** is selected from hydrogen, C_1-C_3 alkyl, and halogen; and
- **R^8** is selected from:
    - hydrogen,
    - C_1-C_8 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl,
        - oxo,
        - amino,
        - cyano,
        - halogen,
        - C_1-C_3 alkoxy (substituted with 0-1 oxo group),

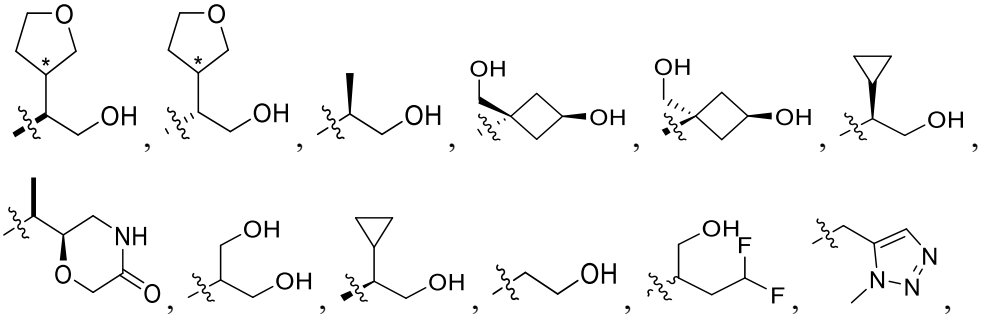
- C_3-C_6 cycloalkyl (substituted with 0-2 groups independently selected from hydroxyl, halogen, and C_1-C_3 alkyl),
- 3- to 6-membered heterocyclyl (substituted with 0-3 groups independently selected from halogen, hydroxyl, oxo, and C_1-C_3 alkyl (substituted with 0-1 hydroxyl group)), and
- 5- to 6-membered heteroaryl (substituted with 0-3 groups independently selected from oxo, C_1-C_3 alkyl, and C_3-C_6 cycloalkyl);

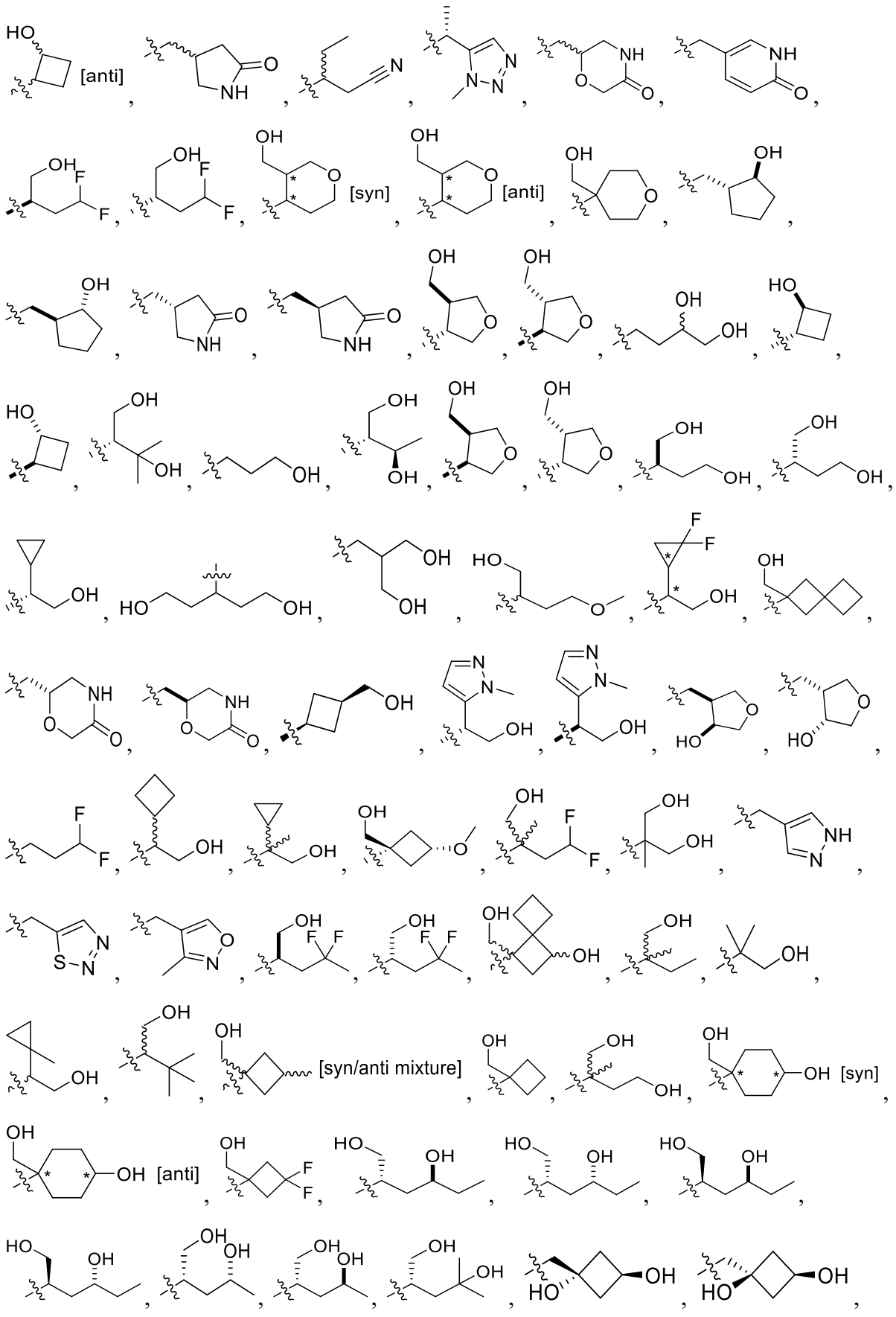
o C_3-C_7 cycloalkyl substituted with 0-3 groups independently selected from:
- hydroxyl,
- halogen,
- C_1-C_3 alkyl (substituted with 0-3 groups independently selected from hydroxyl and halogen), and
- C_1-C_3 alkoxy; and

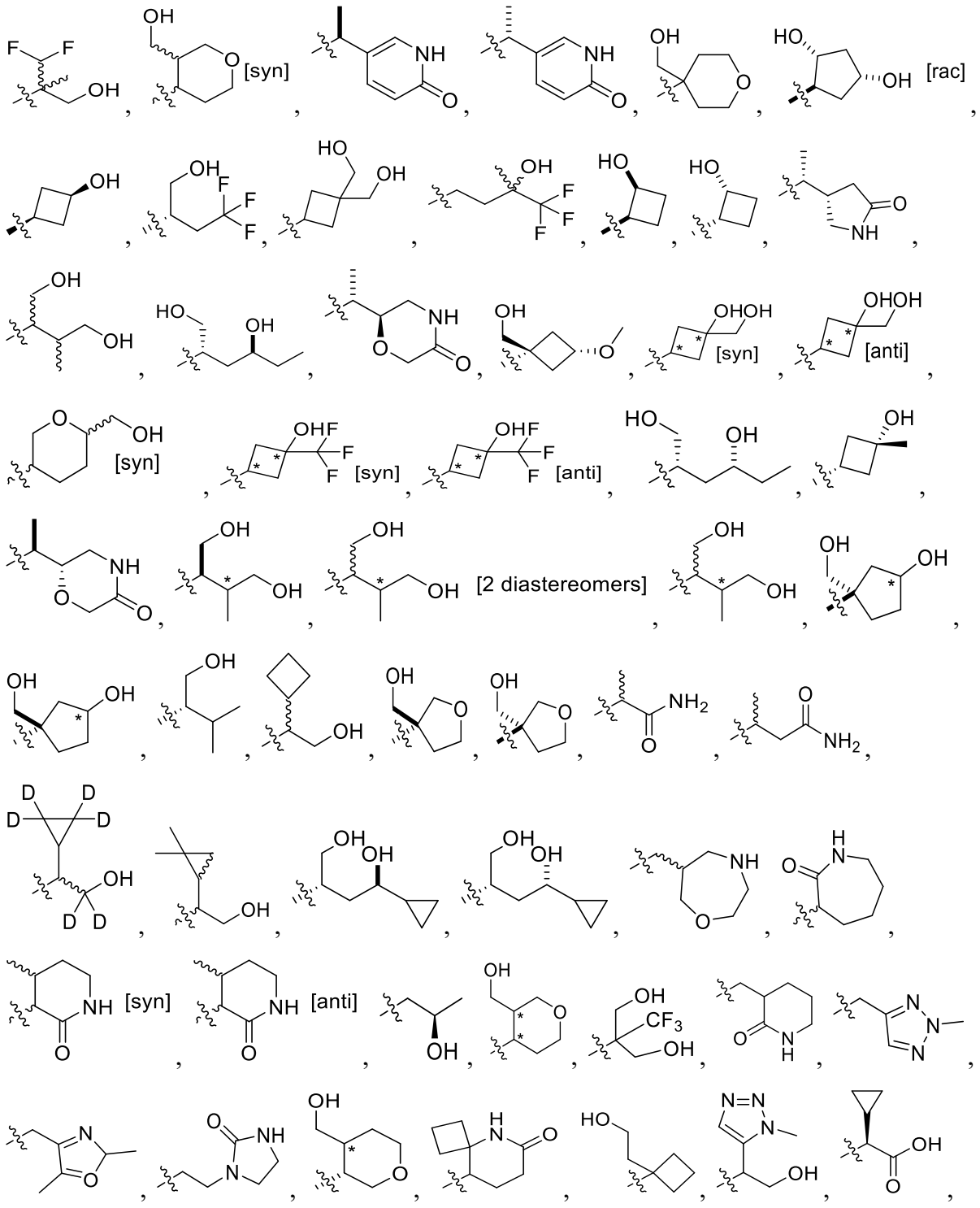
o 5- to 9-membered heterocyclyl substituted with 0-2 groups independently selected from:
- oxo,
- hydroxyl, and
- C_1-C_3 alkyl (substituted with 0-1 hydroxyl group).

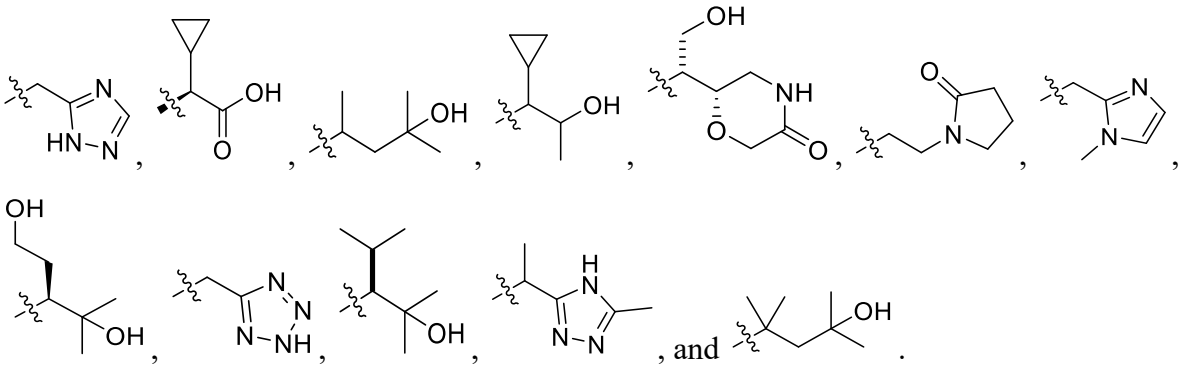
12. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, wherein **R^8** is selected from C_1-C_8 alkyl substituted with 0-5 groups, C_3-C_7 cycloalkyl substituted with 0-3 groups, and 5- to 9-membered heterocyclyl substituted with 0-2 groups.

13. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 12, wherein **R^8** is selected from:

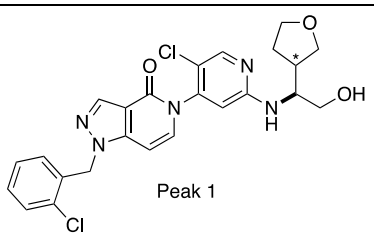
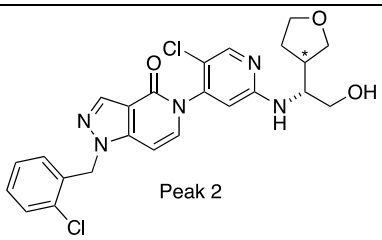
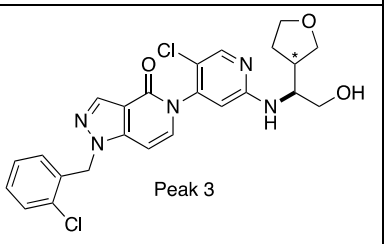
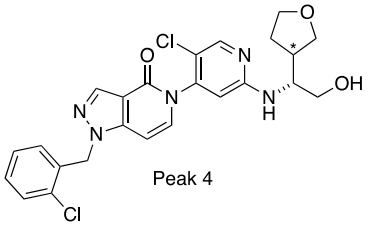
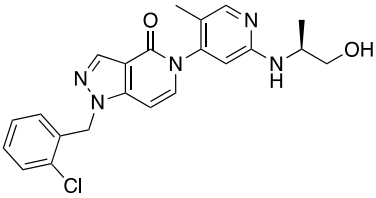
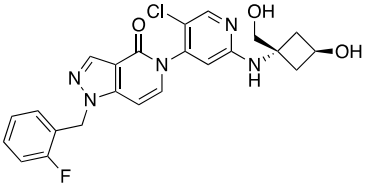
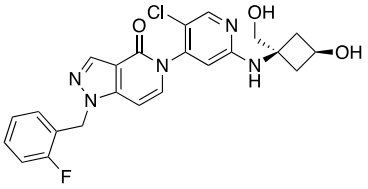
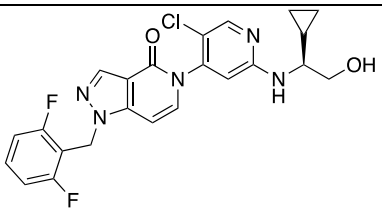
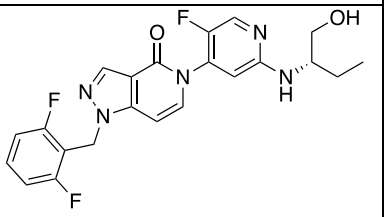
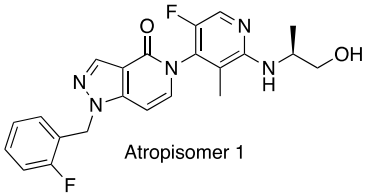
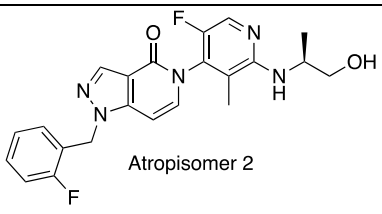
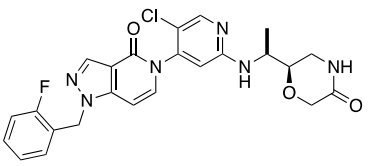
hydrogen, 

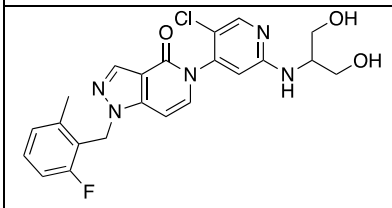
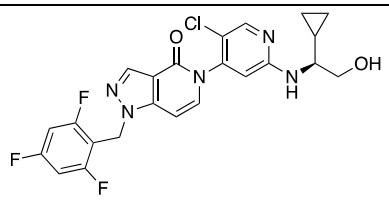
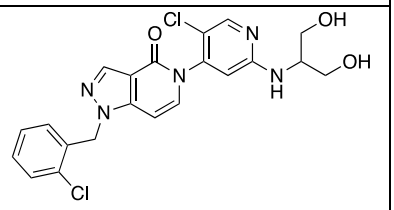
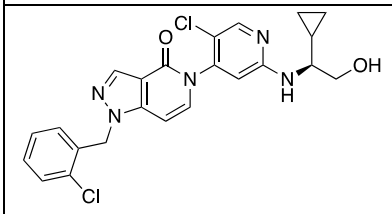
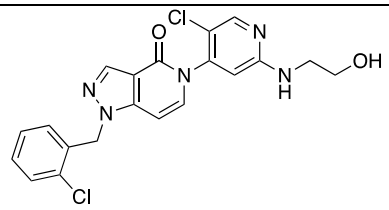
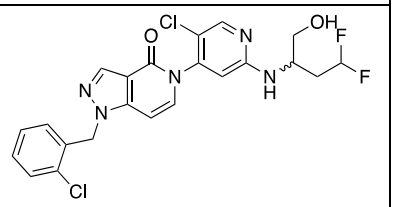
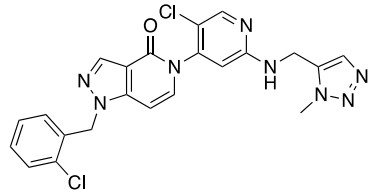
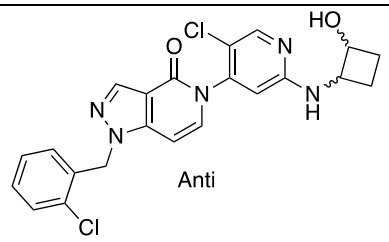
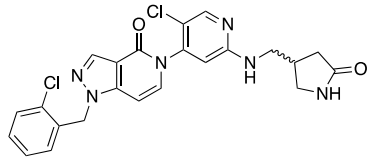
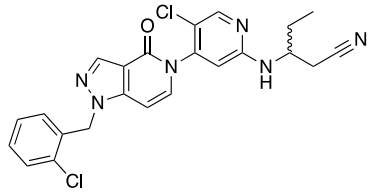
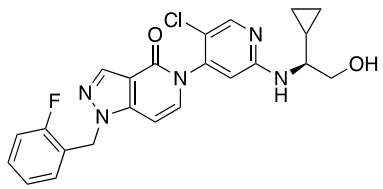
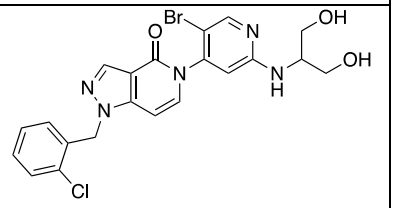
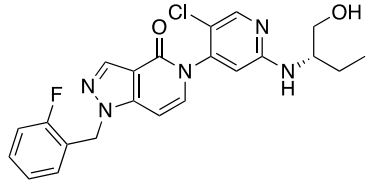
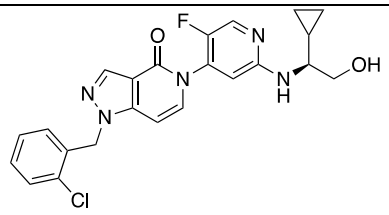
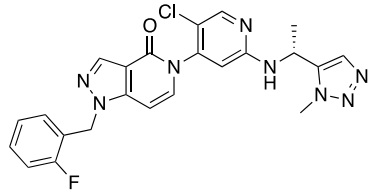
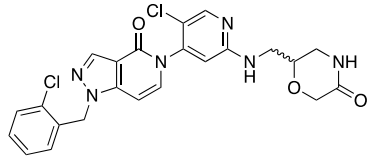
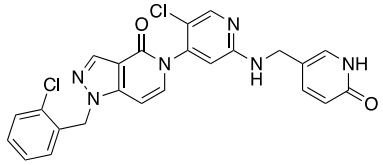
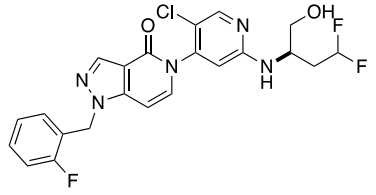


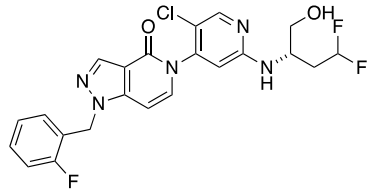
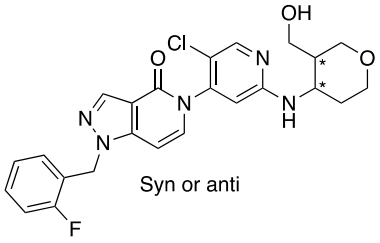
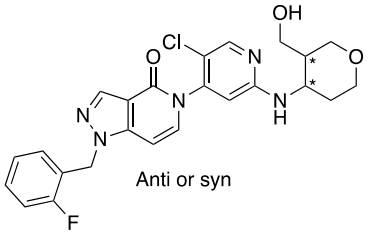
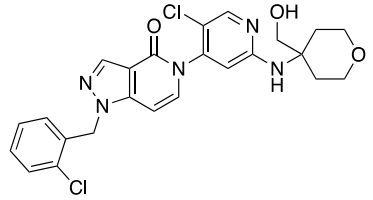
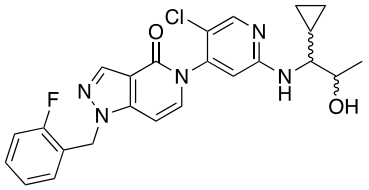
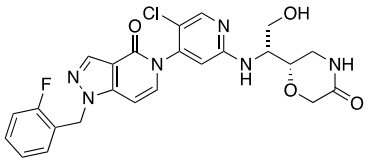
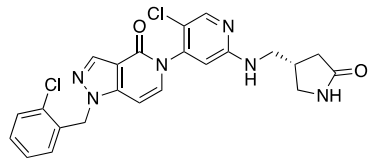
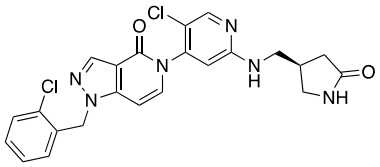
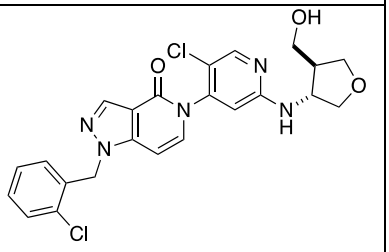
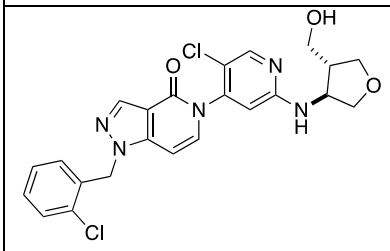
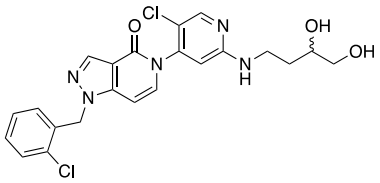
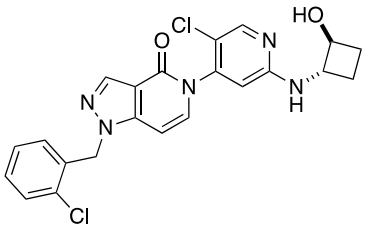
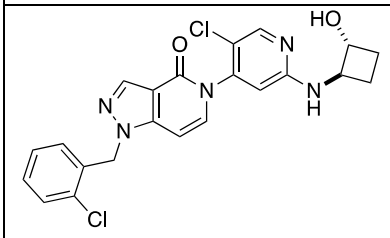
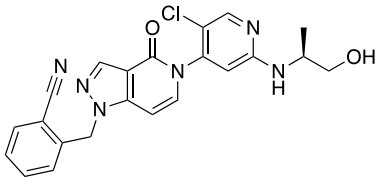
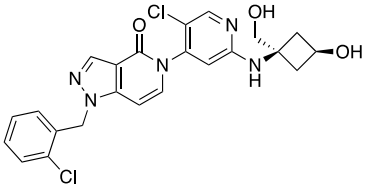
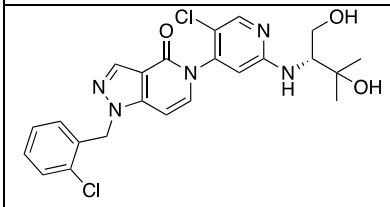
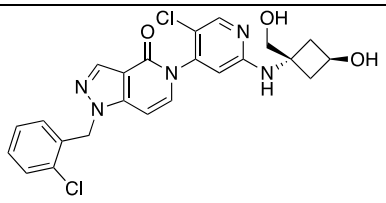
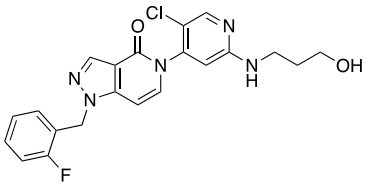

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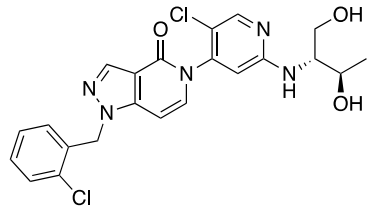
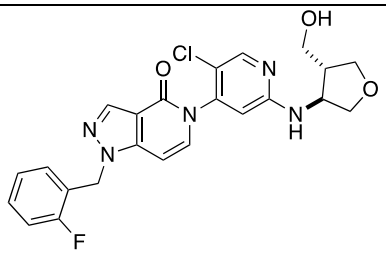
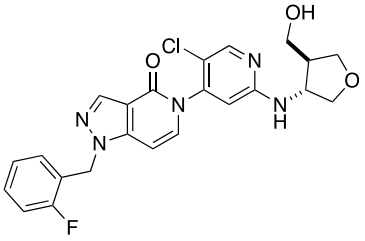
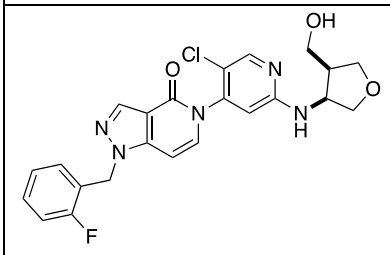
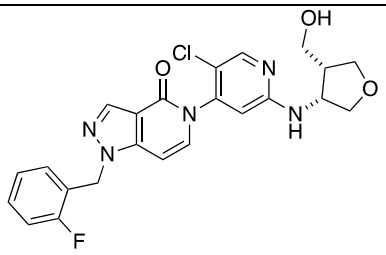
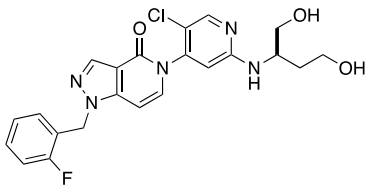
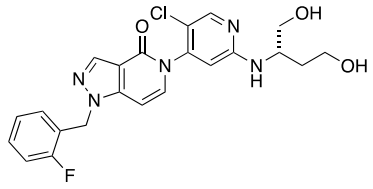
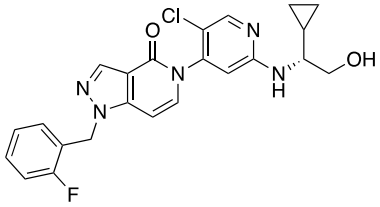
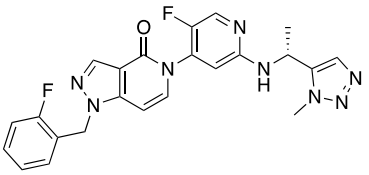
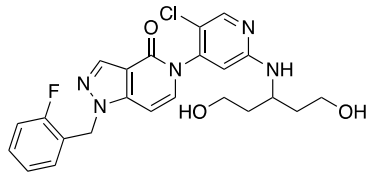
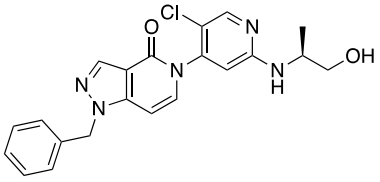
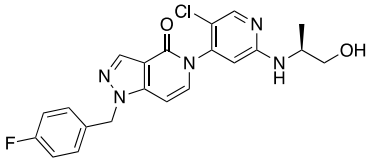
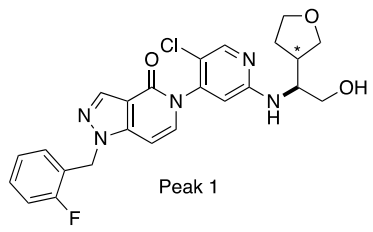
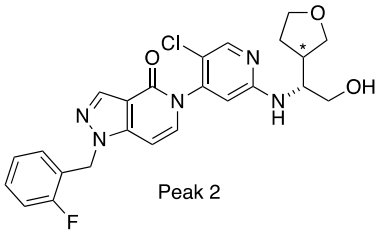
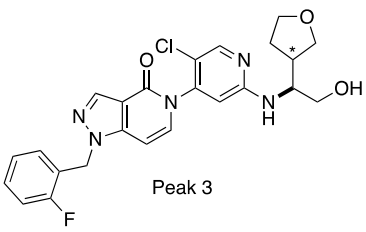
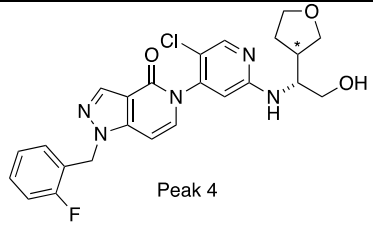
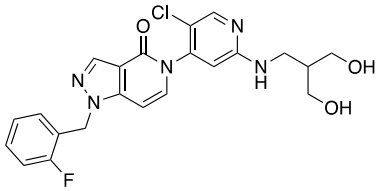
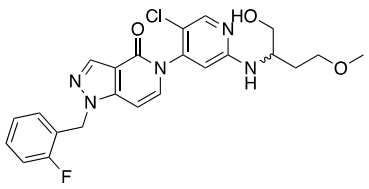


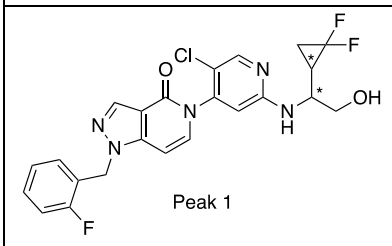
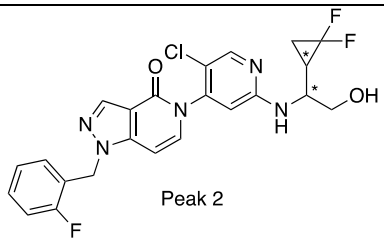
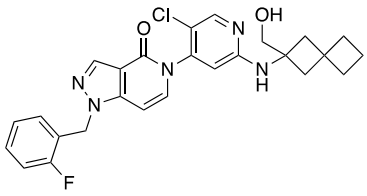
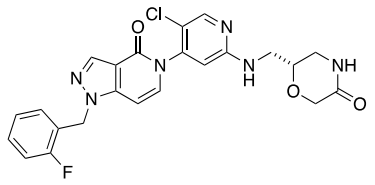
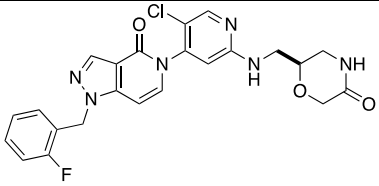
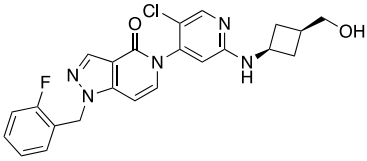
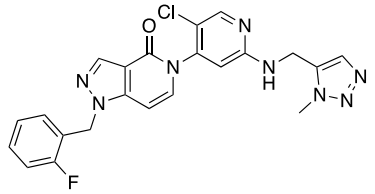
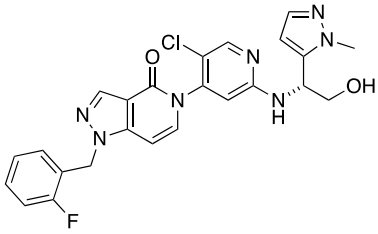
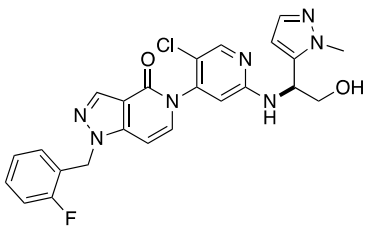
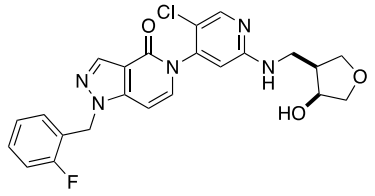
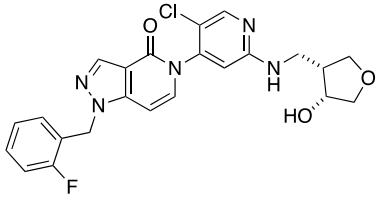
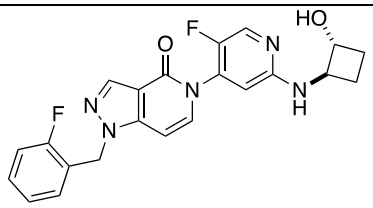
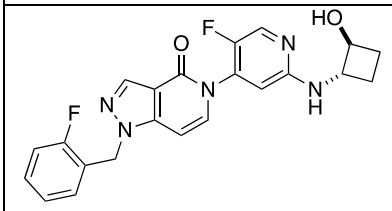
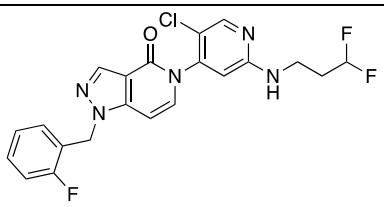
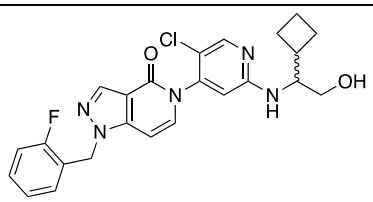
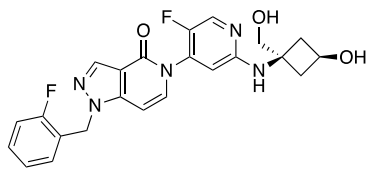
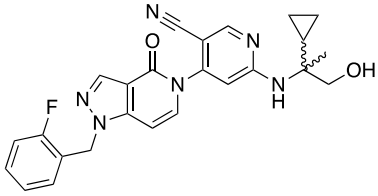
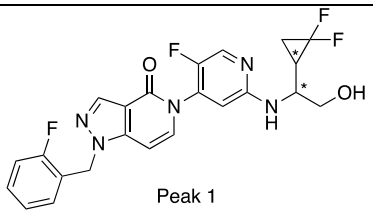
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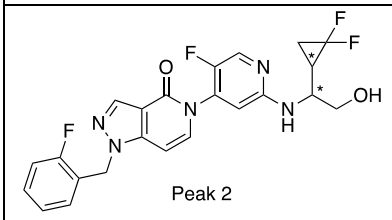
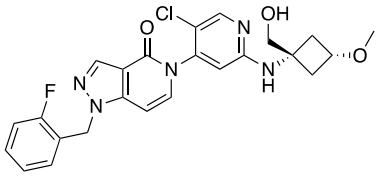
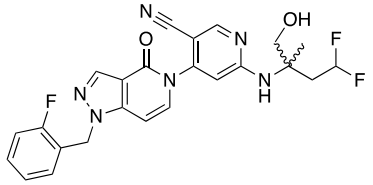
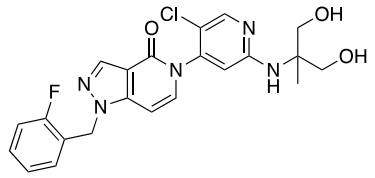
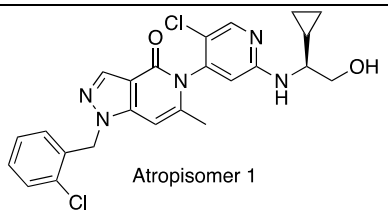
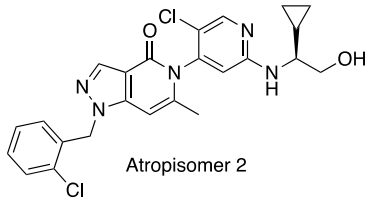
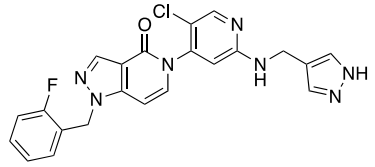
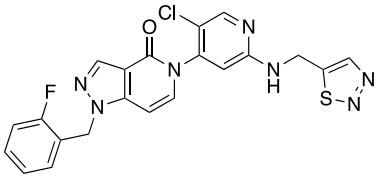
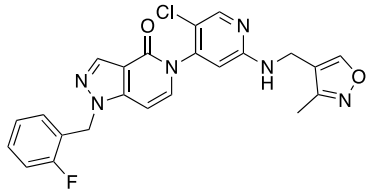
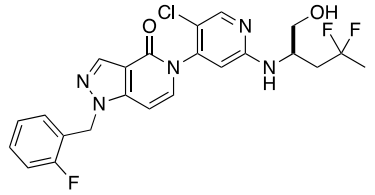
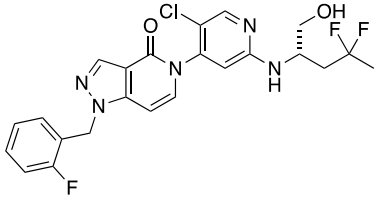
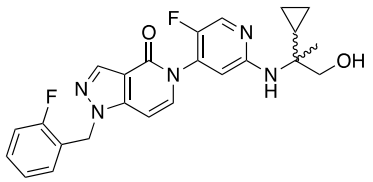
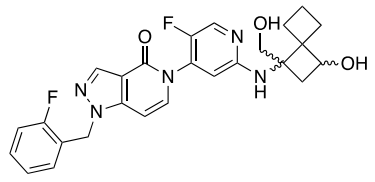
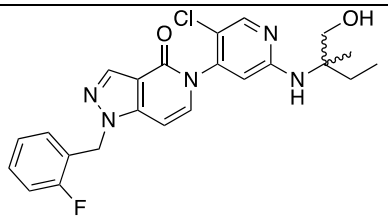
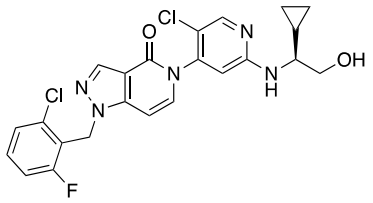
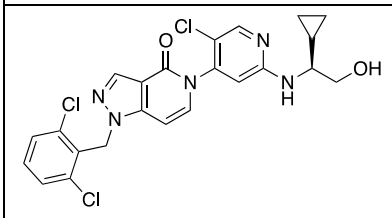
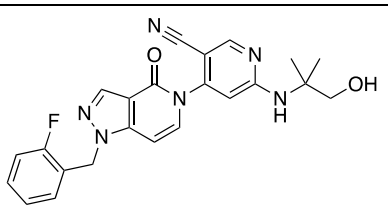
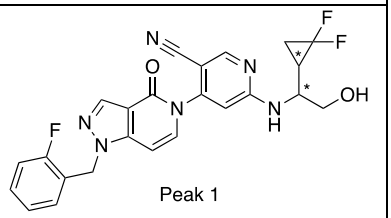
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 Peak 4		
7	**8**	**9**
		
10	**11**	**12**
 Atropisomer 1	 Atropisomer 2	

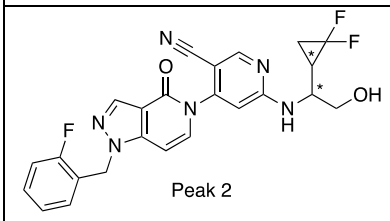
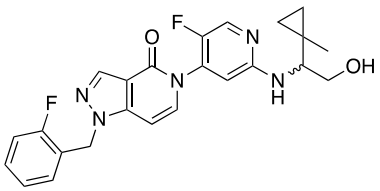
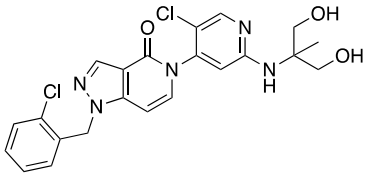
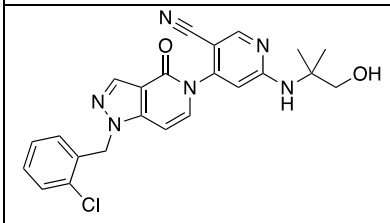
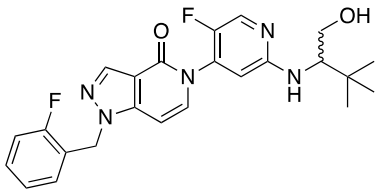
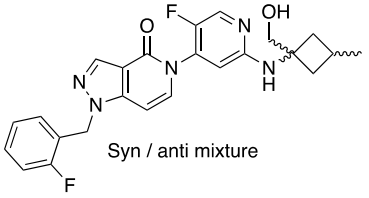
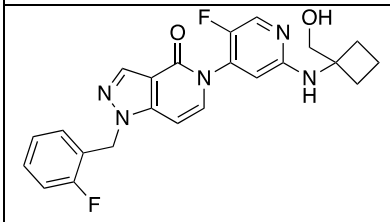
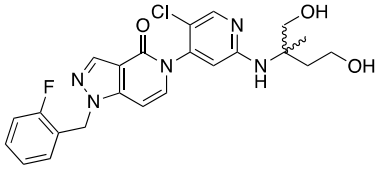
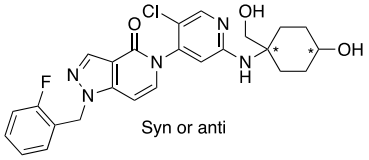
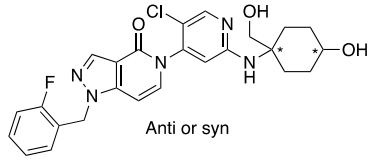
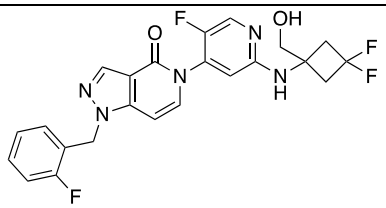
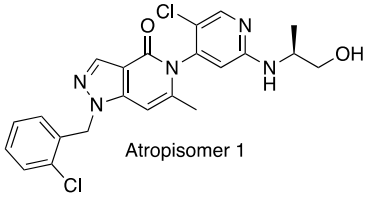
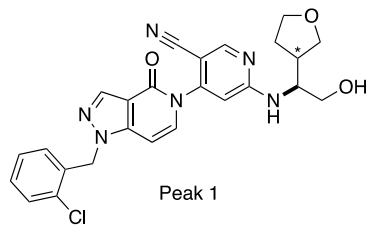
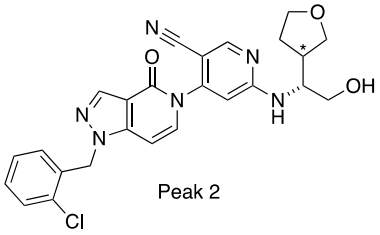
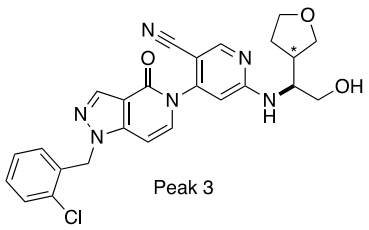
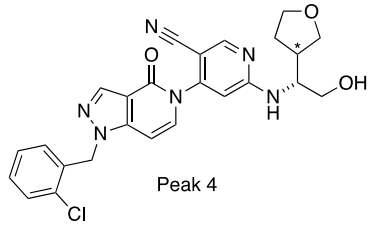
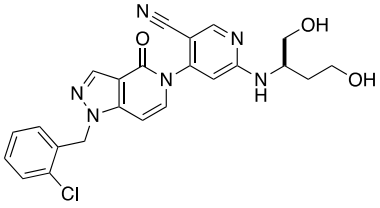
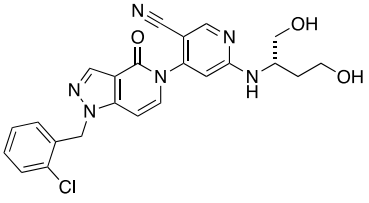
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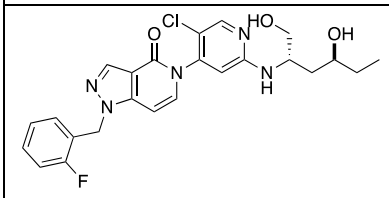
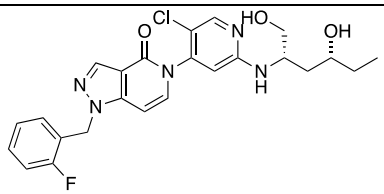
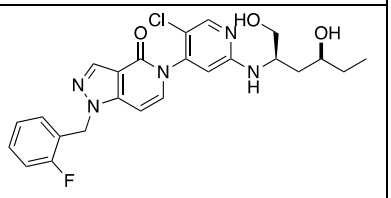
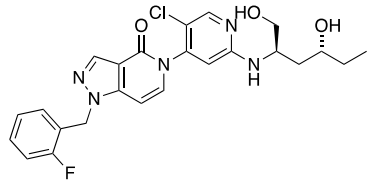
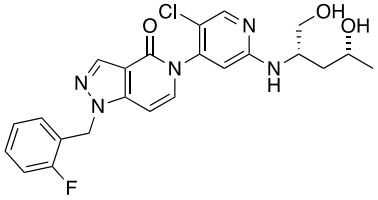
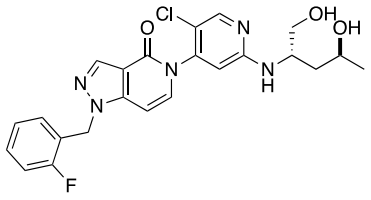
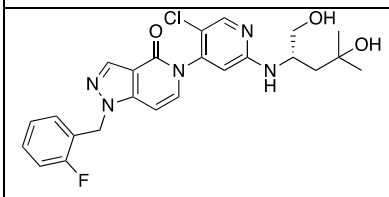
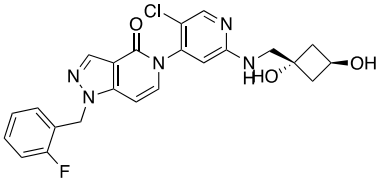
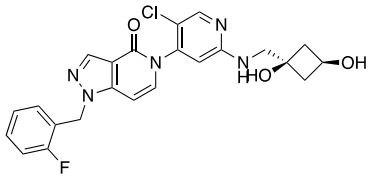
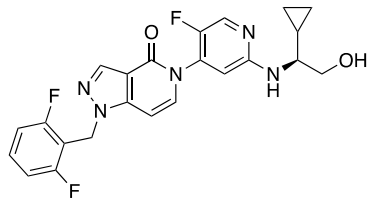
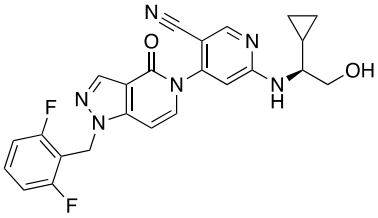
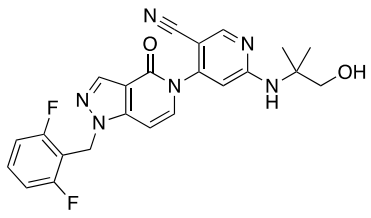
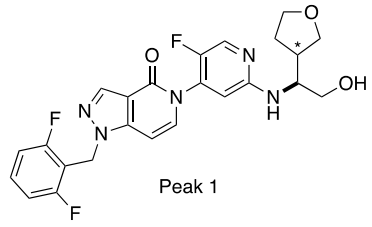
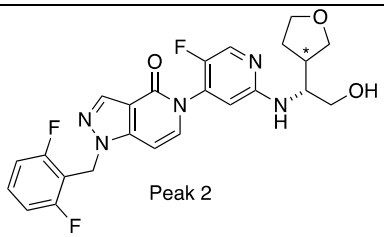
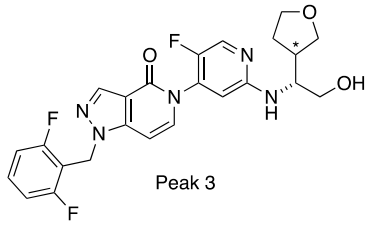
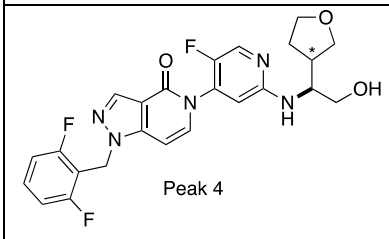
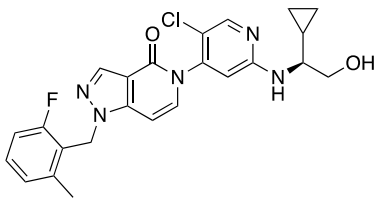
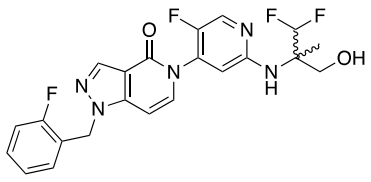
31	32	33
	 Syn or anti	 Anti or syn
34	**35**	**36**
		
37	**38**	**39**
		
40	**41**	**42**
		
43	**44**	**45**
		
46	**47**	**48**
		

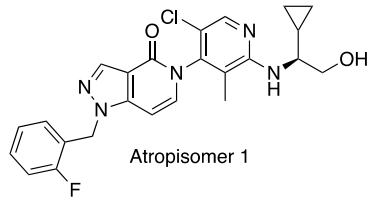
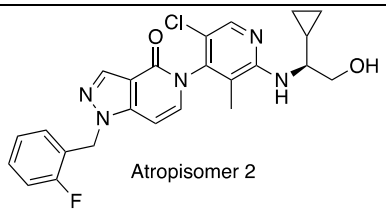
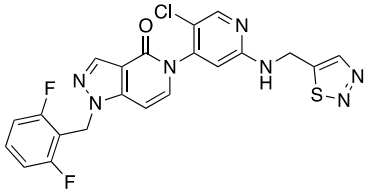
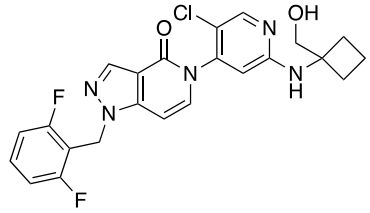
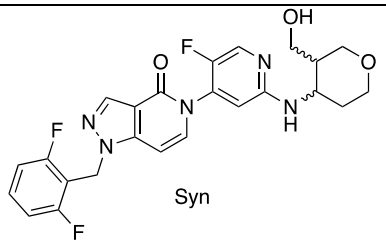
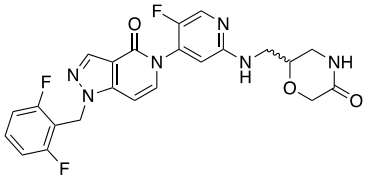
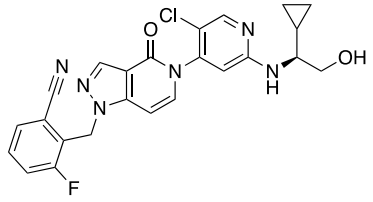
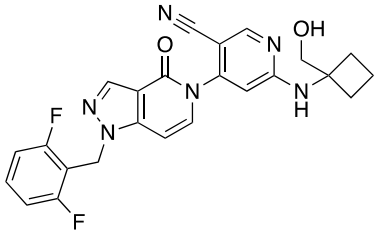
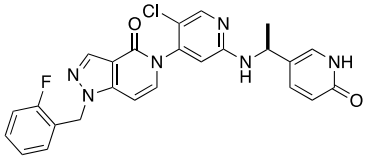
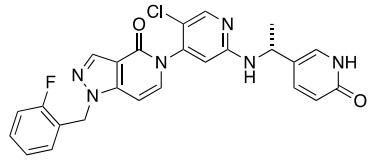
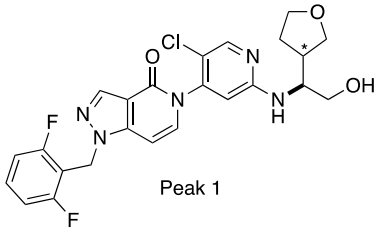
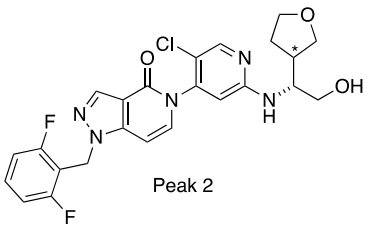
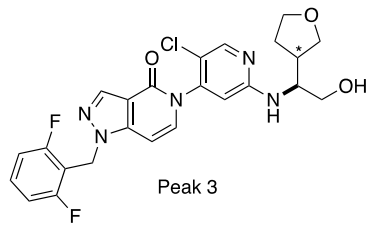
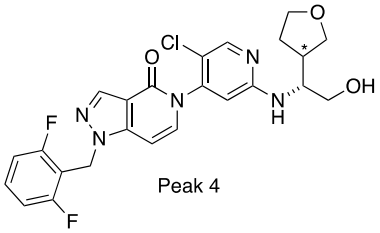
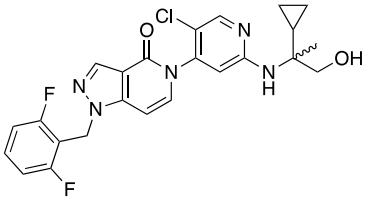
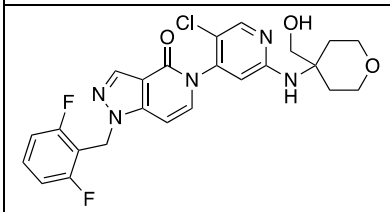
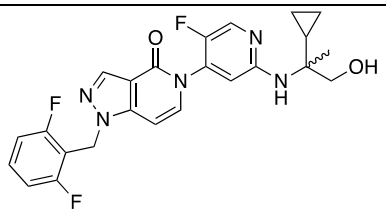
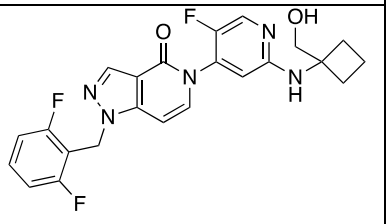
49	50	51
		
52	**53**	**54**
		
55	**56**	**57**
		
58	**59**	**60**
		
61	**62**	**63**
 Peak 1	 Peak 2	 Peak 3
64	**65**	**66**
 Peak 4		

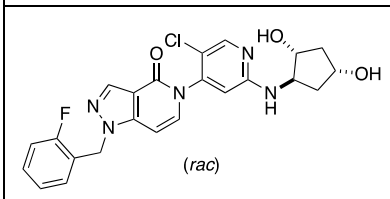
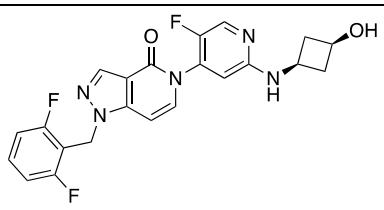
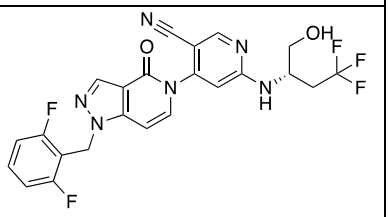
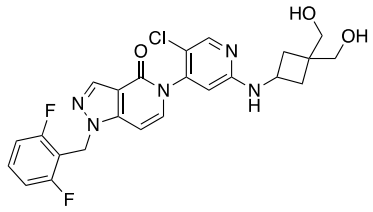
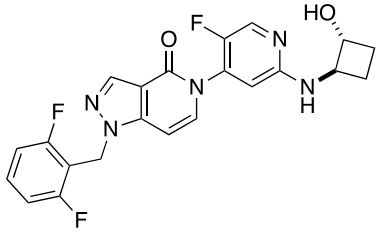
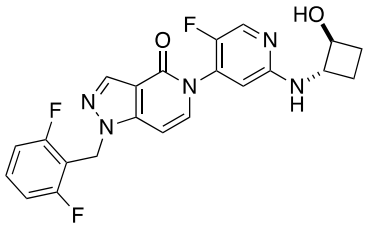
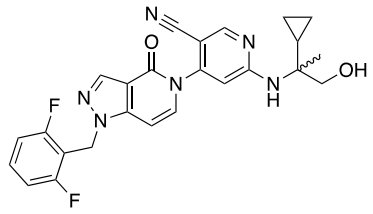
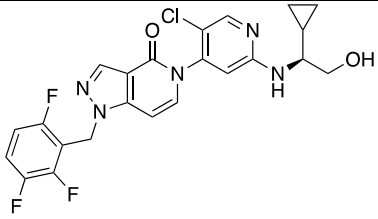
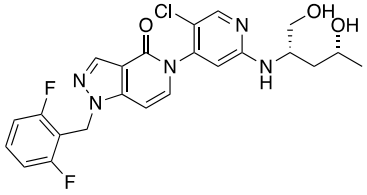
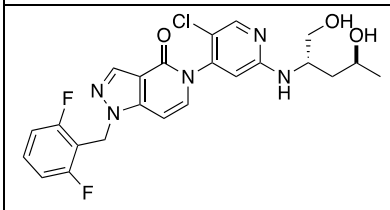
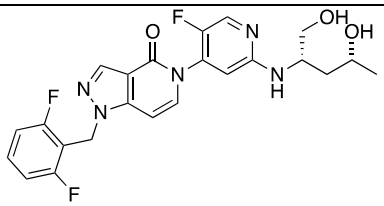
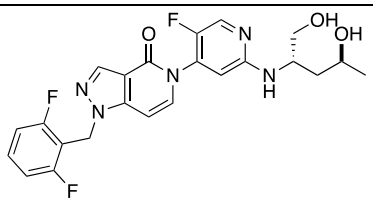
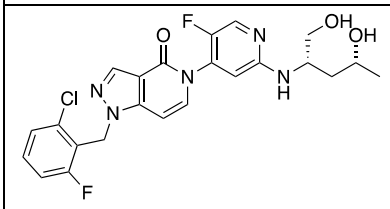
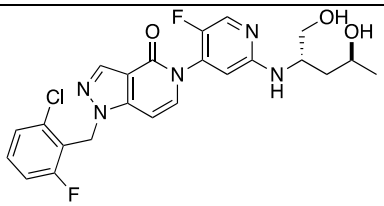
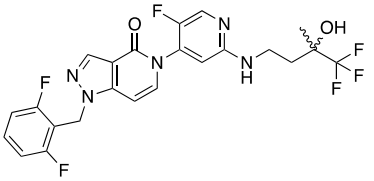
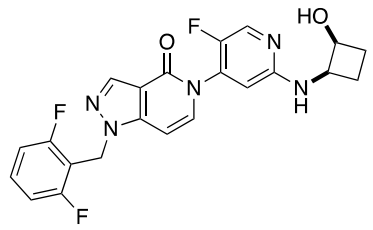
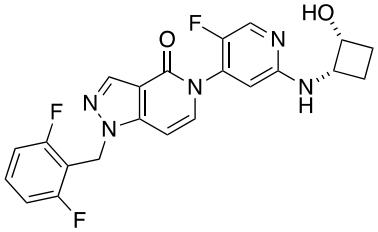
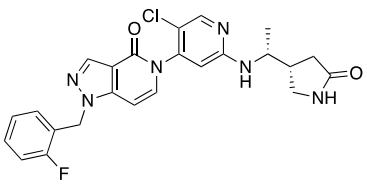
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 Peak 1	 Peak 2	
70	**71**	**72**
		
73	**74**	**75**
		
76	**77**	**78**
		
79	**80**	**81**
		
82	**83**	**84**
		 Peak 1

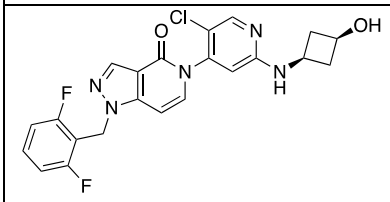
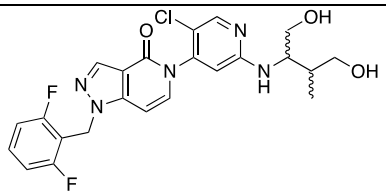
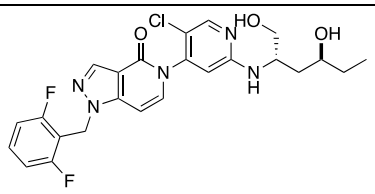
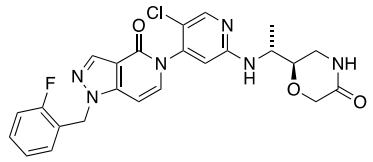
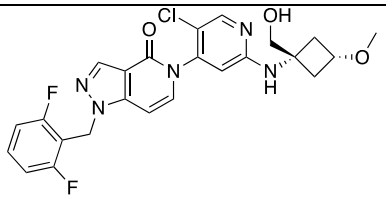
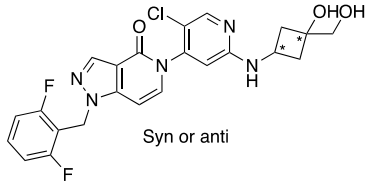
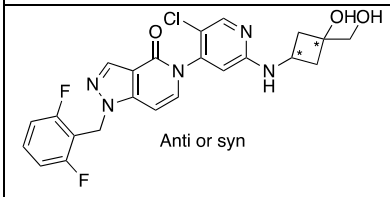
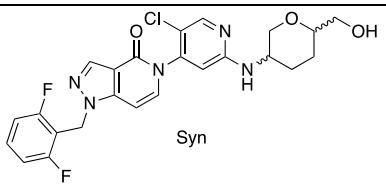
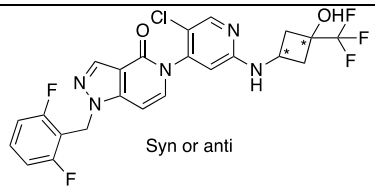
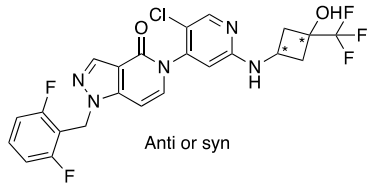
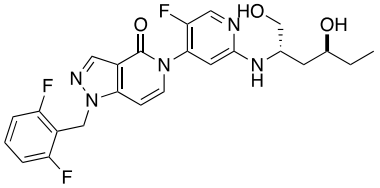
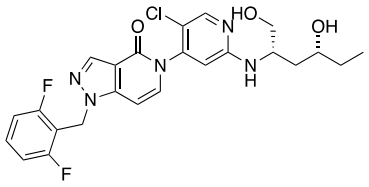
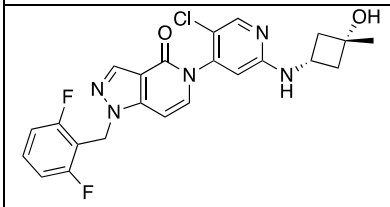
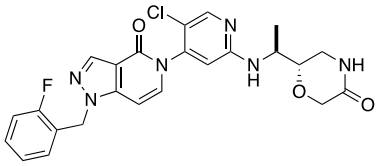
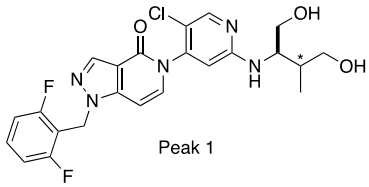
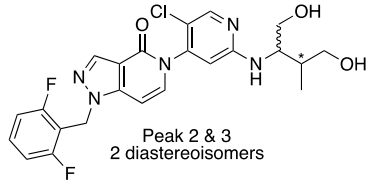
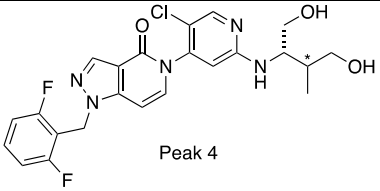
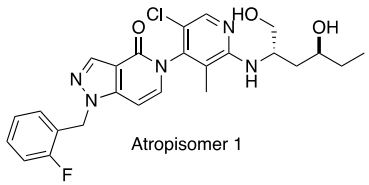
85	86	87
 Peak 2		
88	**89**	**90**
	 Atropisomer 1	 Atropisomer 2
91	**92**	**93**
		
94	**95**	**96**
		
97	**98**	**99**
		
100	**101**	**102**
		 Peak 1

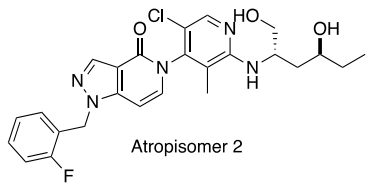
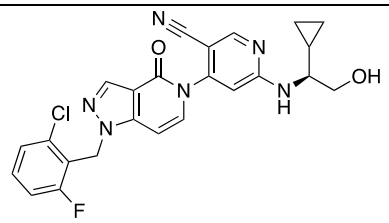
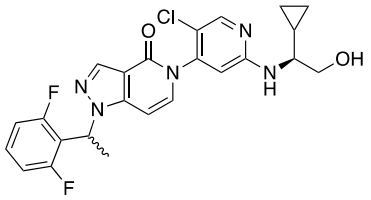
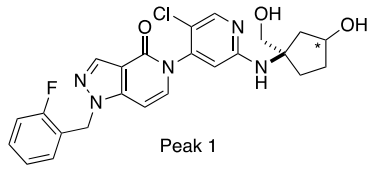
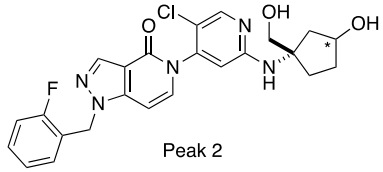
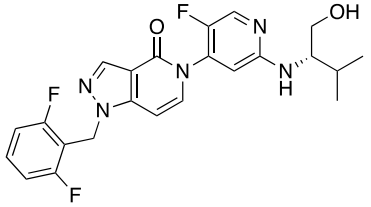
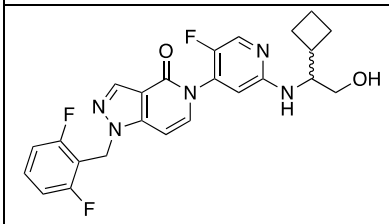
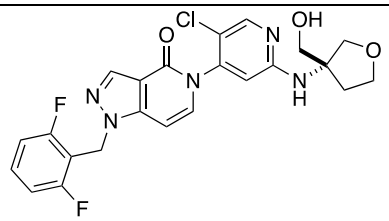
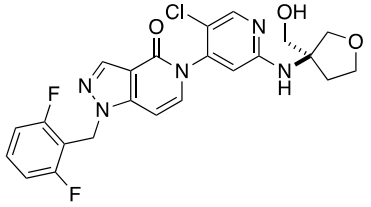
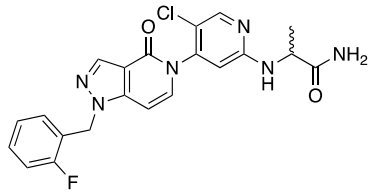
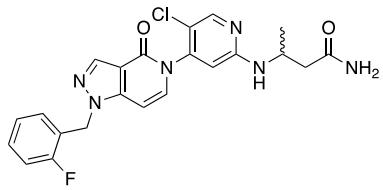
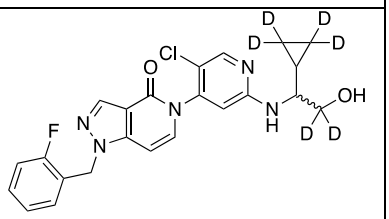
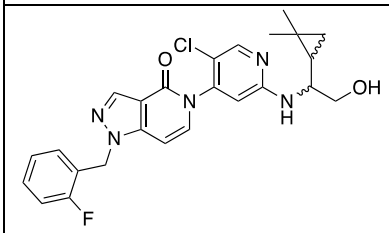
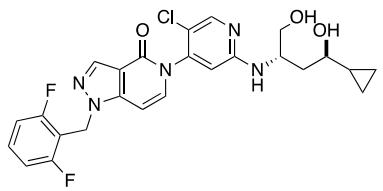
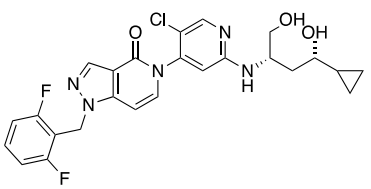
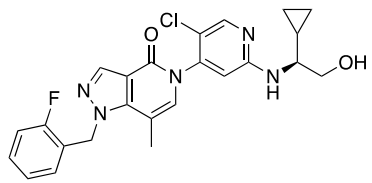
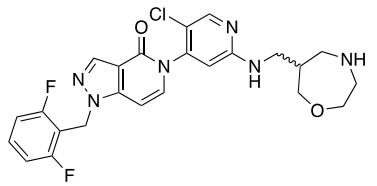
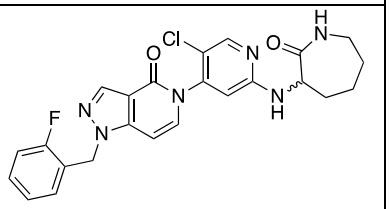
103	104	105
 Peak 2		
106	**107**	**108**
		 Syn / anti mixture
109	**110**	**111**
		 Syn or anti
112	**113**	**114**
 Anti or syn		 Atropisomer 1
115	**116**	**117**
 Peak 1	 Peak 2	 Peak 3
118	**119**	**120**
 Peak 4		

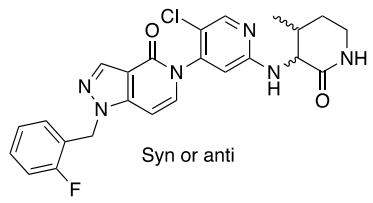
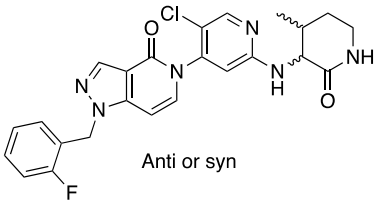
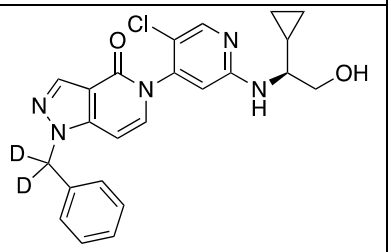
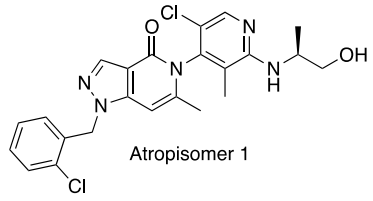
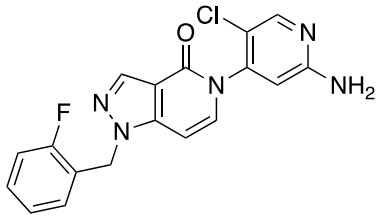
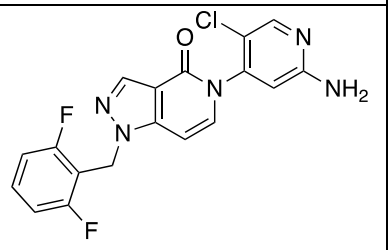
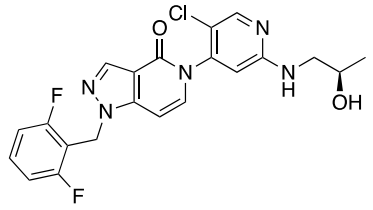
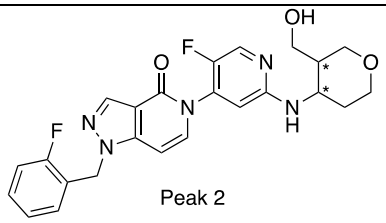
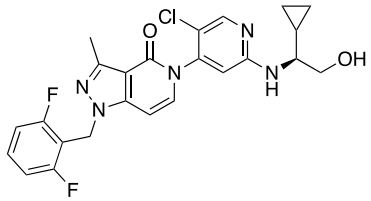
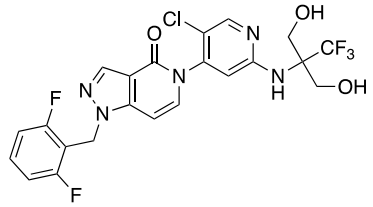
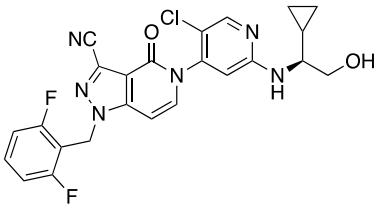
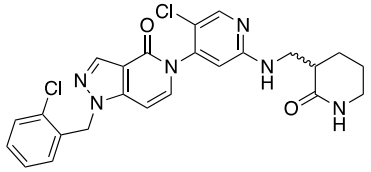
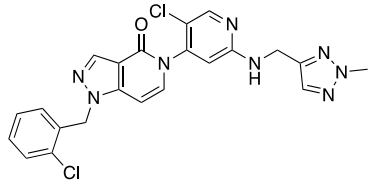
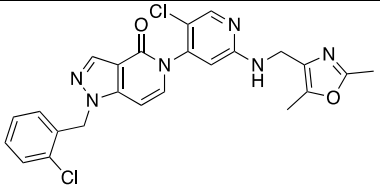
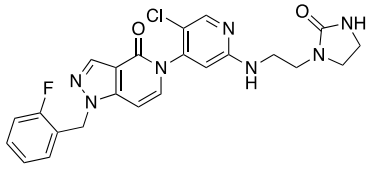
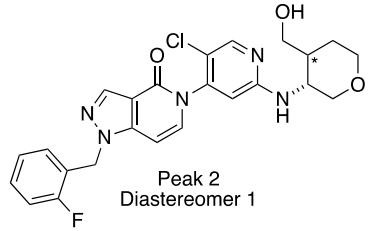
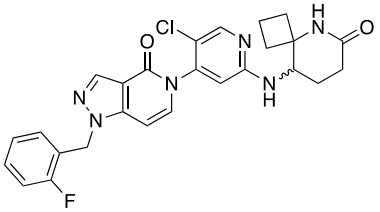
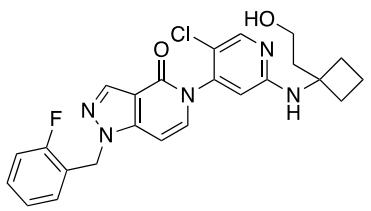
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124	**125**	**126**
		
127	**128**	**129**
		
130	**131**	**132**
		
133	**134**	**135**
 Peak 1	 Peak 2	 Peak 3
136	**137**	**138**
 Peak 4		

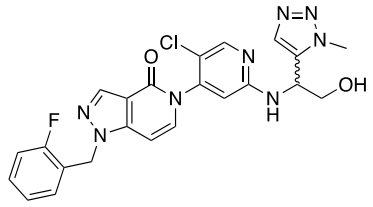
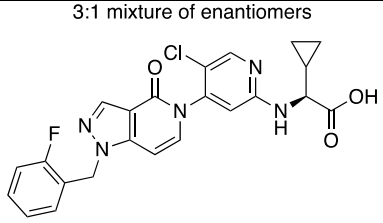
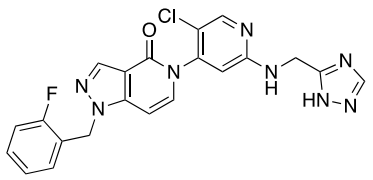
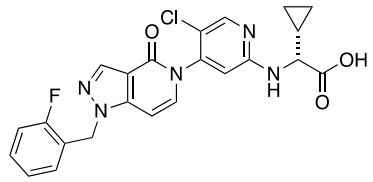
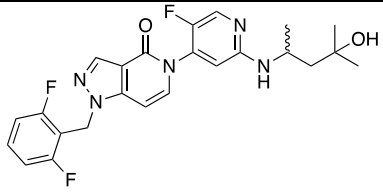
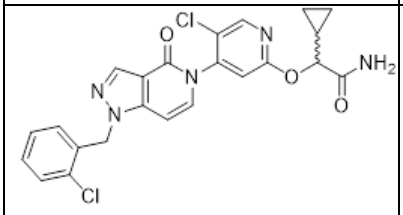
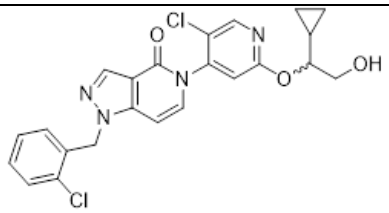
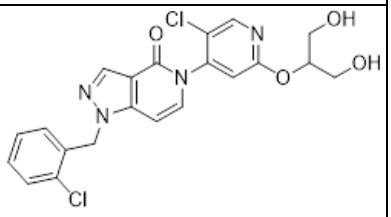
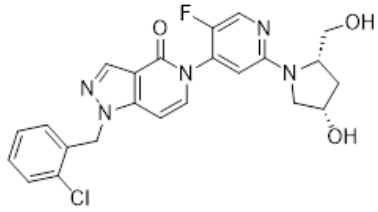
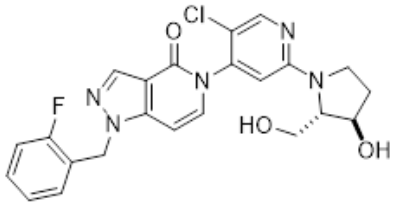
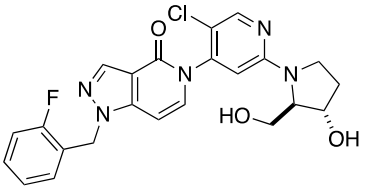
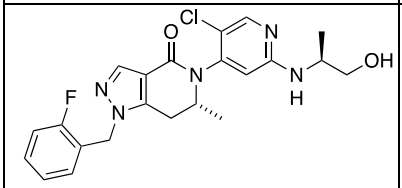
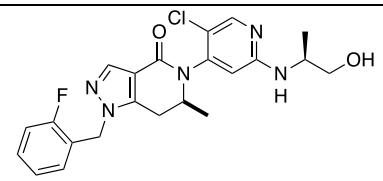
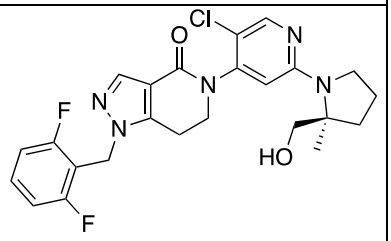
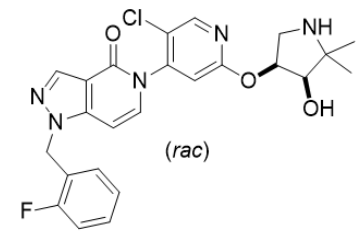
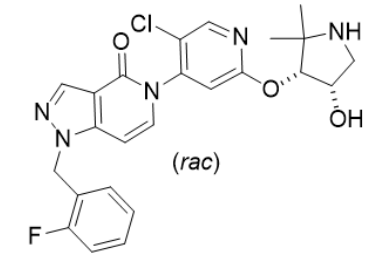
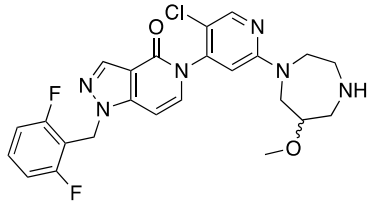
139	140	141
 Atropisomer 1	 Atropisomer 2	
142	**143**	**144**
	 Syn	
145	**146**	**147**
		
148	**149**	**150**
	 Peak 1	 Peak 2
151	**152**	**153**
 Peak 3	 Peak 4	
154	**155**	**156**
		

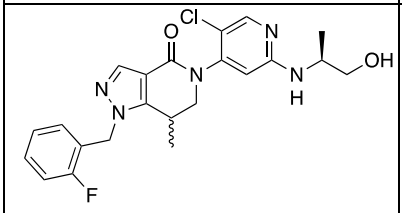
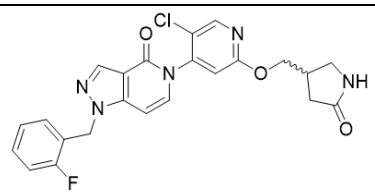
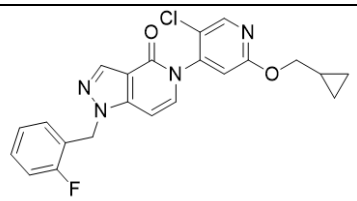
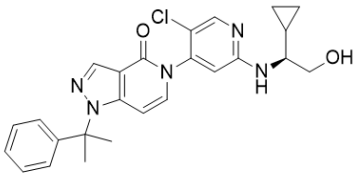
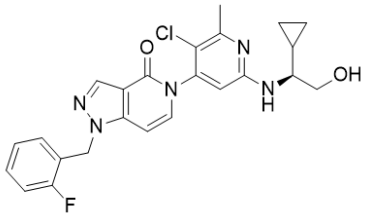
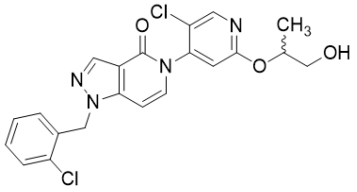
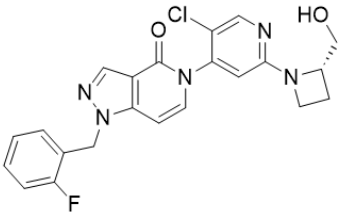
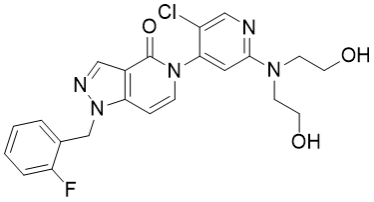
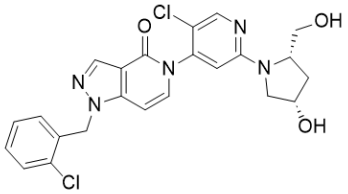
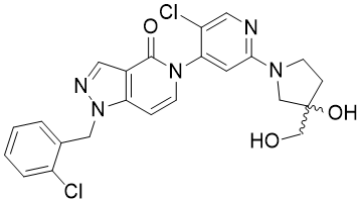
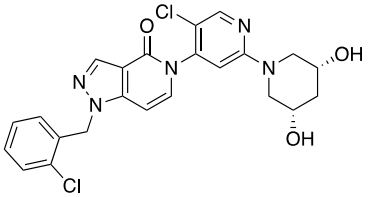
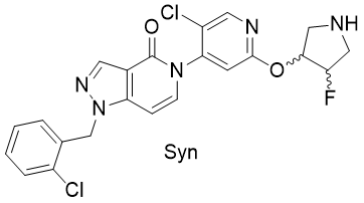
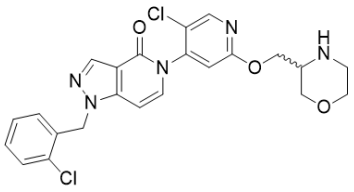
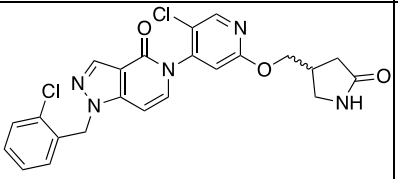
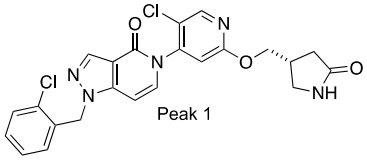
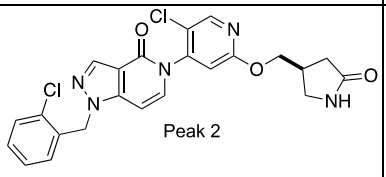
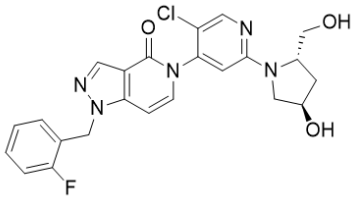
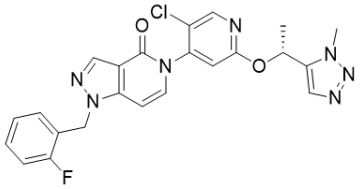
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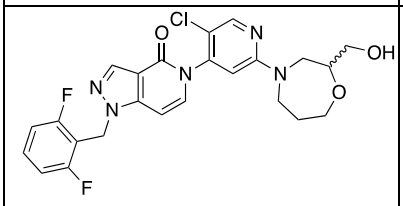
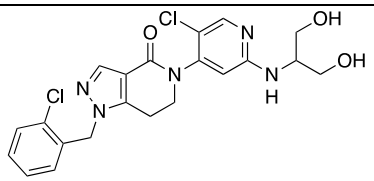
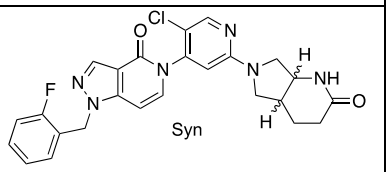
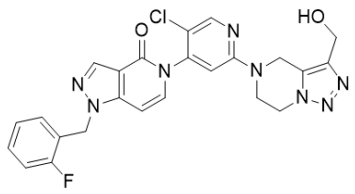
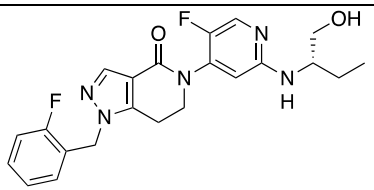
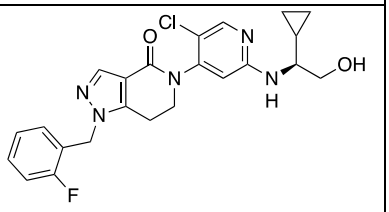
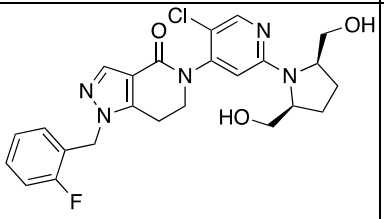
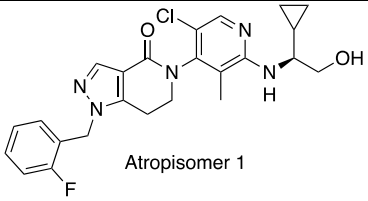
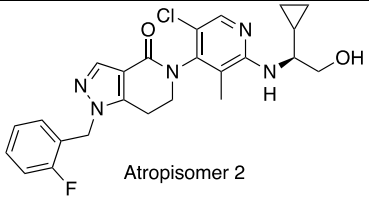
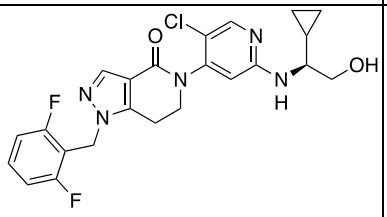
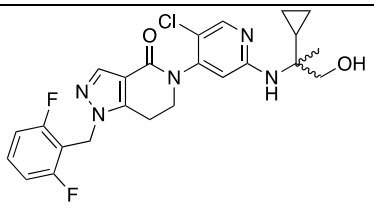
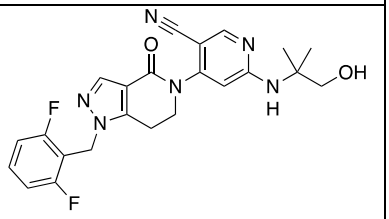
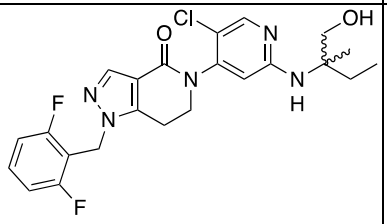
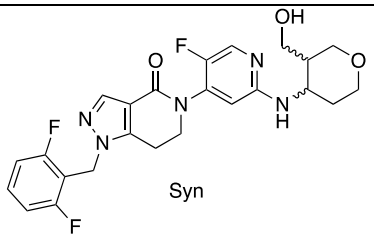
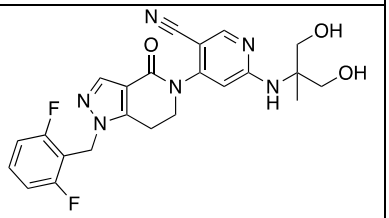
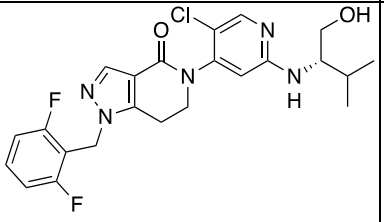
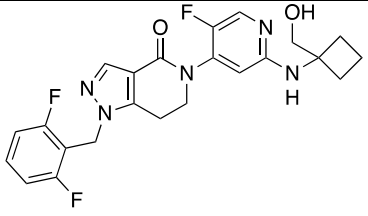
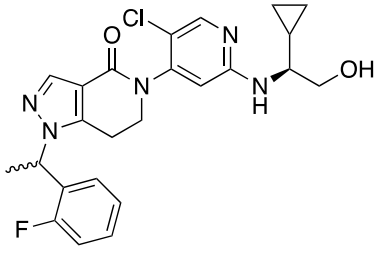
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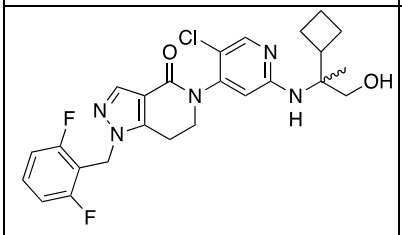
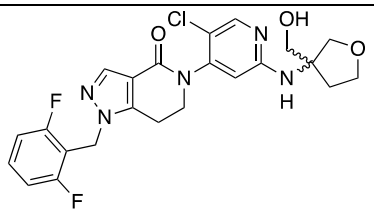
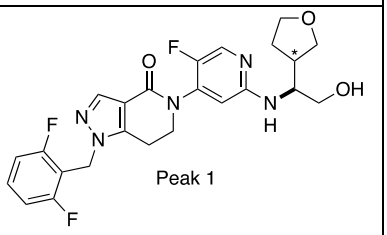
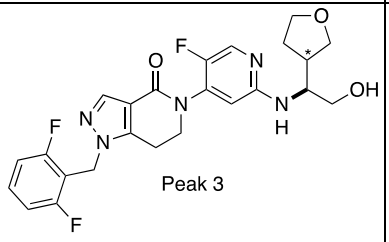
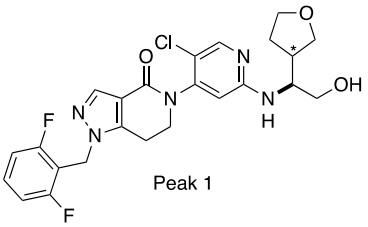
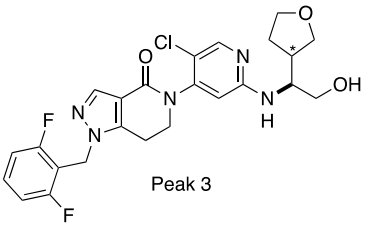
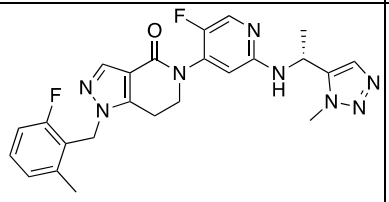
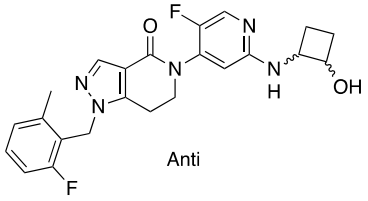
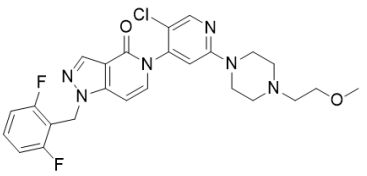
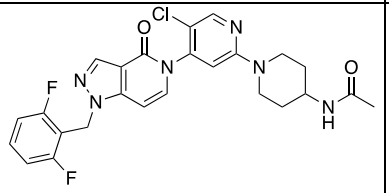
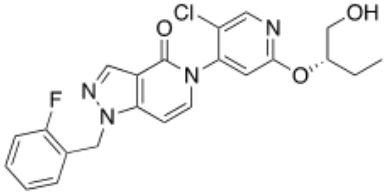
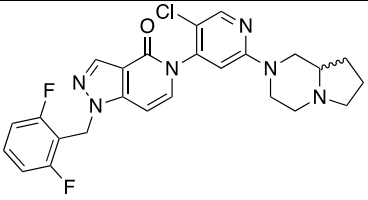
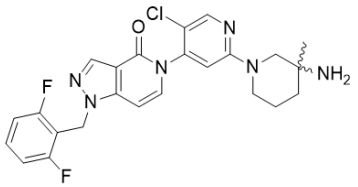
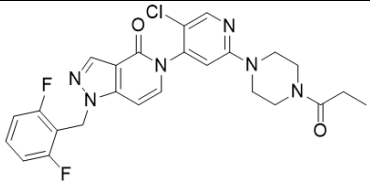
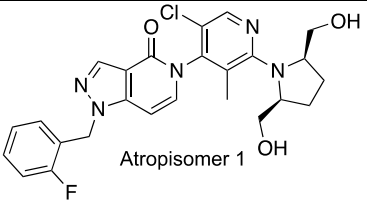
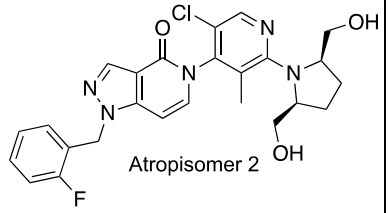
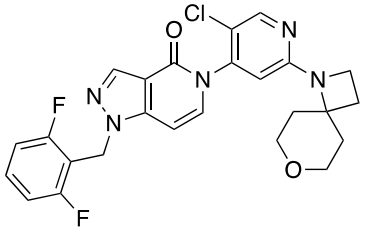
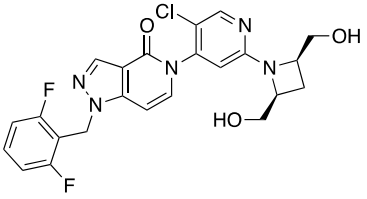
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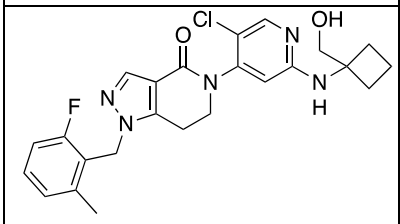
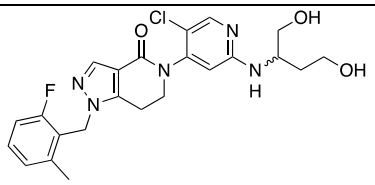
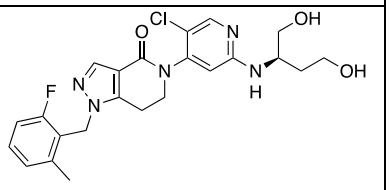
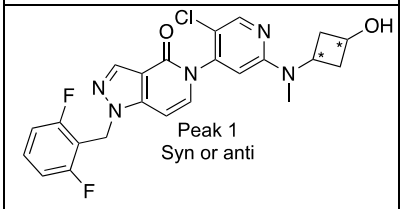
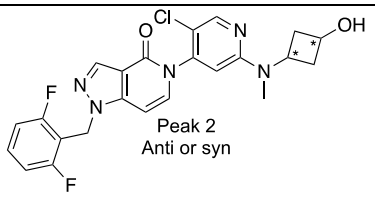
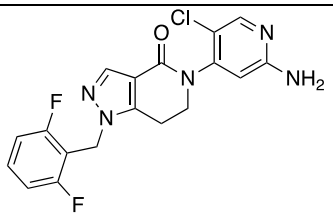
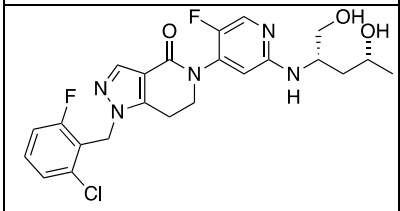
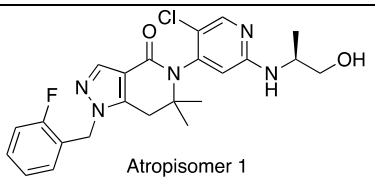
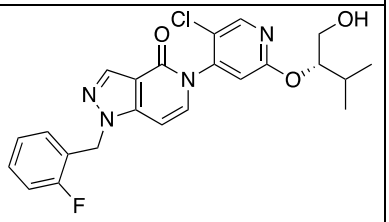
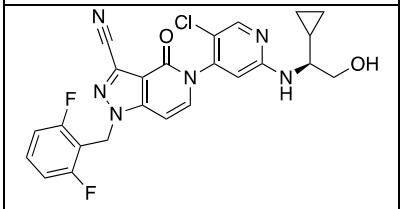
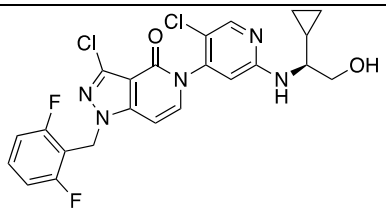
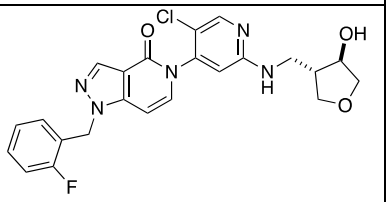
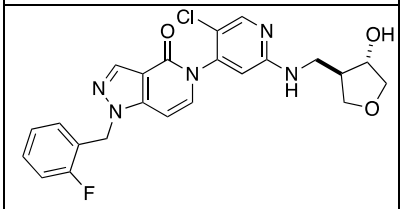
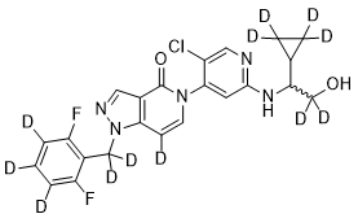
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214	**215**	**216**
 Atropisomer 1		
217	**218**	**219**
	 Peak 2	
220	**221**	**222**
		
223	**224**	**225**
		
226	**227**	**228**
 Peak 2 Diastereomer 1		

229	230	231
	3:1 mixture of enantiomers 	
232	**233**	
		
248	**249**	**250**
		
251	**252**	**253**
		
254	**255**	**256**
		
257	**258**	**259**
		

260	261	262
		
263	**264**	**265**
		
266	**267**	**268**
		
269	**270**	**271**
		 Syn
272	**273**	**274**
		 Peak 1
275	**276**	**277**
 Peak 2		

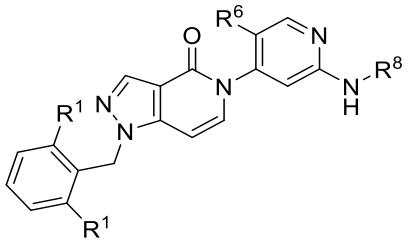
278	279	280
		 Syn
281	**282**	**283**
		
284	**285**	**286**
	 Atropisomer 1	 Atropisomer 2
287	**288**	**289**
		
290	**291**	**292**
	 Syn	
293	**294**	**295**
		

296	297	298
		 Peak 1
299	**300**	**301**
 Peak 3	 Peak 1	 Peak 3
302	**303**	**304**
	 Anti	
305	**306**	**307**
		
308	**309**	**310**
		 Atropisomer 1
311	**312**	**313**
 Atropisomer 2		

314	315	316
		
317	**318**	**319**
 Peak 1 Syn or anti	 Peak 2 Anti or syn	
320	**321**	**322**
	 Atropisomer 1	
323	**324**	**325**
		
326	**327**	
		

tautomers or atropisomers thereof, deuterated derivatives of the compounds, tautomers, or atropisomers, and pharmaceutically acceptable salts or prodrugs of any of the foregoing.

15. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 1, selected from a compound of Formula IIb:

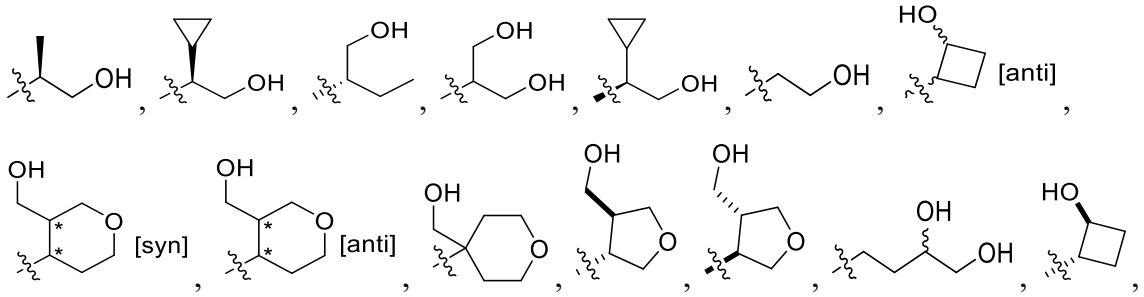


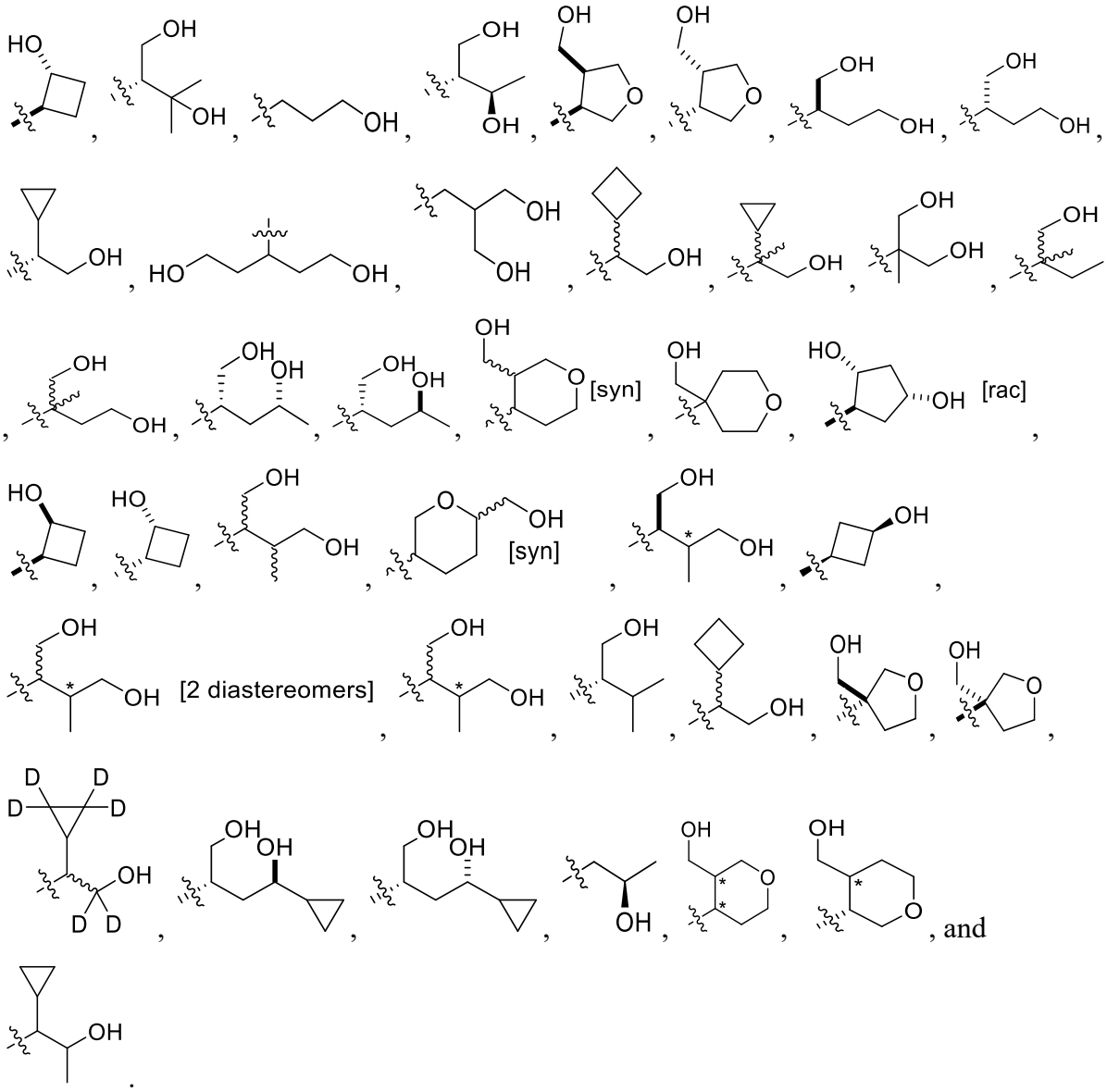
(Formula IIb),

a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing, wherein:

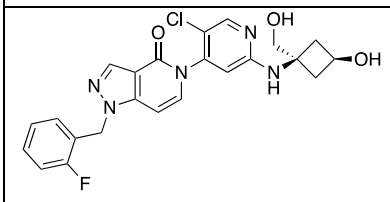
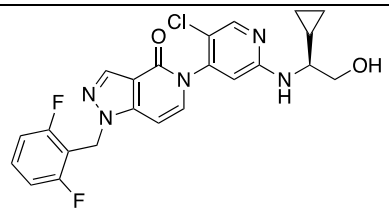
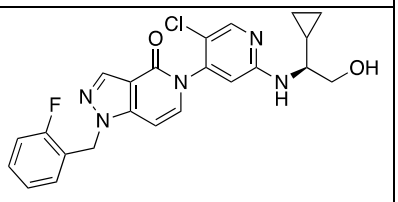
- each **R^1** is independently selected from hydrogen and halogen;
- **R^6** is selected from halogen; and
- **R^8** is selected from:
    - C_1-C_5 alkyl substituted with 0-5 groups independently selected from:
        - hydroxyl, and
        - C_3-C_6 cycloalkyl;
    - C_3-C_6 cycloalkyl, substituted with 0-2 groups selected from hydroxyl and halogen; and
    - 5- to 6-membered heterocyclyl unsubstituted or substituted with C_1-C_3 alkyl, wherein the C_1-C_3 alkyl is substituted with 0-2 substituents selected from hydroxyl and halogen.

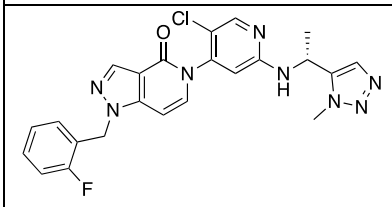
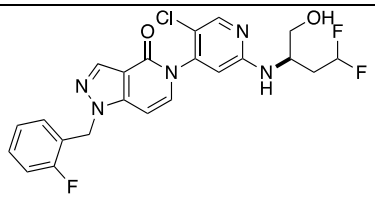
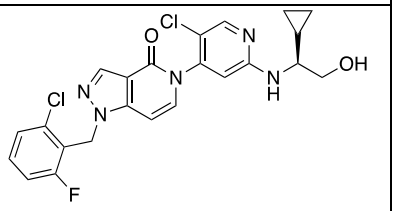
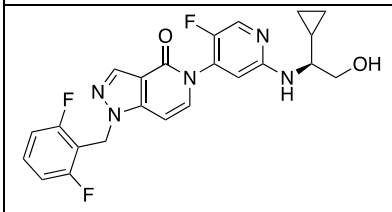
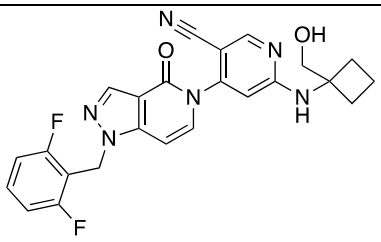
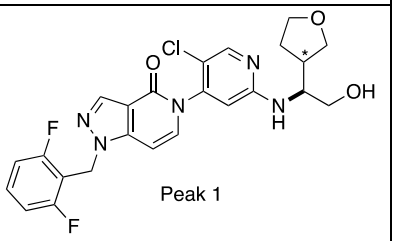
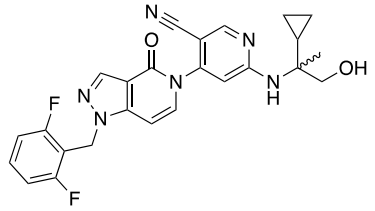
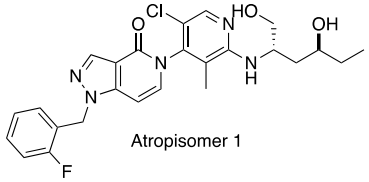
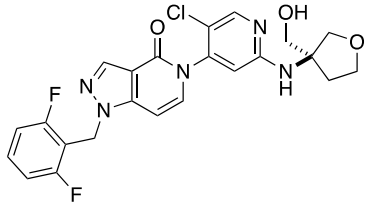
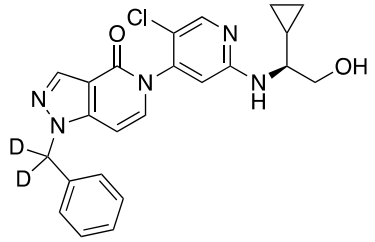
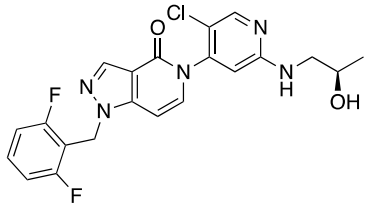
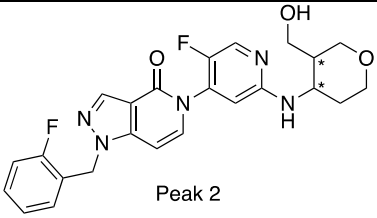
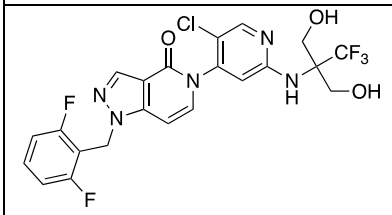
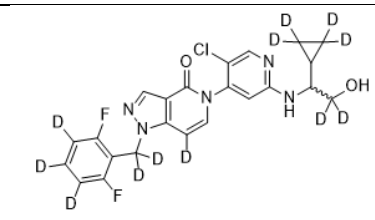
16. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to claim 15, wherein **R^8** is selected from:





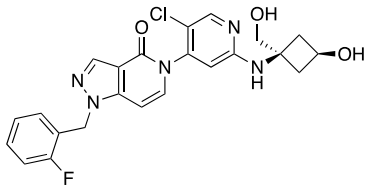
17. A compound selected from:

Compound 7	Compound 8	Compound 23
		

Compound 27	Compound 30	Compound 99
		
Compound 130	**Compound 146**	**Compound 149**
		 Peak 1
Compound 163	**Compound 192**	**Compound 201**
	 Atropisomer 1	
Compound 213	**Compound 217**	**Compound 218**
		 Peak 2
Compound 220	**Compound 327**	
		

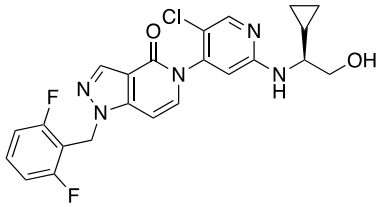
a tautomer or atropisomer thereof, a deuterated derivative of the compound, tautomer, or atropisomer, and a pharmaceutically acceptable salt or prodrug of any of the foregoing.

18. A compound having the following formula:



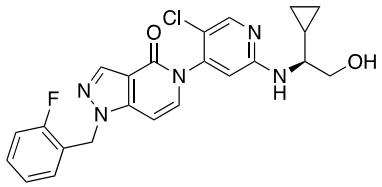
(Compound 7).

19. A compound having the following formula:



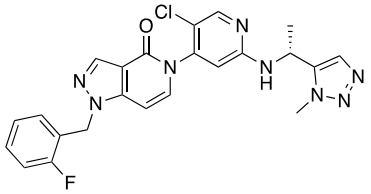
(Compound 8).

20. A compound having the following formula:



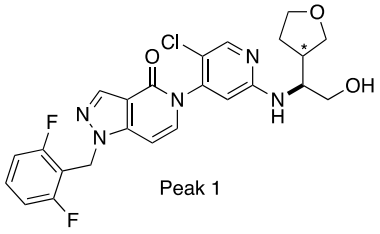
(Compound 23).

21. A compound having the following formula:



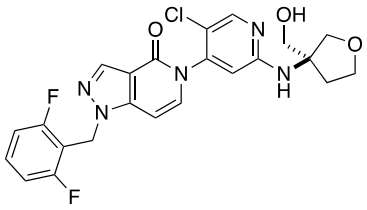
(Compound 27).

22. A compound having the following formula:



(Compound 149).

23. A compound having the following formula:



(Compound 201).

24. A pharmaceutical composition comprising the compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 23, and a pharmaceutically acceptable carrier.

25. Use of the compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 23, or the pharmaceutical composition according to claim 24, in the manufacture of a medicament for treating autosomal dominant polycystic kidney disease (ADPKD) in a patient in need thereof.

26. The compound, tautomer, atropisomer, deuterated derivative, or pharmaceutically acceptable salt or prodrug according to any one of claims 1 to 23, or the pharmaceutical composition according to claim 24, for use in therapy.