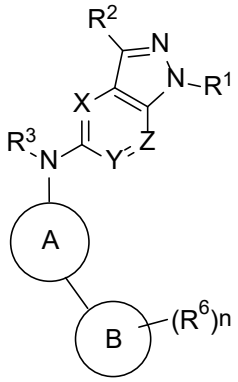
CLAIMS

What is claimed is:

1. A compound of Formula (**I**):



(**I**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof,

wherein:

R^1 is hydrogen, substituted or unsubstituted alkyl, or a nitrogen protecting group;

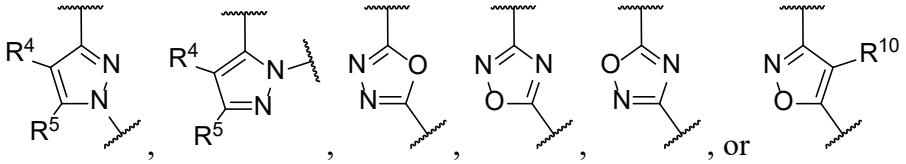
R^2 is hydrogen, halogen, -CN, substituted or unsubstituted alkyl, or substituted or unsubstituted carbocyclyl;

X is CR^7 or N;

Y is CR^8 or N;

Z is CR^9 or N;

R^3 is hydrogen, substituted or unsubstituted alkyl, or a nitrogen protecting group;

A is , or ;

R^4 is hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^5 is hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; or R^4 and R^5 together with the atoms to which they are attached form a substituted

or unsubstituted carbocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted heteroaryl;

B is aryl, heterocyclyl, heteroaryl, or carbocyclyl;

each R^6 is independently halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroaliphatic, oxo, $–OR^A$, $–N_3$, $–N(R^A)_2$, $–SR^A$, –CN, –SCN, $–C(=NR^A)R^A$, $–C(=NR^A)OR^A$, $–C(=NR^A)N(R^A)_2$, $–C(=O)R^A$, $–C(=O)OR^A$, $–C(=O)N(R^A)_2$, $–NO_2$, $–NR^AC(=O)R^A$, $–NR^AC(=O)OR^A$, $–NR^AC(=O)N(R^A)_2$, $–NR^AC(=NR^A)N(R^A)_2$, $–OC(=O)R^A$, $–OC(=O)OR^A$, $–OC(=O)N(R^A)_2$, $–NR^AS(O)_2R^A$, $-OS(O)_2R^A$, or $-S(O)_2R^A$;

n is 1, 2, 3, 4, or 5;

each R^7, R^8, and R^9 is independently hydrogen, halogen, -CN, or substituted or unsubstituted alkyl;

R^{10} is hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted carbocyclyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; and

each occurrence of R^A is, independently, hydrogen, substituted or unsubstituted acyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted carbocyclyl, substituted or unsubstituted carbocyclylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted hetaralkyl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom, or two R^A groups are joined to form a substituted or unsubstituted heterocyclyl ring, or a substituted or unsubstituted heteroaryl ring.

2. The compound of claim 1, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^1 is hydrogen or substituted or unsubstituted alkyl.

3. The compound of claim 1, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^1 is hydrogen.

4. The compound of any of claims 1-3, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^2 is hydrogen, halogen, or substituted or unsubstituted alkyl.

5. The compound of claim 4, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^2 is hydrogen or halogen.

6. The compound of claim 4, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^2 is hydrogen.

7. The compound of any of claims 1-6, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^3 is hydrogen or substituted or unsubstituted alkyl.

8. The compound of claim 7, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^3 is hydrogen.

9. The compound of any of claims 1-8, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein X is CR^7.

10. The compound of claim 9, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein:

X is CR^7; and

R^7 is hydrogen or halogen, preferably hydrogen.

11. The compound of any of claims 1-10, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein Y is CR^8.

12. The compound of any of claims 1-11, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein Z is CR^9.

13. The compound of any of claims 1-8, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein:

X is CR^7, wherein R^7 is hydrogen or halogen, preferably hydrogen;

Y is CR^8, wherein R^8 is hydrogen; and

Z is CR^9, wherein R^9 is hydrogen.

14. The compound of any of claims 1-13, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein B is aryl, heterocyclyl, or heteroaryl.

15. The compound of claim 14, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein B is aryl or heteroaryl.

16. The compound of claim 14, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein B is phenyl or pyridinyl.

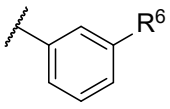
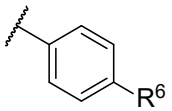
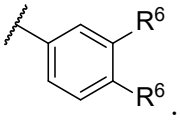
17. The compound of claim 14, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein B is phenyl.

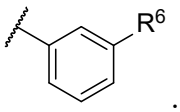
18. The compound of claim 14, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein B is pyridinyl.

19. The compound of any of claims 1-18, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein n is 1 or 2.

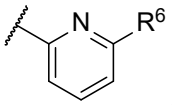
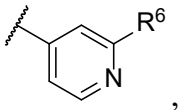
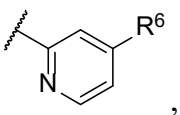
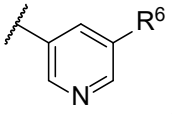
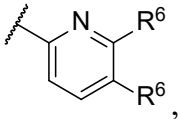
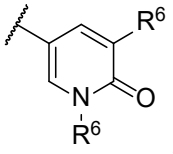
20. The compound of claim 19, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein n is 1.

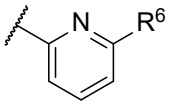
21. The compound of claim 19, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein n is 2.

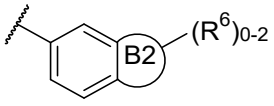
22. The compound of any of claims 1-18, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein $-B(R^6)_n$ is , , or .

23. The compound of claim 22, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein $-B(R^6)_n$ is .

24. The compound of any of claims 1-18, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched

compound, or prodrug thereof, wherein $-B(R^6)_n$ is , , , , , or .

25. The compound of any of claims 1-18, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein $-B(R^6)_n$ is .

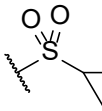
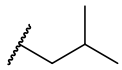
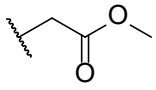
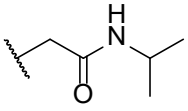
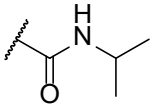
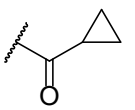
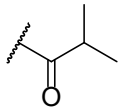
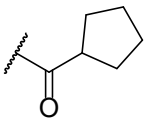
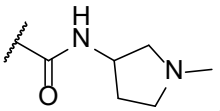
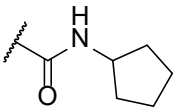
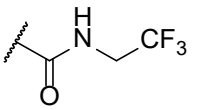
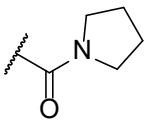
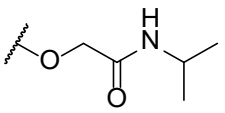
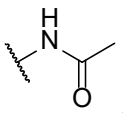
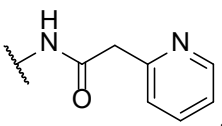
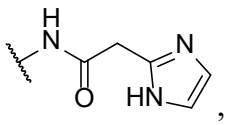
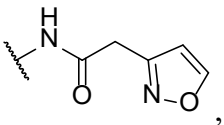
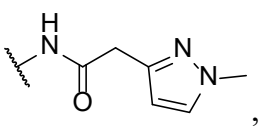
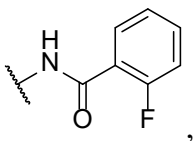
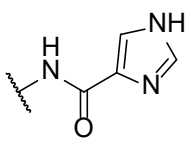
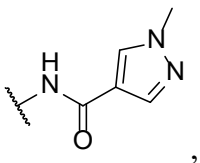
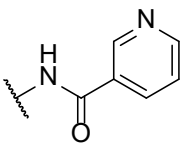
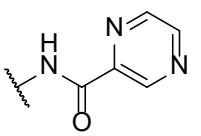
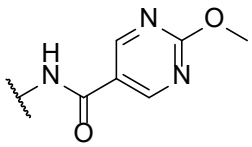
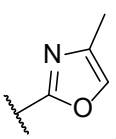
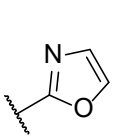
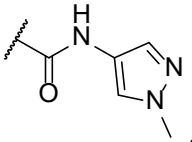
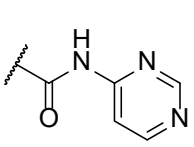
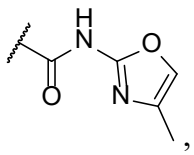
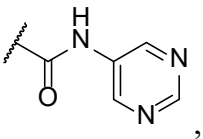
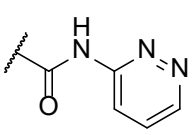
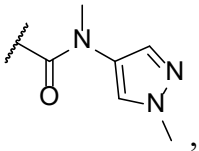
26. The compound of any of claims 1-15, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein $-B(R^6)_n$ is , wherein B2 is 5-6-membered, monocyclic, unsubstituted heteroaryl, or 5-6-membered, monocyclic, unsubstituted heterocyclyl, and R^6 is directly attached to B2.

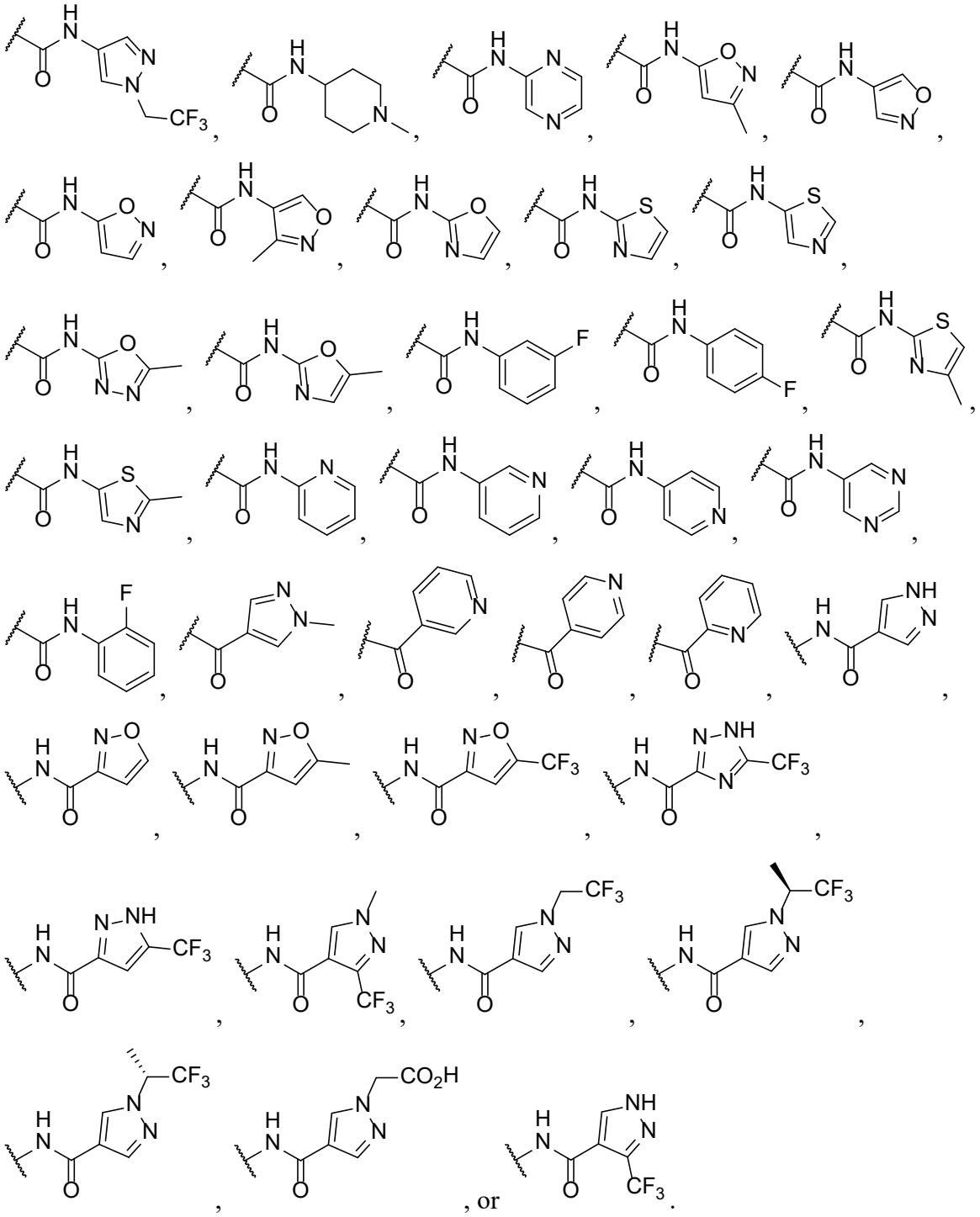
27. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently halogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroaliphatic, oxo, $-OR^A$, $-N(R^A)_2$, $-CN$, $-C(=NR^A)R^A$, $-C(=NR^A)OR^A$, $-C(=NR^A)N(R^A)_2$, $-C(=O)R^A$, $-C(=O)OR^A$, $-C(=O)N(R^A)_2$, $-NR^AC(=O)R^A$, $-NR^AC(=O)OR^A$, $-NR^AC(=O)N(R^A)_2$, $-NR^AC(=NR^A)N(R^A)_2$, $-OC(=O)R^A$, $-OC(=O)OR^A$, $-OC(=O)N(R^A)_2$, $-NR^AS(O)_2R^A$, $-OS(O)_2R^A$, or $-S(O)_2R^A$.

28. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, oxo, $-OR^A$, $-N(R^A)_2$, or $-NR^AC(=O)R^A$.

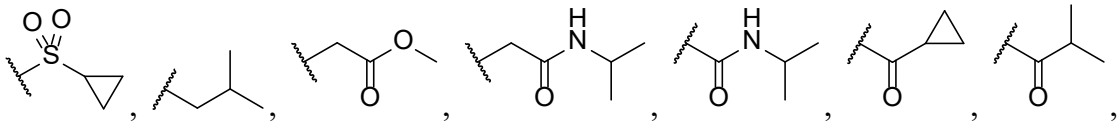
29. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, oxo, $–OC_{1\text{-}4}$ alkyl, $–OCH_2C(=O)N(R^A)_2$, $–N(R^A)_2$, or $–NR^AC(=O)R^A$.

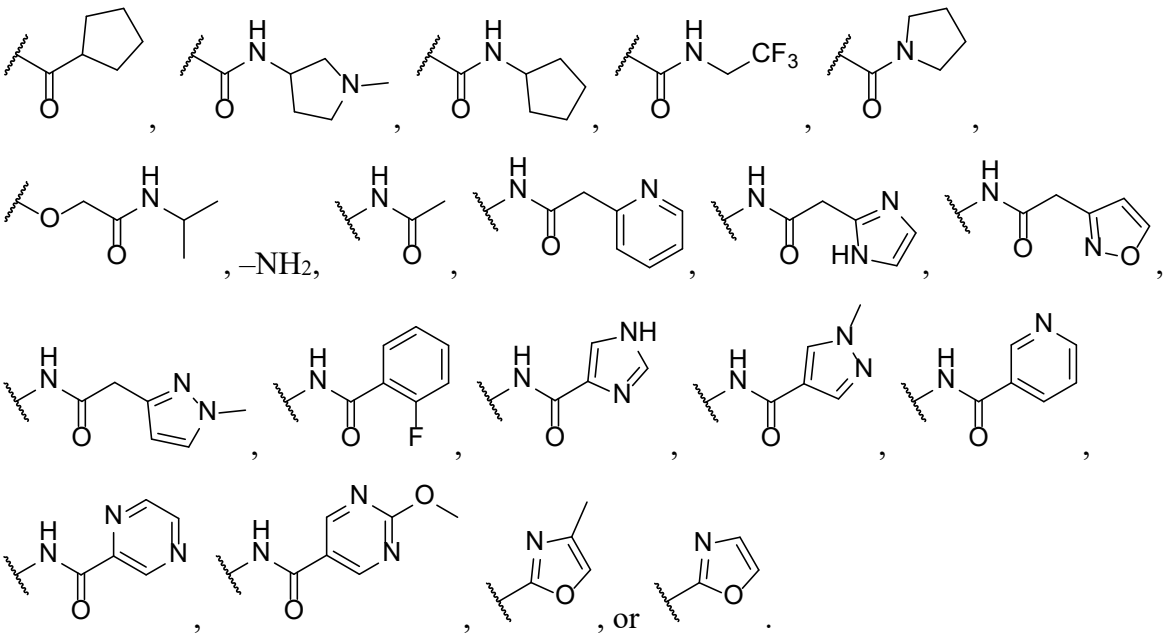
30. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently $C_{1\text{-}4}$ alkyl, substituted or unsubstituted heteroaryl, oxo, $–OC_{1\text{-}4}$ alkyl, $–OCH_2C(=O)NHC_{1\text{-}4}$ alkyl, $–NH_2$, –NHC(=O)aryl, or –NHC(=O)heteroaryl, wherein each alkyl, aryl, and heteroaryl are substituted or unsubstituted.

31. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently each R^6 is independently oxo, $–CH_3$, $–OCH_3$, -F, , , , , , , , , , , , , , –NH_2, , , , , , , , , , , , , , , , , , , .

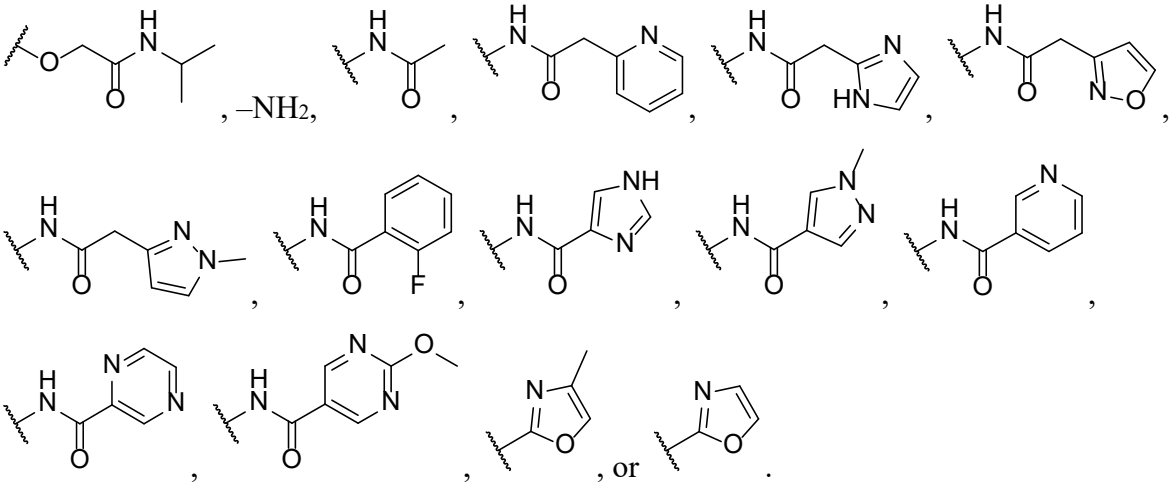


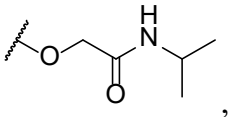
32. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently oxo, $–CH_3$, $–OCH_3$, -F,

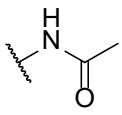
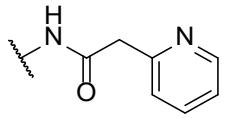
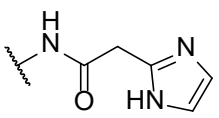
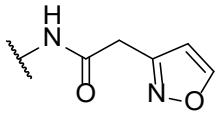
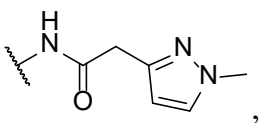


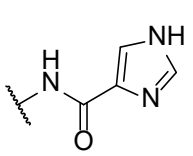
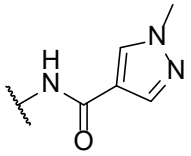
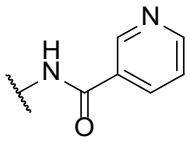
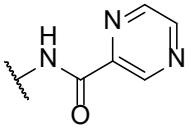
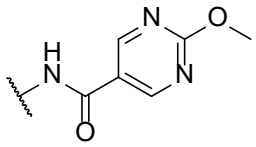


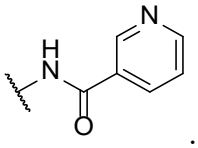
33. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently oxo, $–CH_3$, $–OCH_3$,

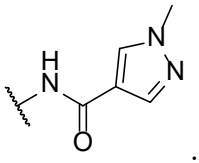


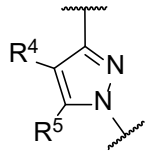
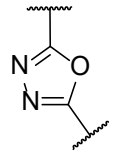
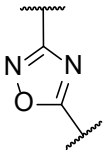
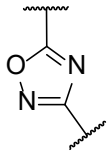
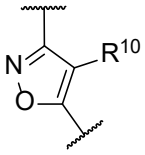
34. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein each R^6 is independently $–OCH_3$, ,

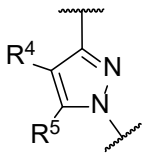
–NH_2, , , , , ,

, , , , or .

35. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^6 is .

36. The compound of any of claims 1-26, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^6 is .

37. The compound of any of claims 1-36, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is , , , , or .

38. The compound of any of claims 1-37, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is 

.

39. The compound of any of claims 1-38, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^4 is hydrogen, halogen, or substituted or unsubstituted alkyl.

40. The compound of claim 39, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^4 is hydrogen.

41. The compound of claim 39, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^4 is substituted or unsubstituted alkyl.

42. The compound of any of claims 1-41, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^5 is hydrogen, halogen, or substituted or unsubstituted alkyl.

43. The compound of claim 42, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^5 is hydrogen.

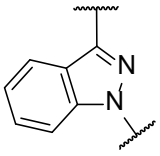
44. The compound of claim 42, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^5 is substituted or unsubstituted alkyl.

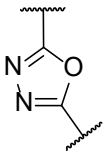
45. The compound of any of claims 1-38, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein:

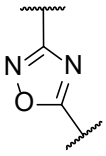
R^4 is hydrogen or substituted or unsubstituted alkyl; and

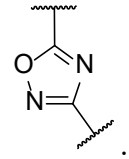
R^5 is hydrogen or substituted or unsubstituted alkyl; or R^4 and R^5 together with the atoms to which they are attached form a substituted or unsubstituted aryl ring.

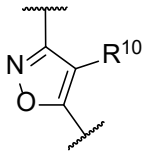
46. The compound of any of claims 1-38, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^4 and R^5 together with the atoms to which they are attached form a substituted or unsubstituted aryl ring.

47. The compound of any of claims 1-46, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is .

48. The compound of any of claims 1-37, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is .

49. The compound of any of claims 1-37, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is .

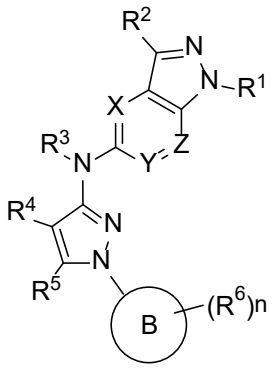
50. The compound of any of claims 1-37, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is .

51. The compound of any of claims 1-37, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein A is .

52. The compound of any of claims 1-37 and 51, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^{10} is hydrogen, halogen, or substituted or unsubstituted alkyl.

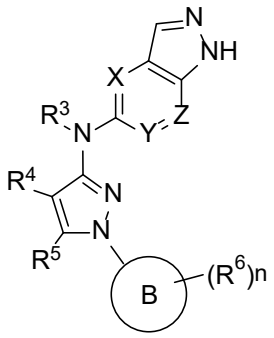
53. The compound of claim 52, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, wherein R^{10} is hydrogen.

54. The compound of any of claims 1-53, wherein:
the compound is of Formula (**I-a**):



(**I-a**),
or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

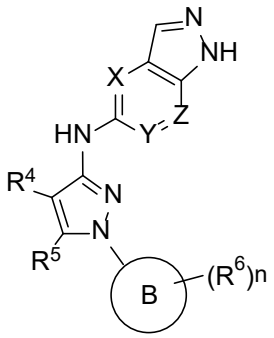
the compound is of Formula (**I-a-1**):



(**I-a-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

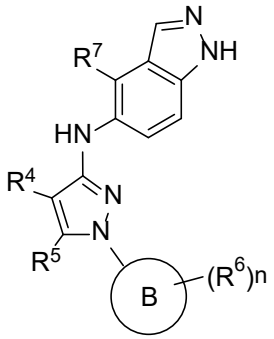
the compound is of Formula (**I-a-2**):



(**I-a-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

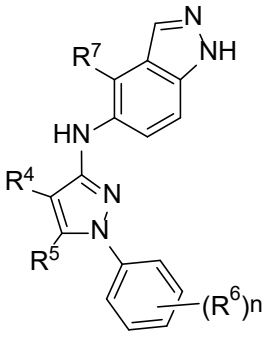
the compound is of Formula (**I-a-3**):



(**I-a-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

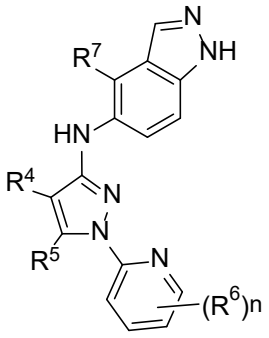
the compound is of Formula (**I-a-4**):



(**I-a-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

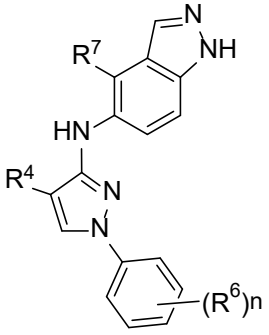
the compound is of Formula (**I-a-4a**):



(**I-a-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

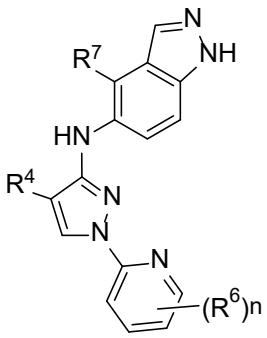
the compound is of Formula (**I-a-5**):



(**I-a-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

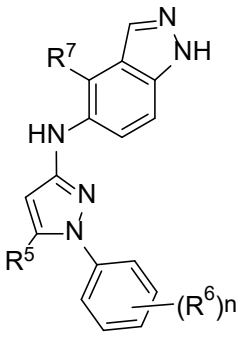
the compound is of Formula (**I-a-5a**):



(**I-a-5a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

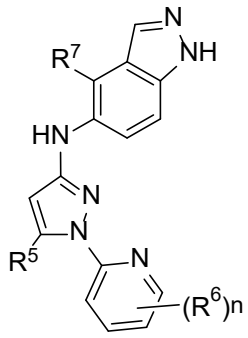
the compound is of Formula (**I-a-6**):



(**I-a-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

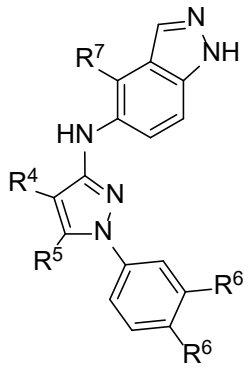
the compound is of Formula (**I-a-6a**):



(**I-a-6a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

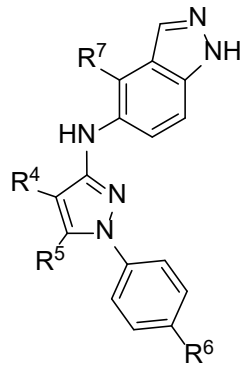
the compound is of Formula (**I-a-7**):



(**I-a-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

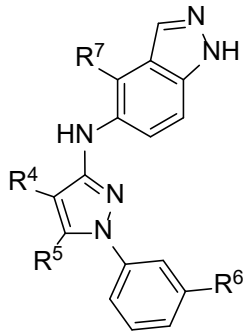
the compound is of Formula (**I-a-8**):



(**I-a-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

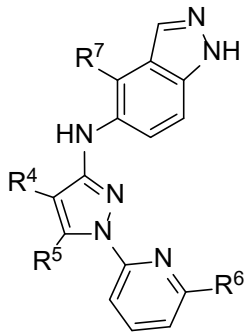
the compound is of Formula (**I-a-9**):



(**I-a-9**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

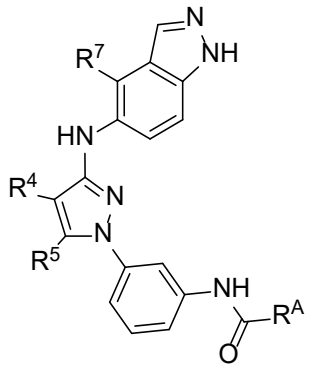
the compound is of Formula (**I-a-9a**):



(**I-a-9a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

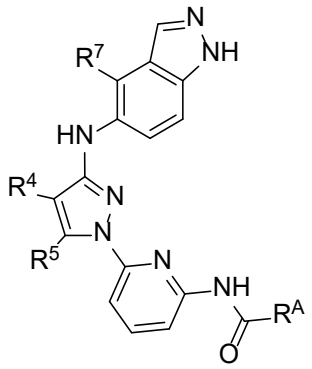
the compound is of Formula (**I-a-10**):



(**I-a-10**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

the compound is of Formula (**I-a-10a**):

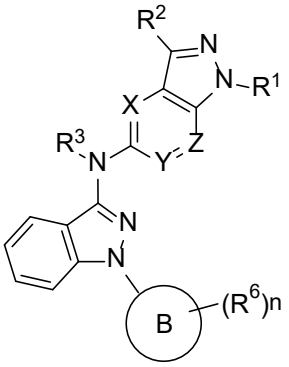


(**I-a-10a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

55. The compound of any of claims 1-53, wherein:

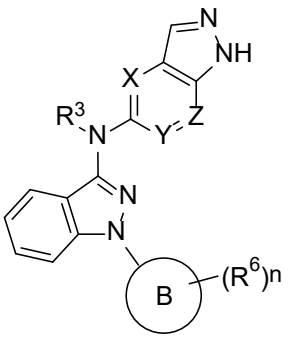
the compound is of Formula (**I-b**):



(**I-b**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

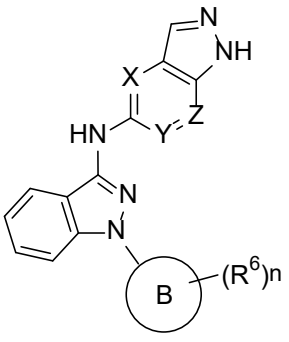
the compound is of Formula (**I-b-1**):



(**I-b-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

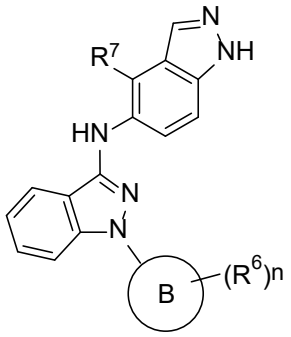
the compound is of Formula (**I-b-2**):



(**I-b-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

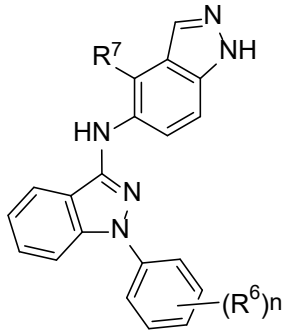
the compound is of Formula (**I-b-3**):



(**I-b-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

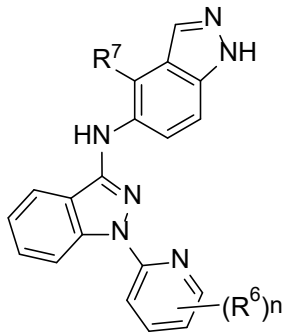
the compound is of Formula (**I-b-4**):



(**I-b-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

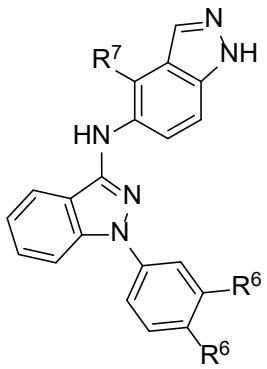
the compound is of Formula (**I-b-4a**):



(**I-b-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

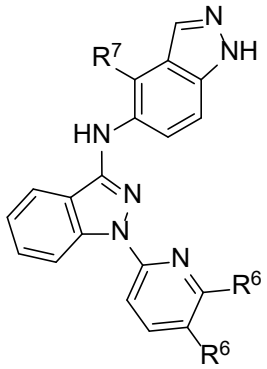
the compound is of Formula (**I-b-5**):



(**I-b-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

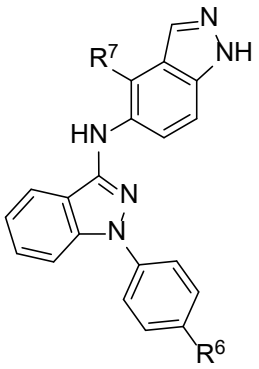
the compound is of Formula (**I-b-5a**):



(**I-b-5a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

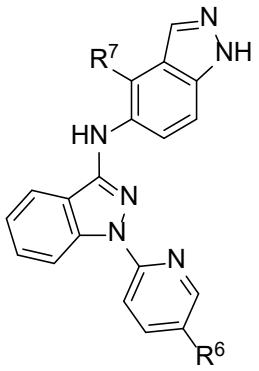
the compound is of Formula (**I-b-6**):



(**I-b-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

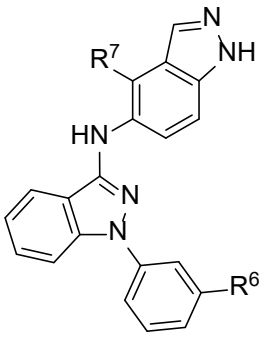
the compound is of Formula (**I-b-6a**):



(**I-b-6a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

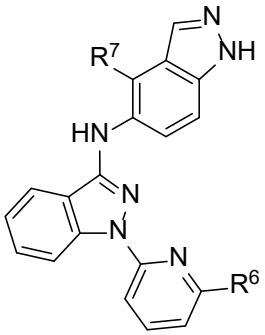
the compound is of Formula (**I-b-7**):



(**I-b-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

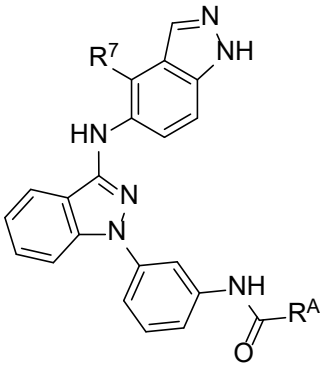
the compound is of Formula (**I-b-7a**):



(**I-b-7a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

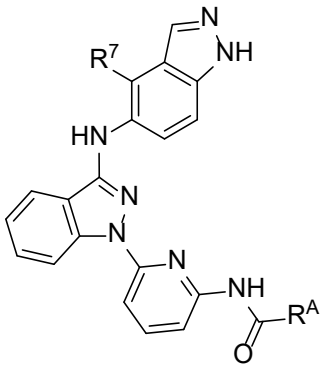
the compound is of Formula (**I-b-8**):



(**I-b-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

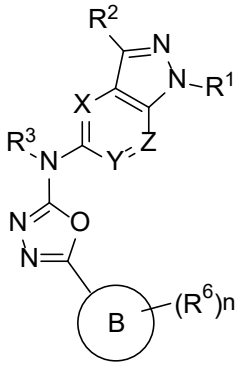
the compound is of Formula (**I-b-8a**):



(**I-b-8a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

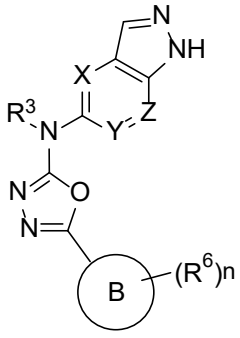
56. The compound of any of claims 1-53, wherein:
the compound is of Formula (**I-c**):



(**I-c**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

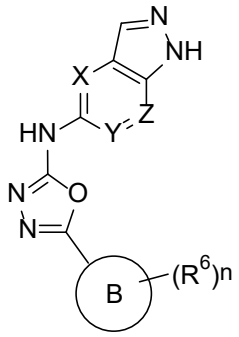
wherein the compound is of Formula (**I-c-1**):



(**I-c-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

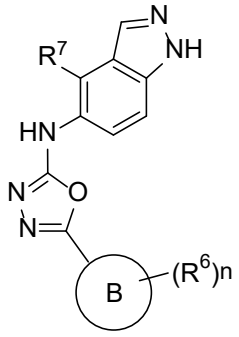
the compound is of Formula (**I-c-2**):



(**I-c-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

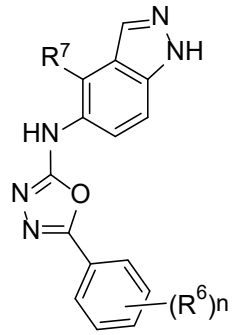
the compound is of Formula (**I-c-3**):



(**I-c-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

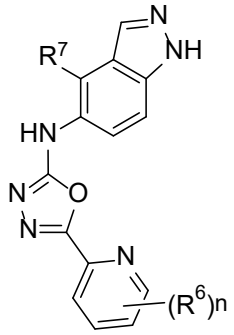
the compound is of Formula (**I-c-4**):



(**I-c-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

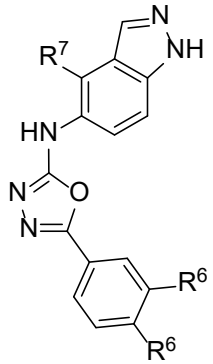
the compound is of Formula (**I-c-4a**):



(**I-c-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

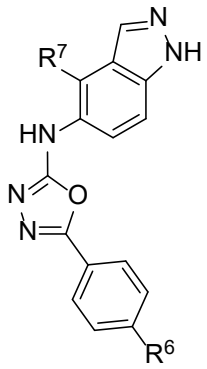
the compound is of Formula (**I-c-5**):



(**I-c-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

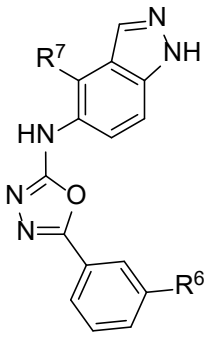
the compound is of Formula (**I-c-6**):



(**I-c-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

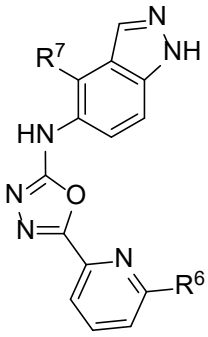
the compound is of Formula (**I-c-7**):



(**I-c-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

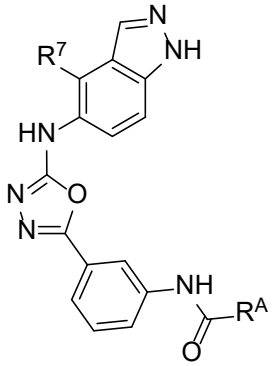
the compound is of Formula (**I-c-7a**):



(**I-c-7a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

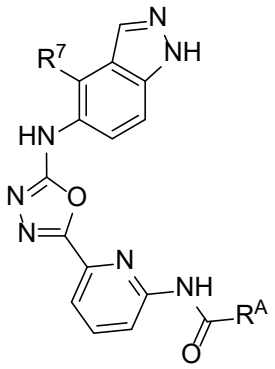
the compound is of Formula (**I-c-8**):



(**I-c-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

the compound is of Formula (**I-c-8a**):

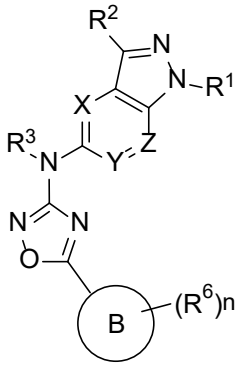


(**I-c-8a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

57. The compound of any of claims 1-53, wherein:

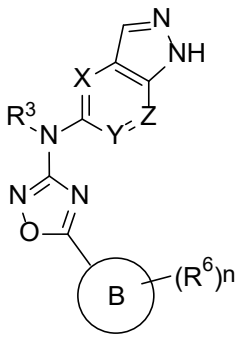
the compound is of Formula (**I-d**):



(**I-d**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

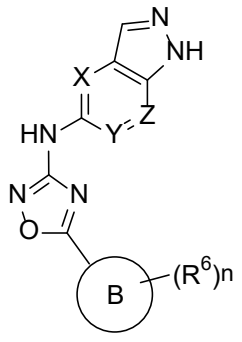
the compound is of Formula (**I-d-1**):



(**I-d-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

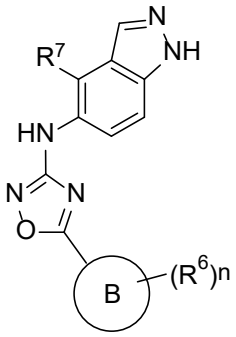
the compound is of Formula (**I-d-2**):



(**I-d-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

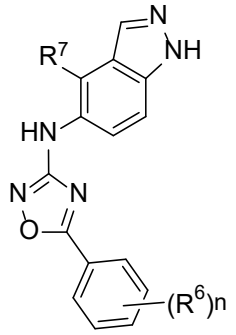
the compound is of Formula (**I-d-3**):



(**I-d-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

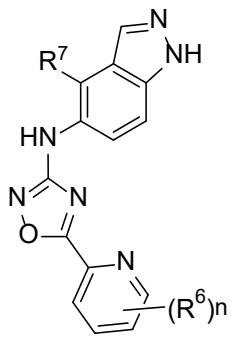
the compound is of Formula (**I-d-4**):



(**I-d-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

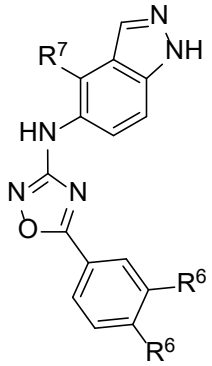
the compound is of Formula (**I-d-4a**):



(**I-d-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

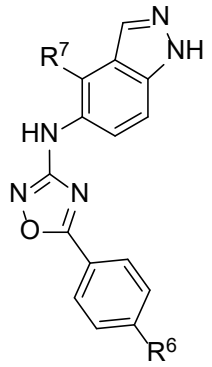
the compound is of Formula (**I-d-5**):



(**I-d-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

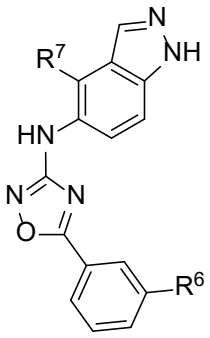
the compound is of Formula (**I-d-6**):



(**I-d-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

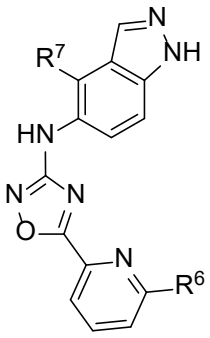
the compound is of Formula (**I-d-7**):



(**I-d-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

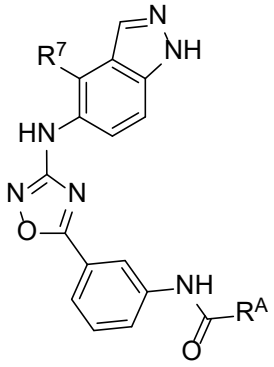
the compound is of Formula (**I-d-7a**):



(**I-d-7a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

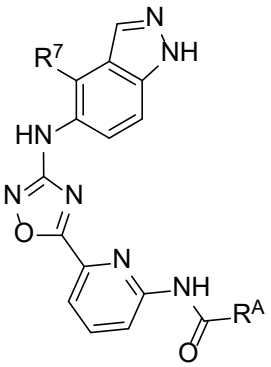
the compound is of Formula (**I-d-8**):



(**I-d-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

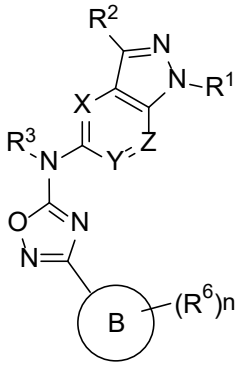
the compound is of Formula (**I-d-8a**):



(**I-d-8a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

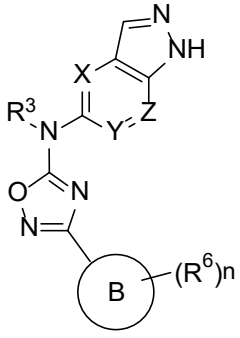
58. The compound of any of claims 1-53, wherein:
the compound is of Formula (**I-e**):



(**I-e**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereofl

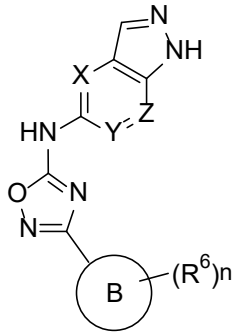
the compound is of Formula (**I-e-1**):



(**I-e-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

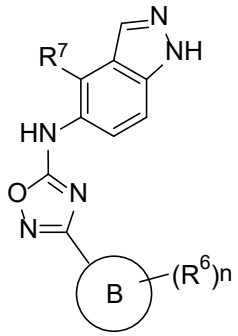
the compound is of Formula (**I-e-2**):



(**I-e-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

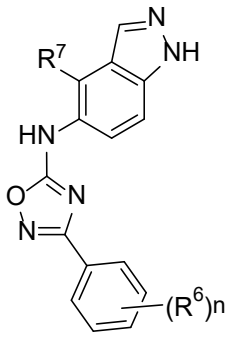
the compound is of Formula (**I-e-3**):



(**I-e-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

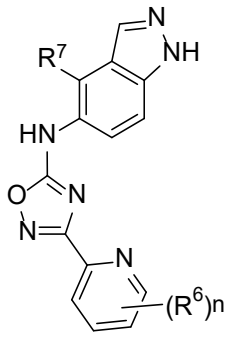
the compound is of Formula (**I-e-4**):



(**I-e-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

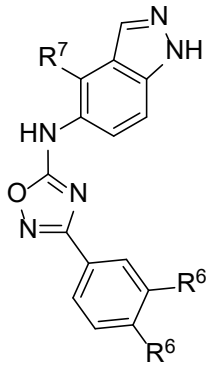
the compound is of Formula (**I-e-4a**):



(**I-e-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

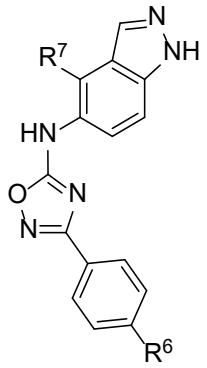
the compound is of Formula (**I-e-5**):



(**I-e-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

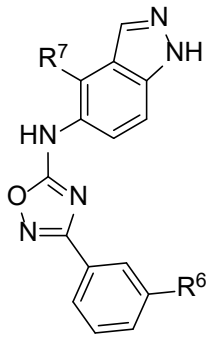
the compound is of Formula (**I-e-6**):



(**I-e-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

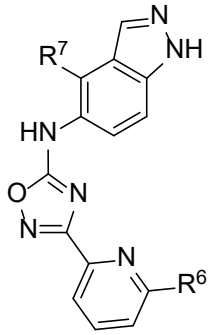
the compound is of Formula (**I-e-7**):



(**I-e-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

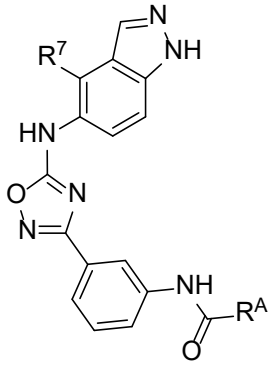
the compound is of Formula (**I-e-7a**):



(**I-e-7a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

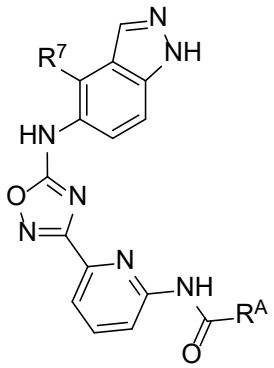
the compound is of Formula (**I-e-8**):



(**I-e-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

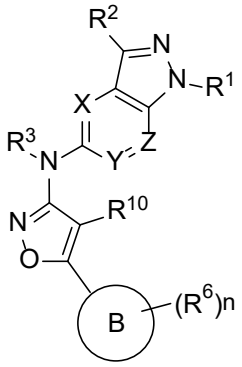
the compound is of Formula (**I-e-8a**):



(**I-e-8a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

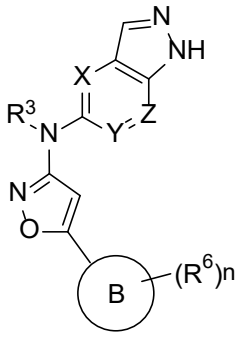
59. The compound of any of claims 1-53, wherein:
the compound is of Formula (**I-f**):



(**I-f**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

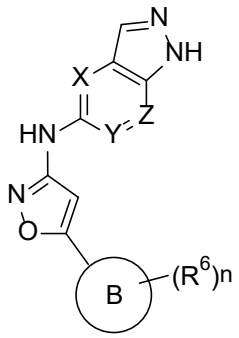
the compound is of Formula (**I-f-1**):



(**I-f-1**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

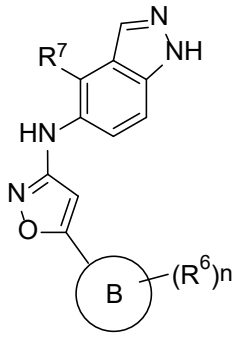
the compound is of Formula (**I-f-2**):



(**I-f-2**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

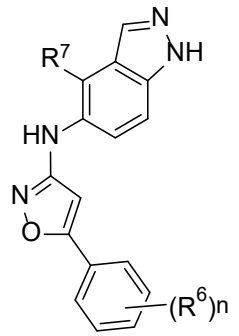
the compound is of Formula (**I-f-3**):



(**I-f-3**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

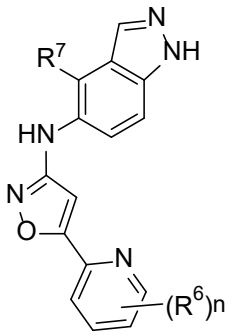
the compound is of Formula (**I-f-4**):



(**I-f-4**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

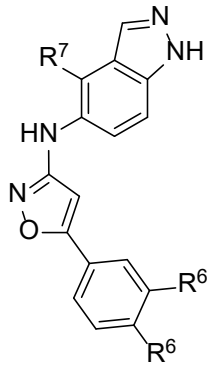
the compound is of Formula (**I-f-4a**):



(**I-f-4a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

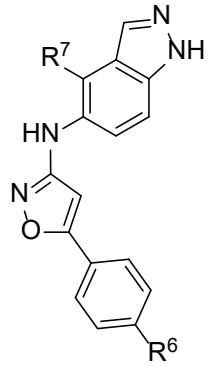
the compound is of Formula (**I-f-5**):



(**I-f-5**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

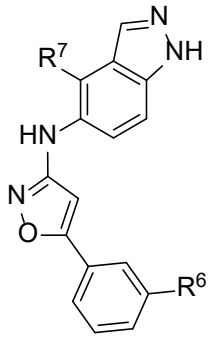
the compound is of Formula (**I-f-6**):



(**I-f-6**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

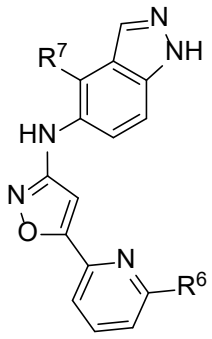
the compound is of Formula (**I-f-7**):



(**I-f-7**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

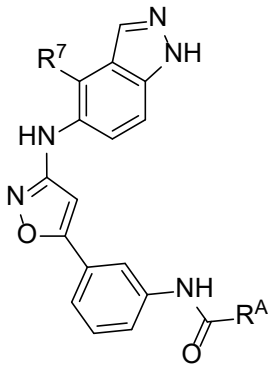
the compound is of Formula (**I-f-7a**):



(**I-f-7a**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof;

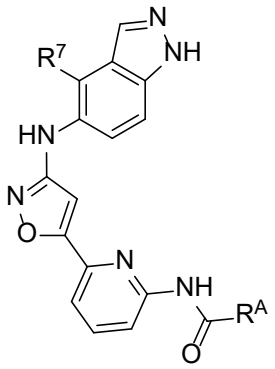
the compound is of Formula (**I-f-8**):



(**I-f-8**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof; or

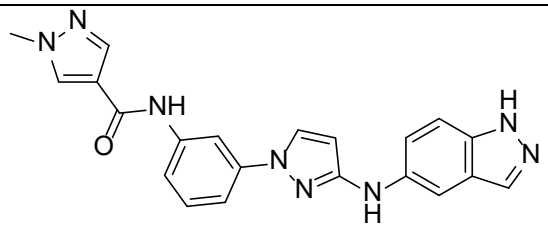
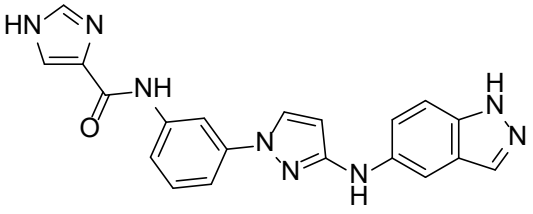
the compound is of Formula (**I-f-8a**):

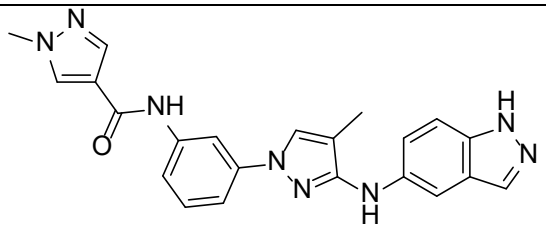
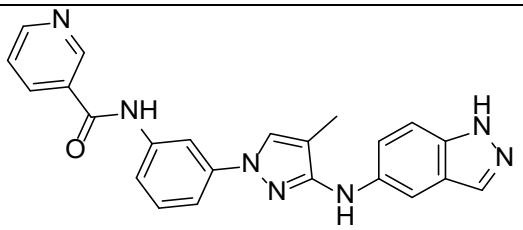
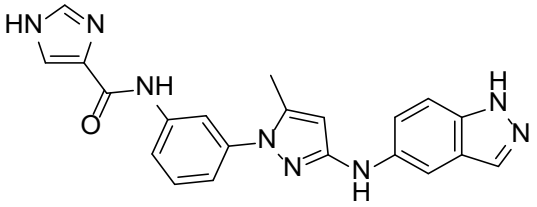
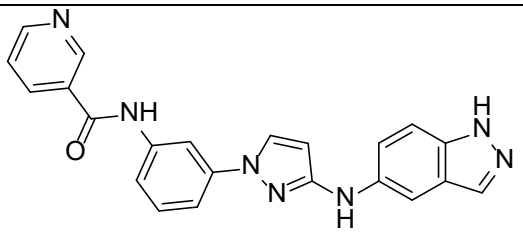
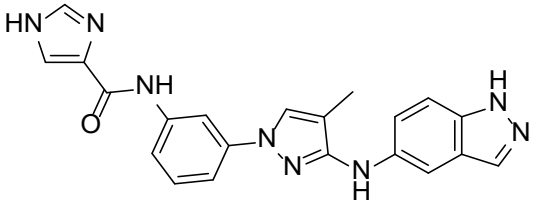
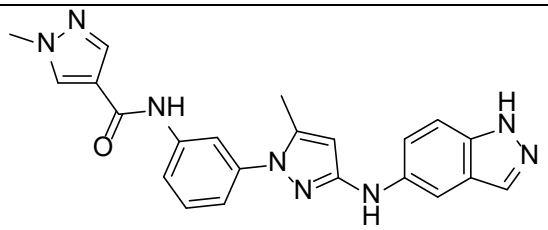
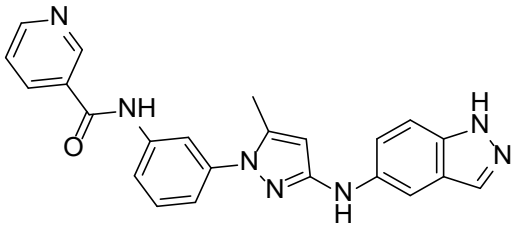
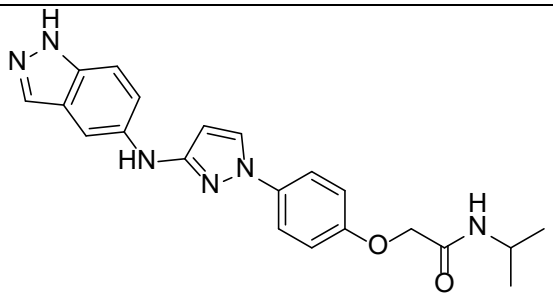
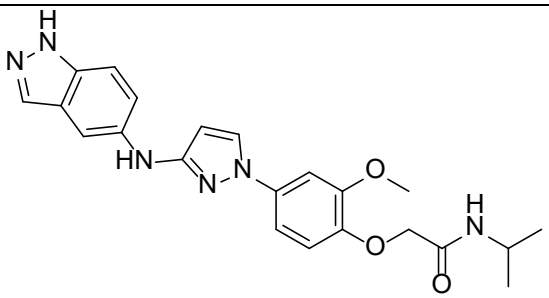
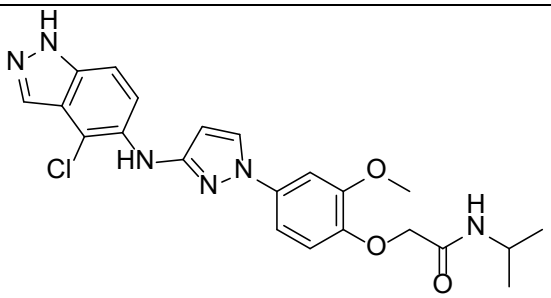
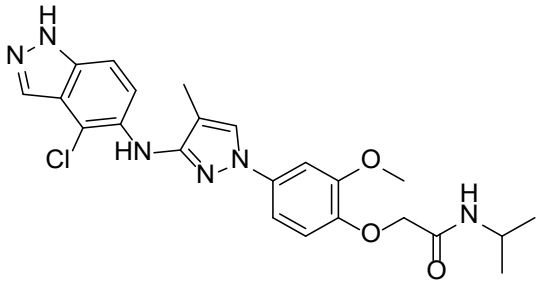
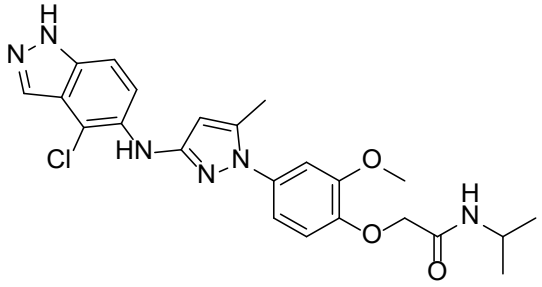


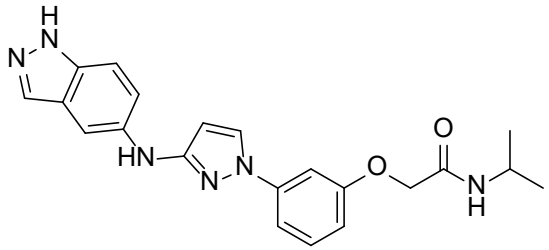
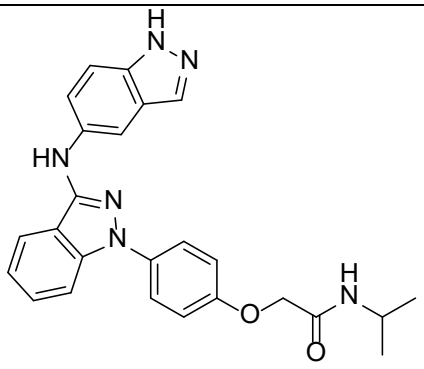
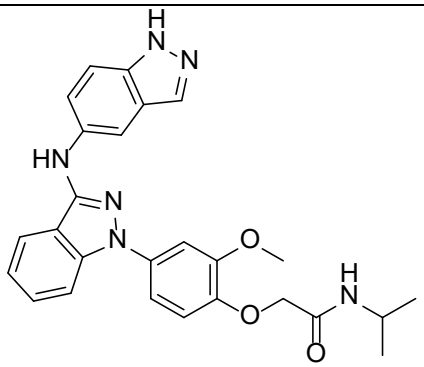
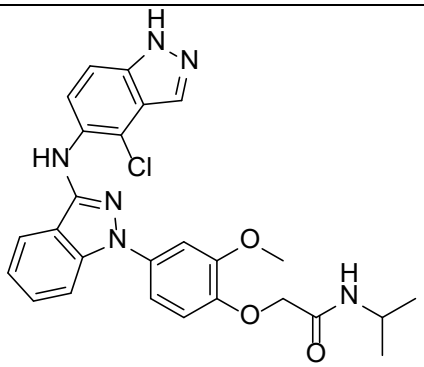
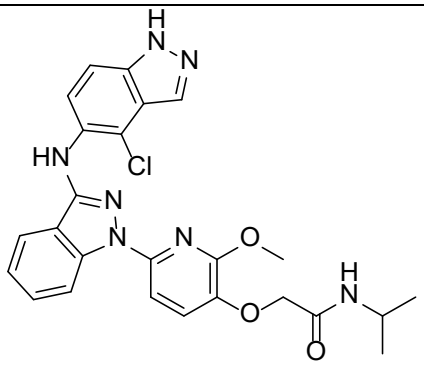
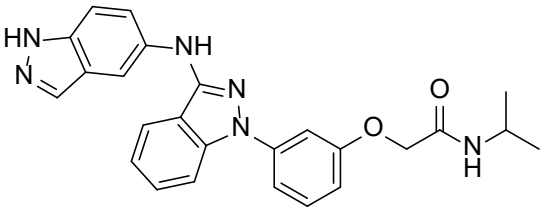
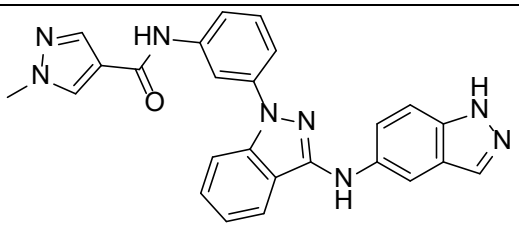
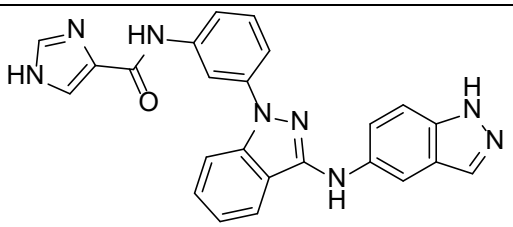
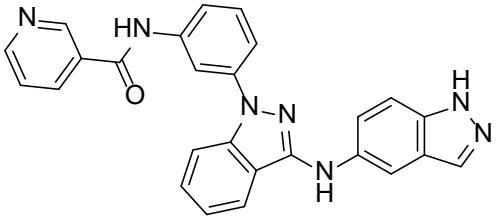
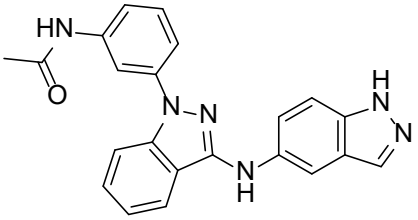
(**I-f-8a**),

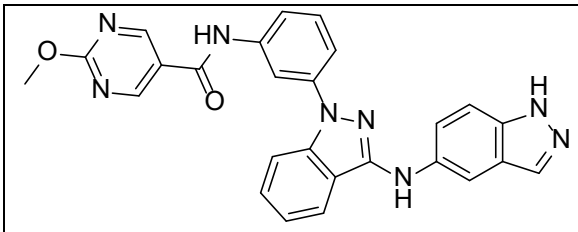
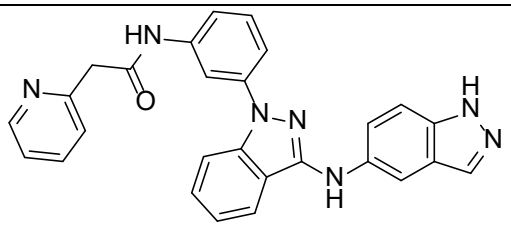
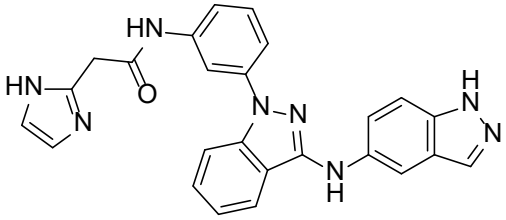
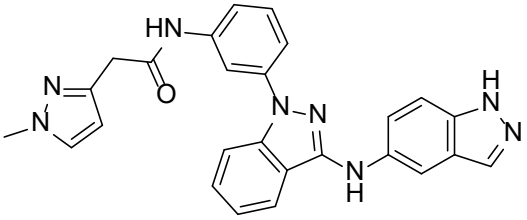
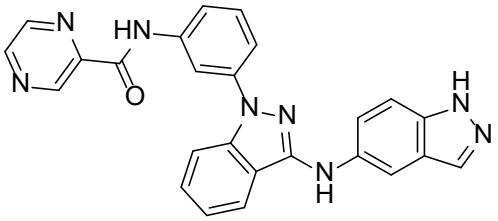
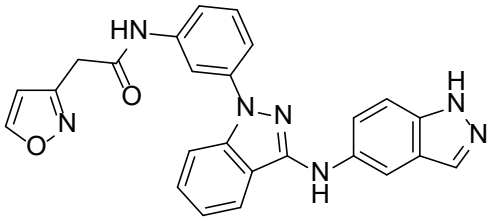
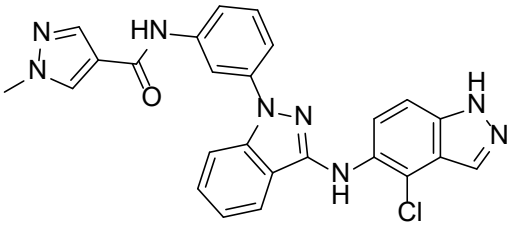
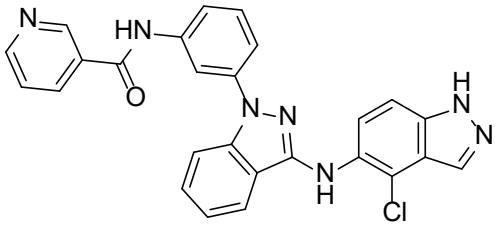
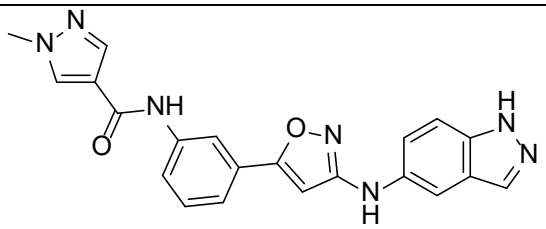
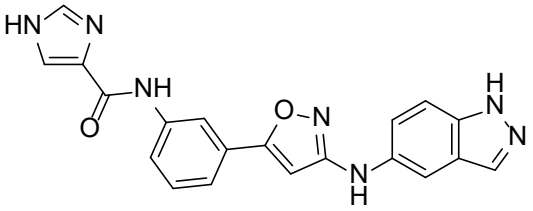
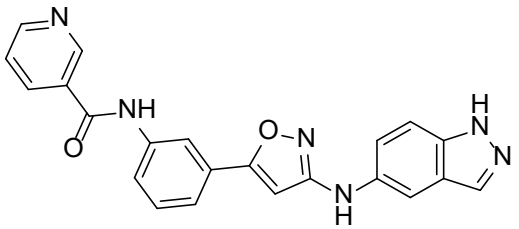
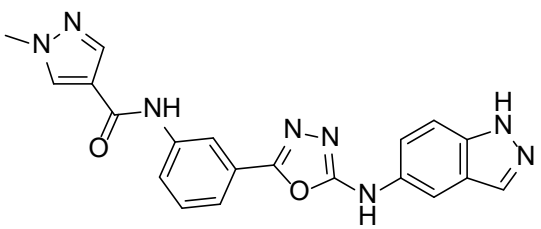
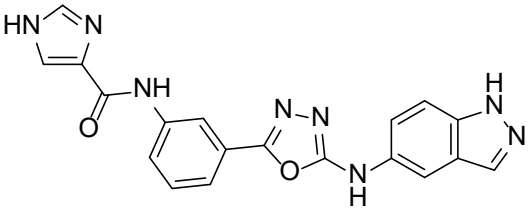
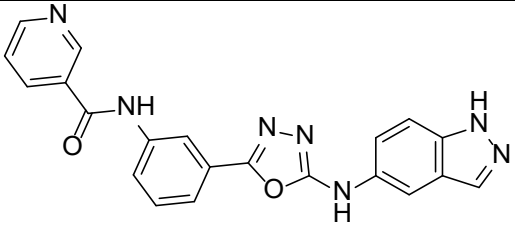
or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

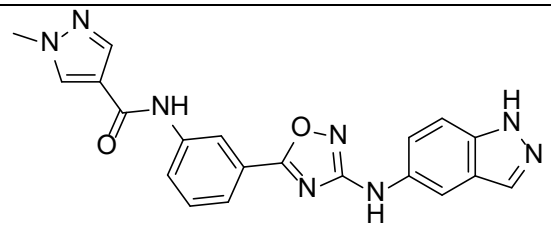
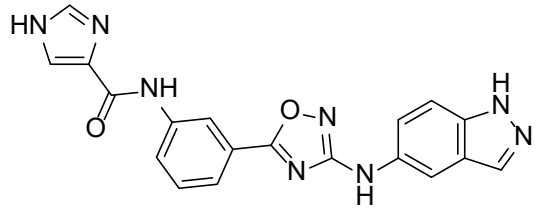
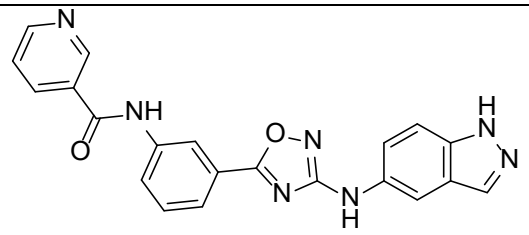
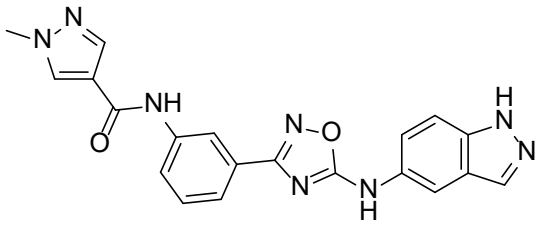
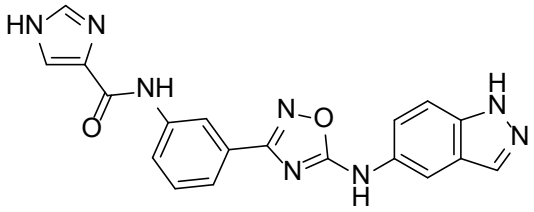
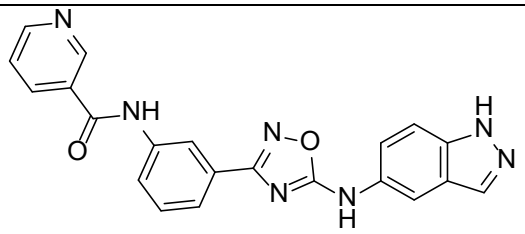
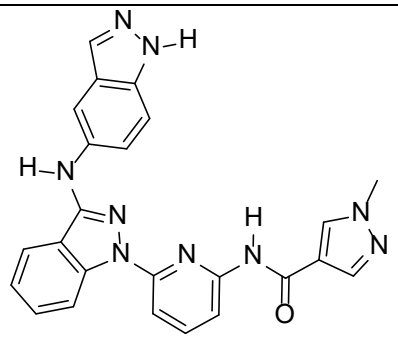
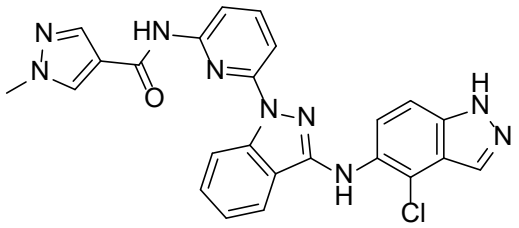
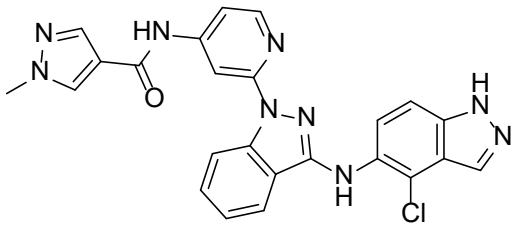
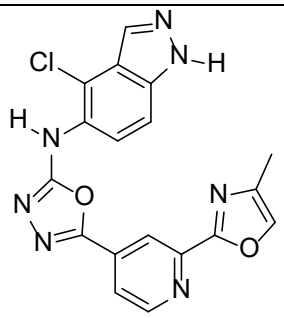
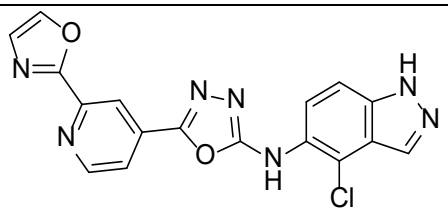
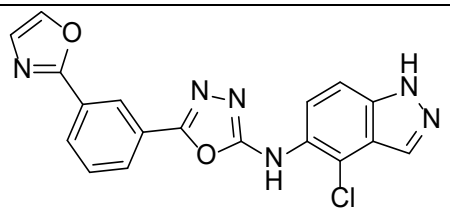
60. The compound of claim 1, wherein the compound is:

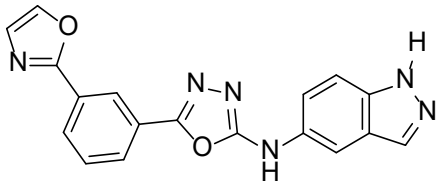
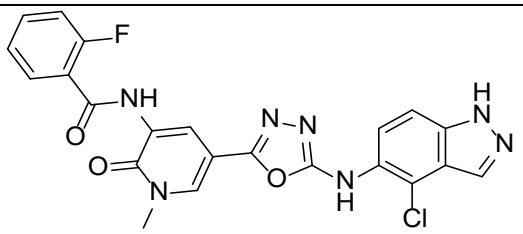
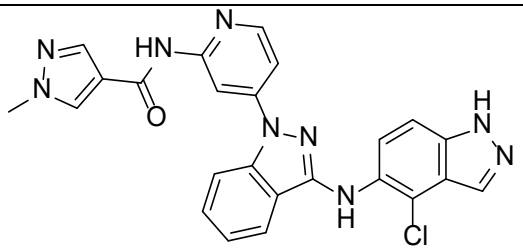
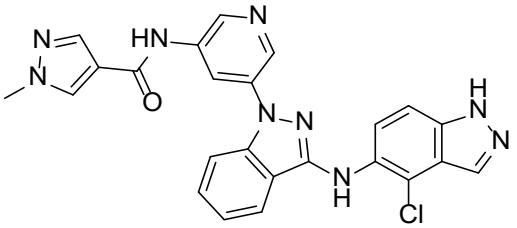
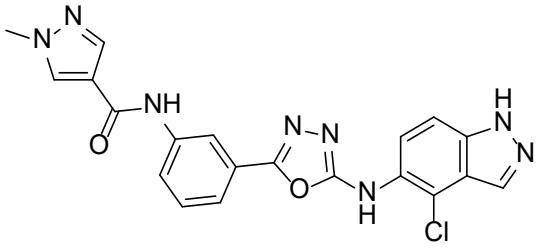
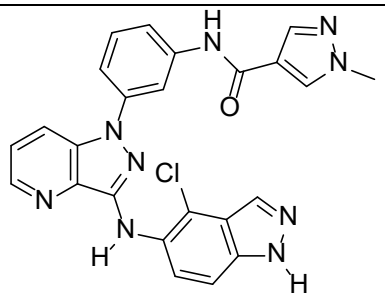
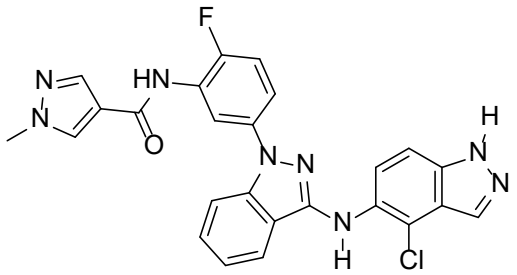
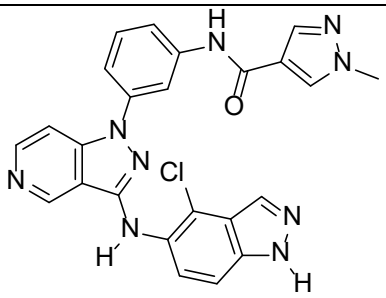
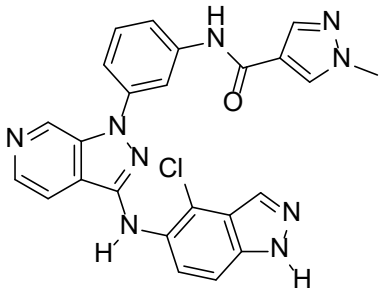
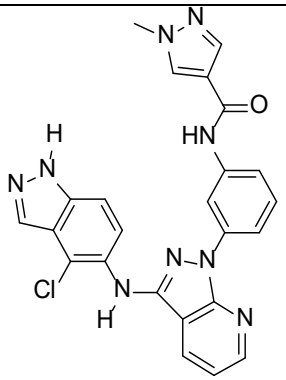
	
1	2

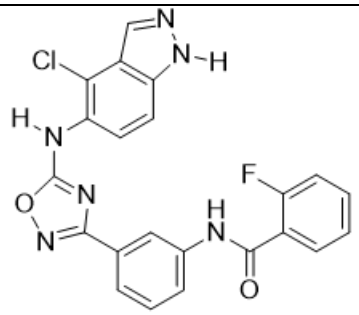
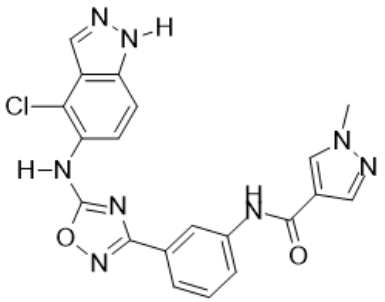
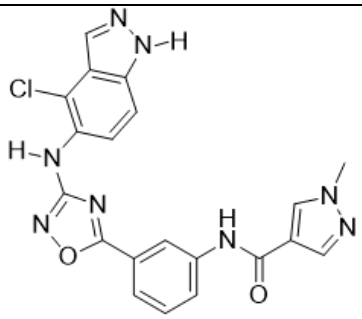
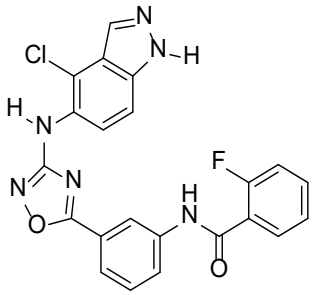
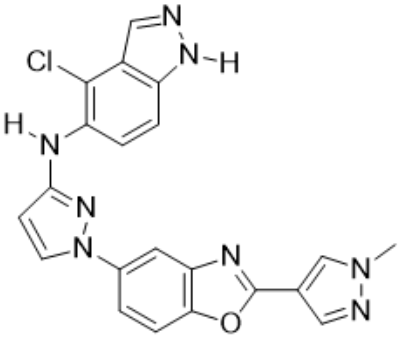
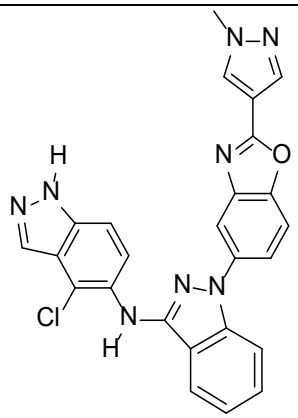
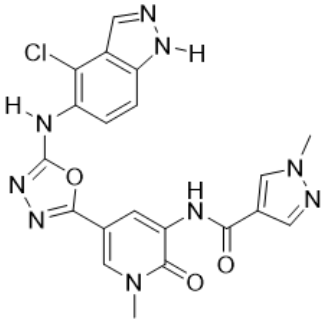
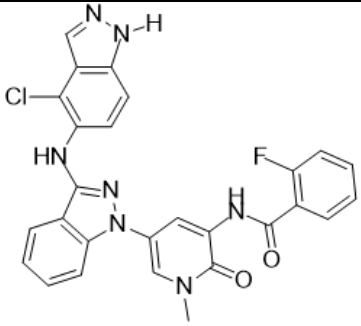
 3	 4
 5	 6
 7	 8
 9	 10
 11	 12
 13	 14

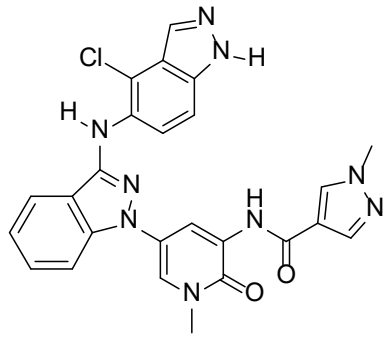
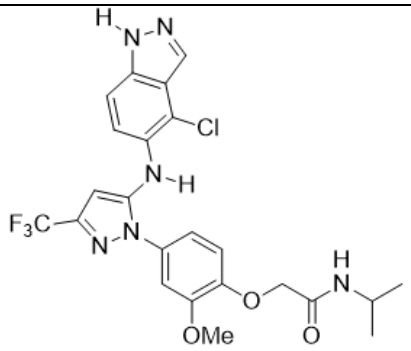
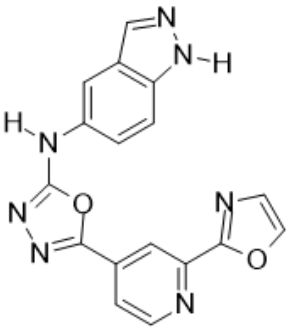
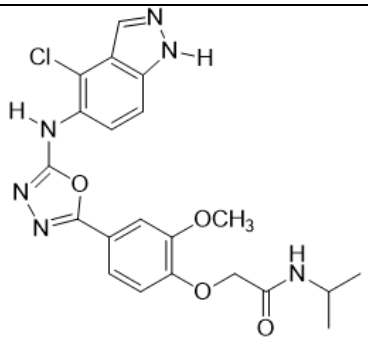
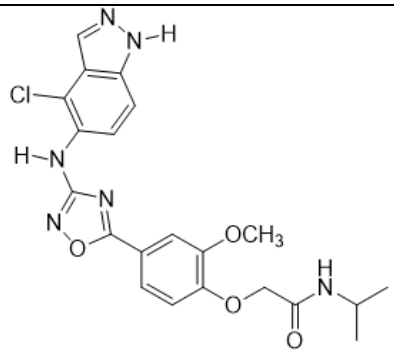
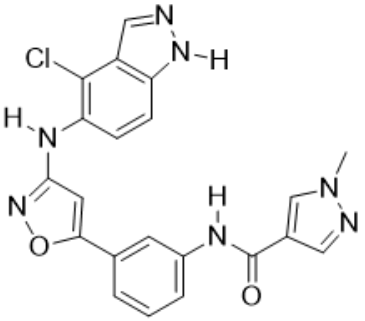
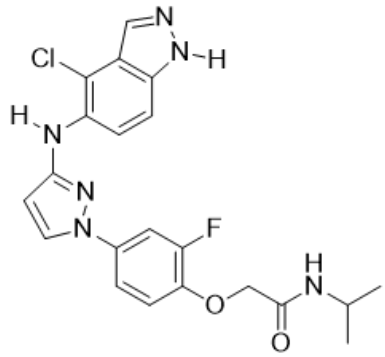
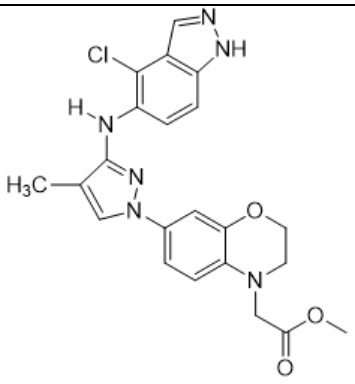
 15	 16
 17	 18
 19	 20
 21	 22
 23	 24

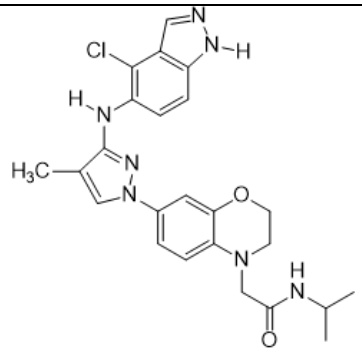
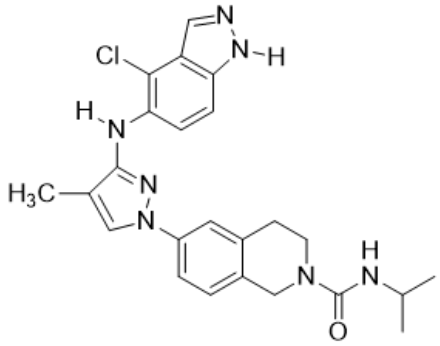
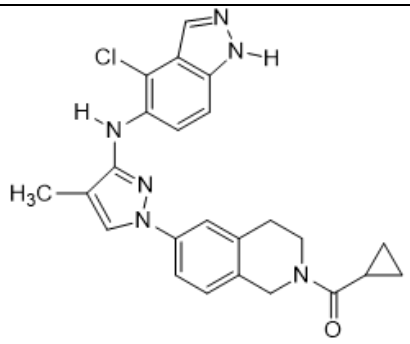
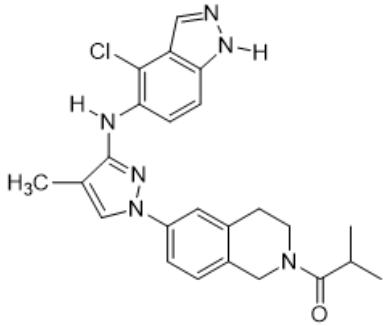
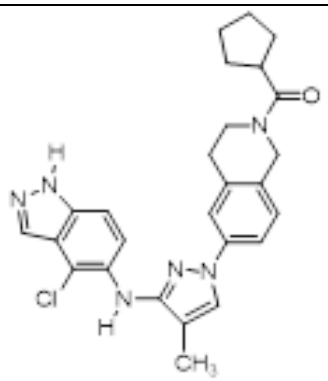
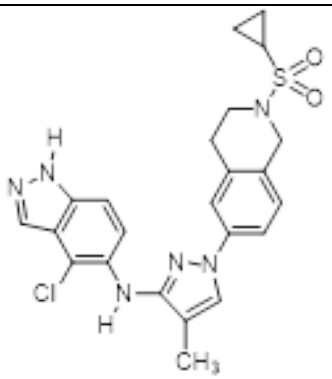
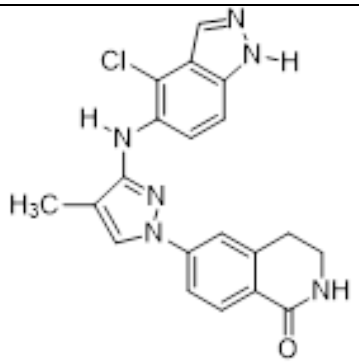
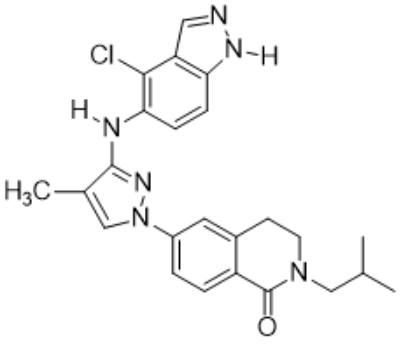
 25	 26
 27	 28
 29	 30
 31	 32
 33	 34
 35	 36
 37	 38

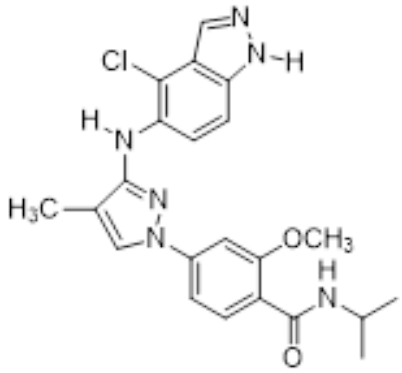
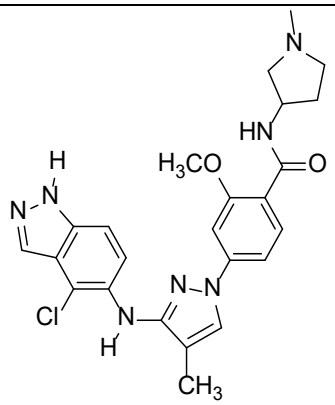
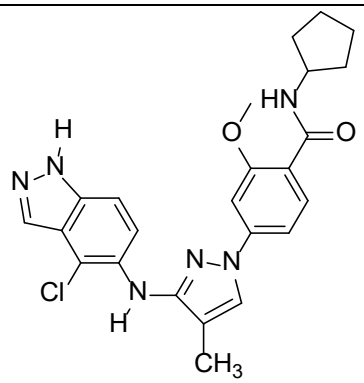
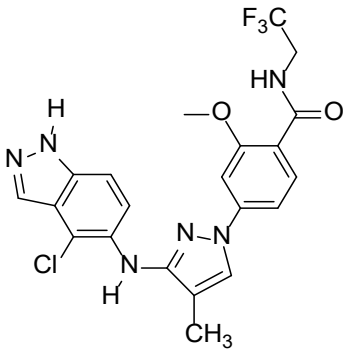
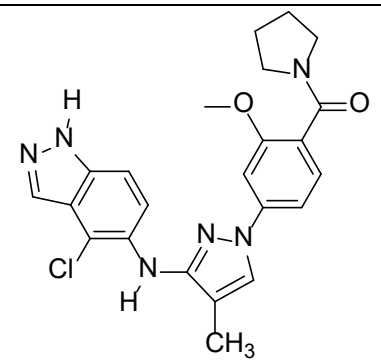
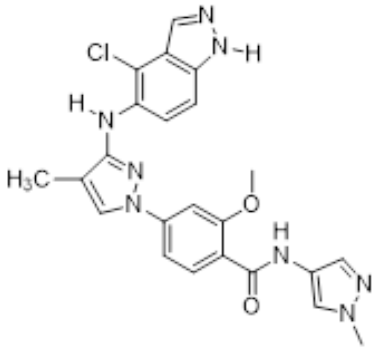
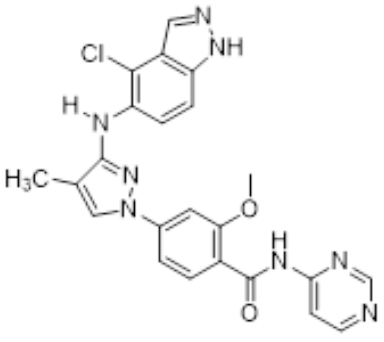
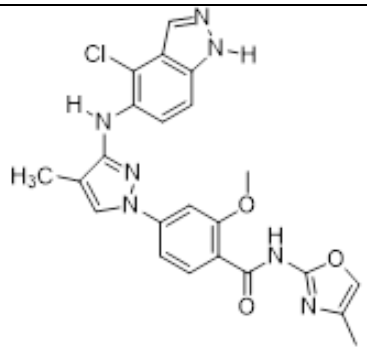
 39	 40
 41	 42
 43	 44
 45	 46
 47	 48
 49	 50

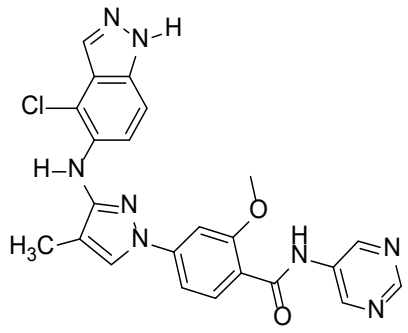
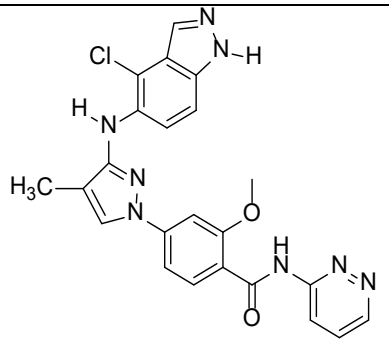
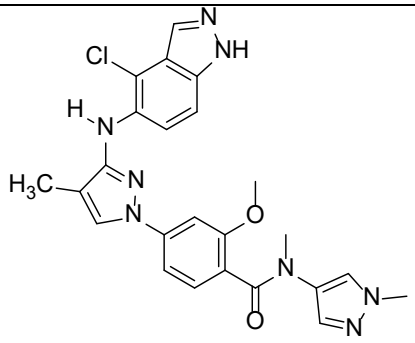
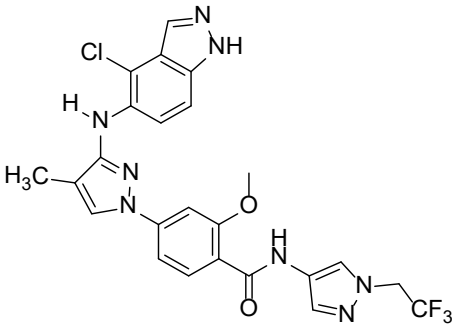
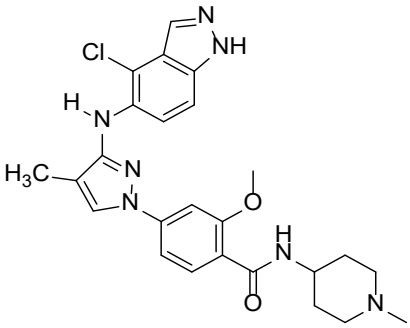
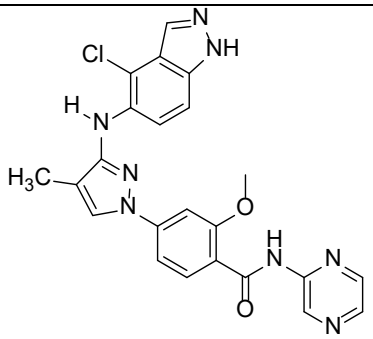
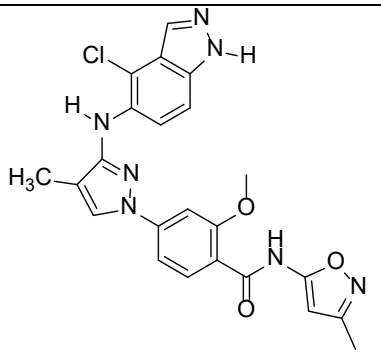
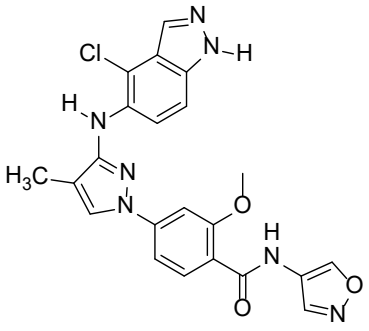
 51	 52
 53	 54
 55	 56
 57	 58
 59	 60

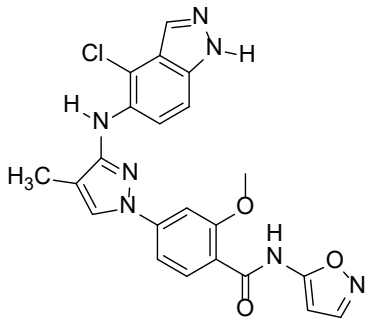
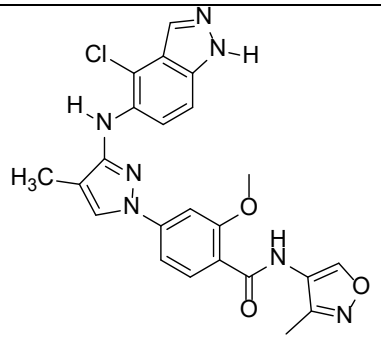
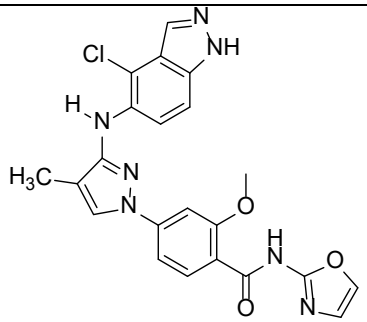
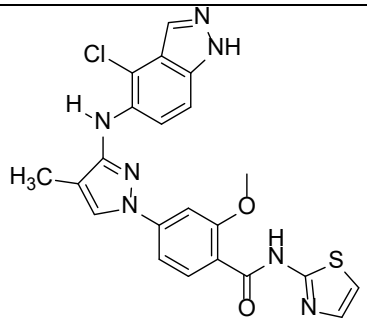
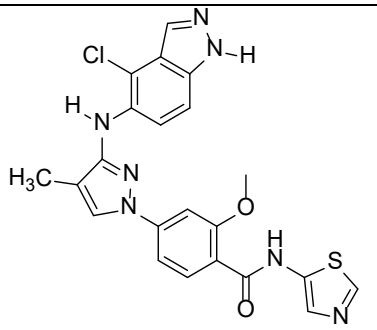
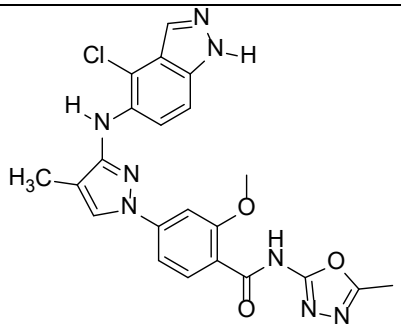
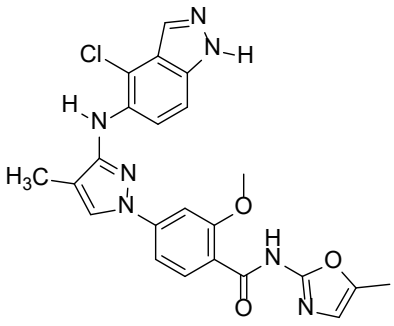
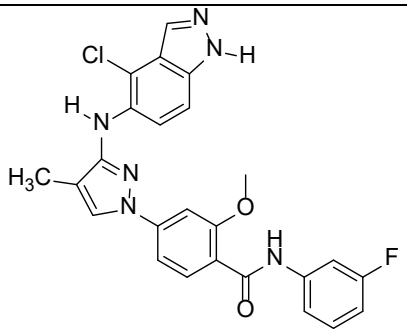
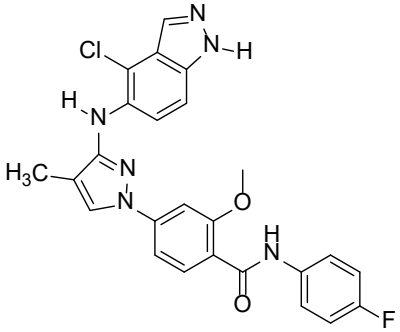
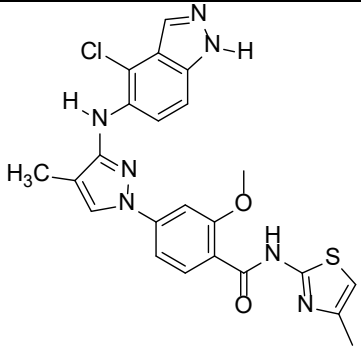
 61	 62
 63	 64
 65	 66
 67	 68

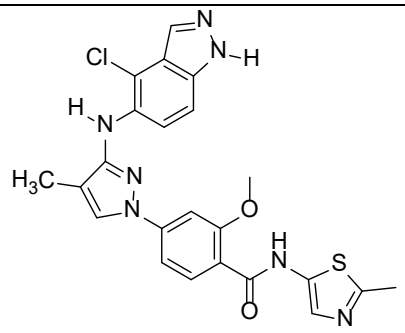
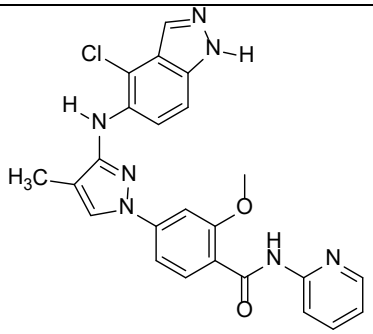
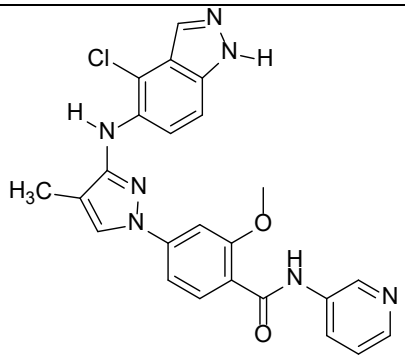
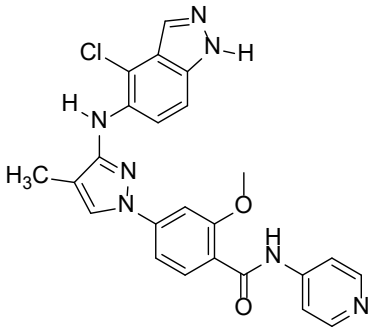
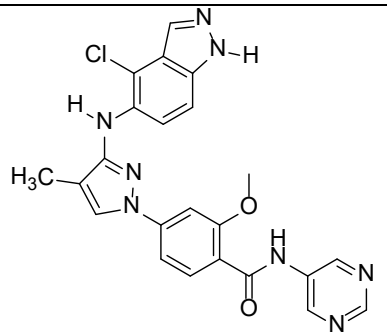
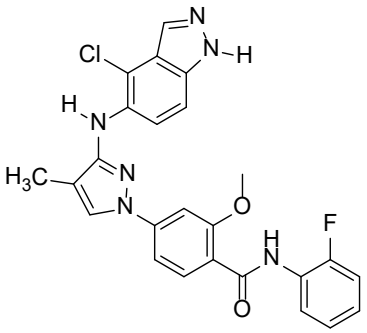
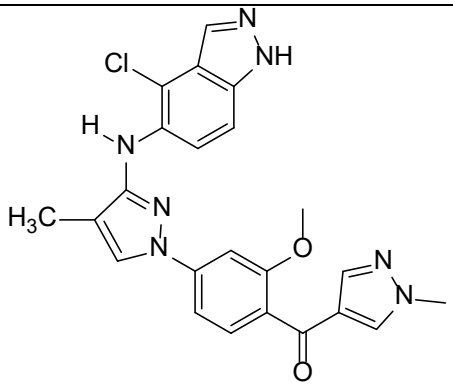
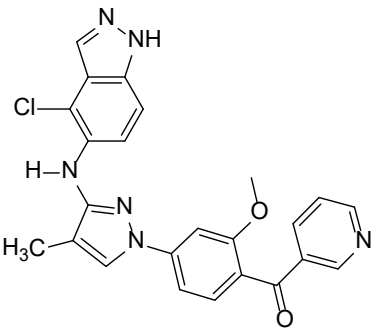
 69	 70
 71	 72
 73	 74
 75	 76

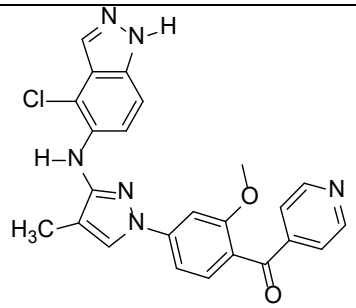
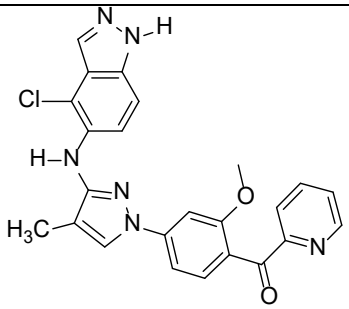
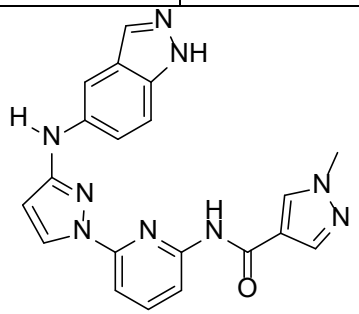
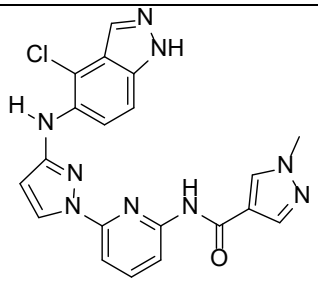
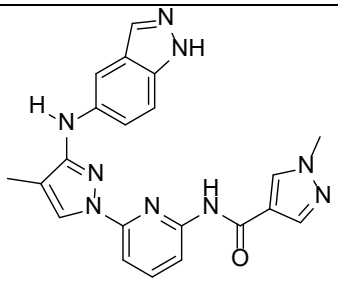
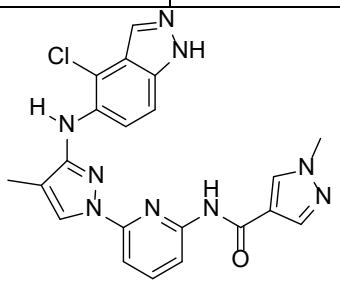
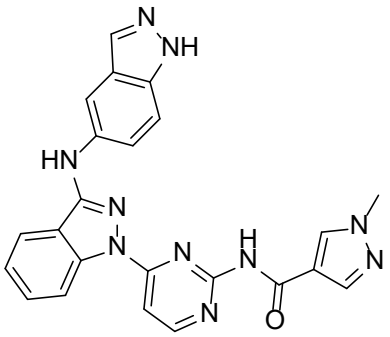
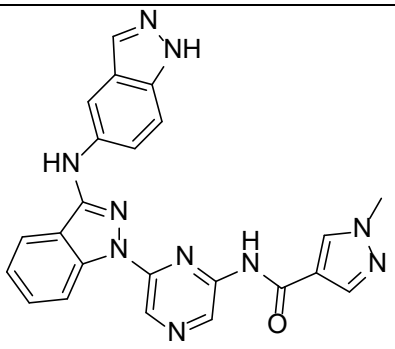
 77	 78
 79	 80
 81	 82
 83	 84

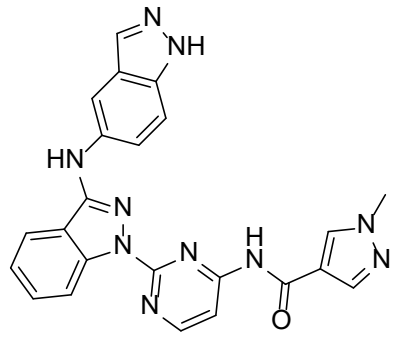
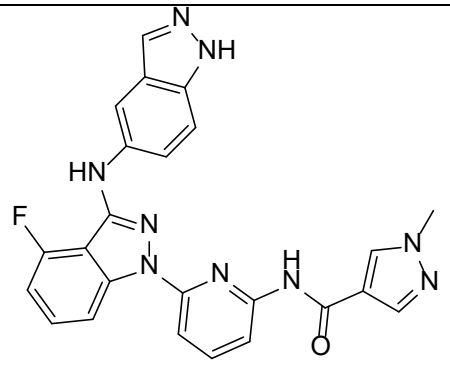
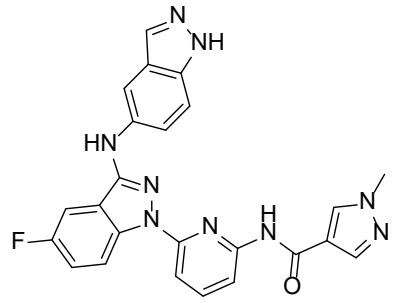
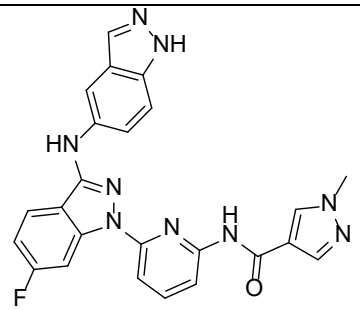
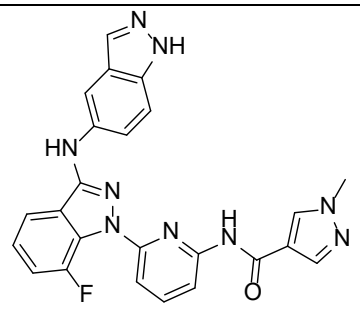
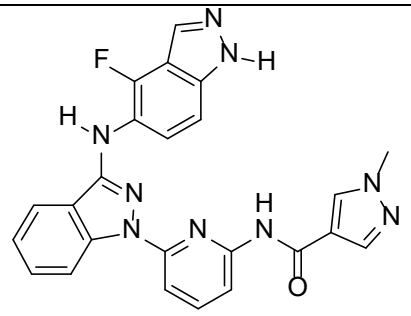
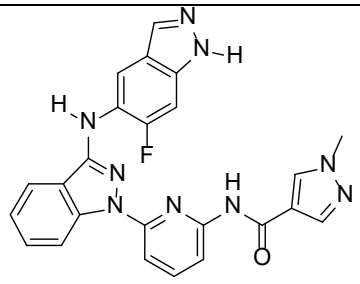
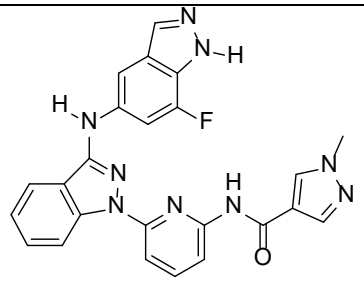
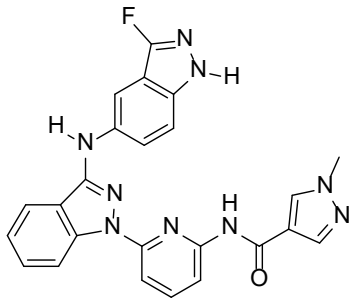
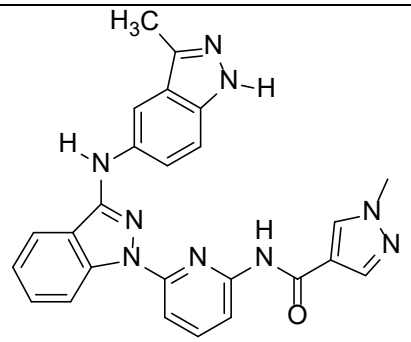
 85	 86
 87	 88
 89	 90
 91	 92

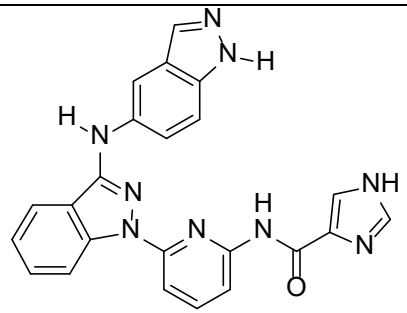
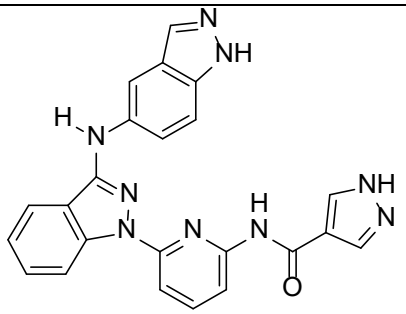
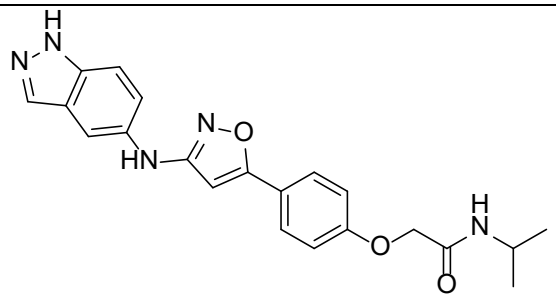
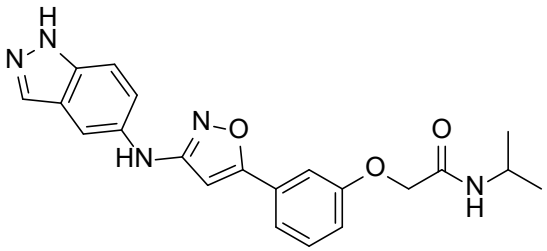
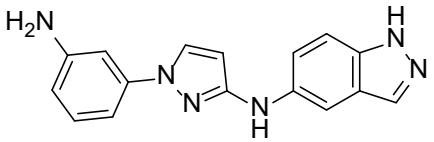
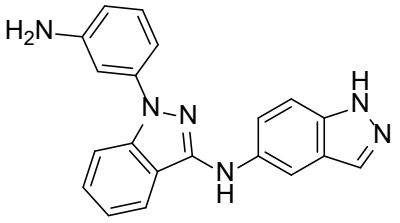
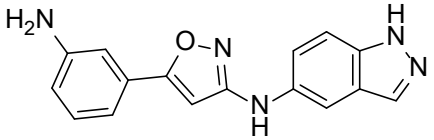
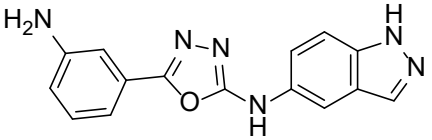
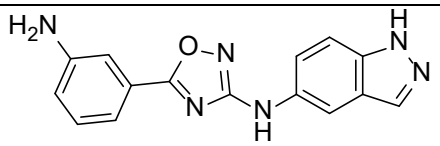
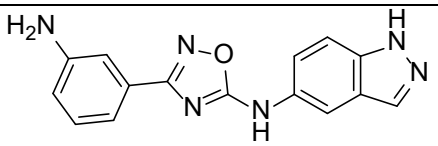
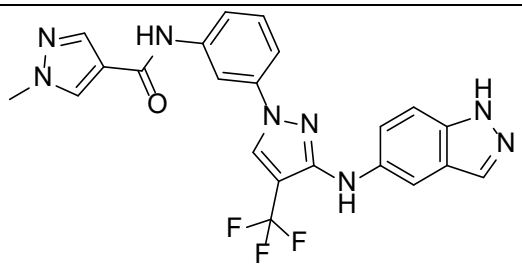
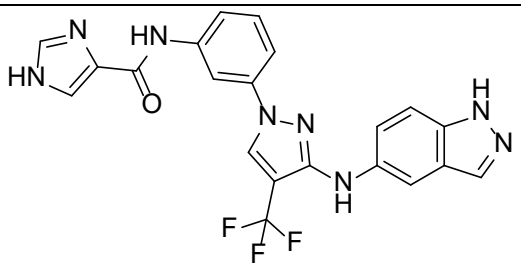
 93	 94
 95	 96
 97	 98
 99	 100

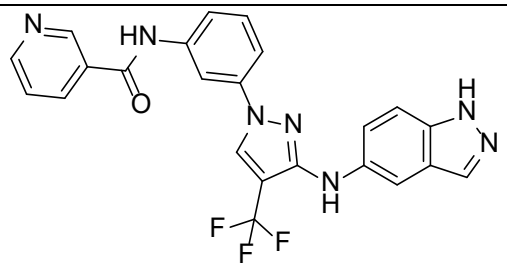
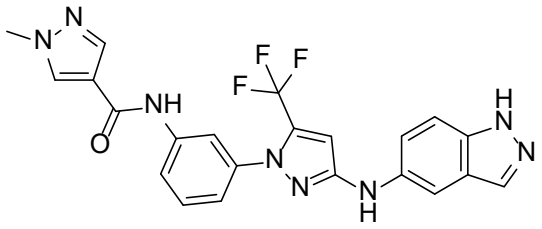
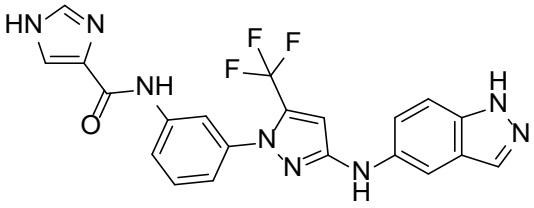
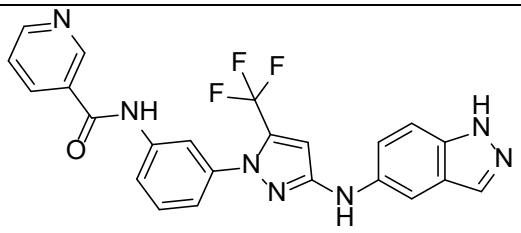
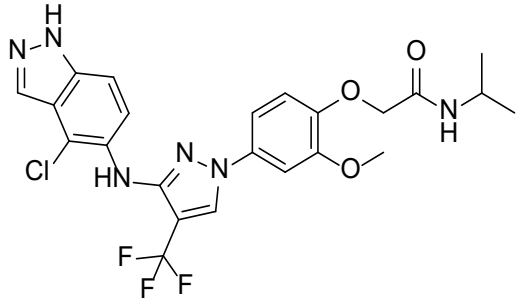
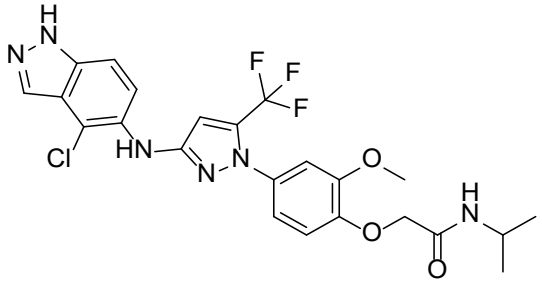
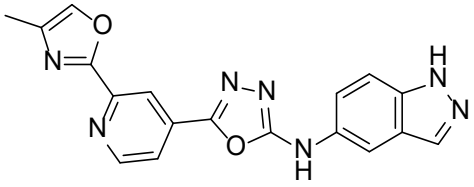
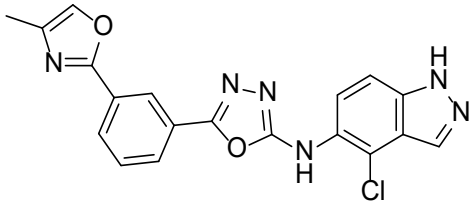
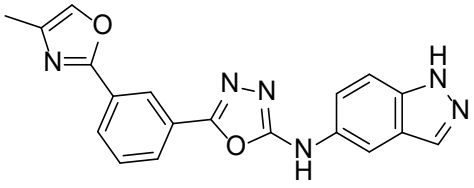
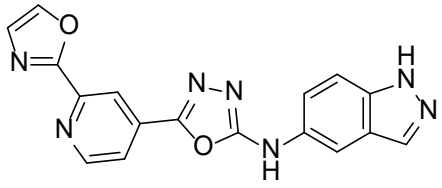
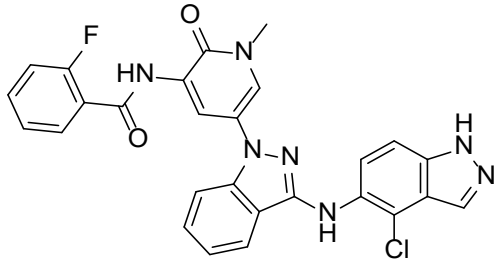
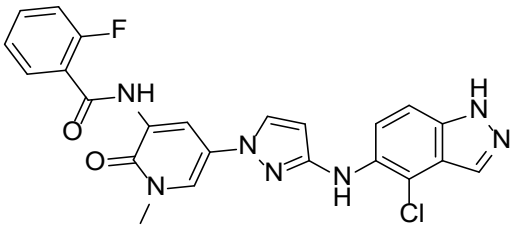
 101	 102
 103	 104
 105	 106
 107	 108
 109	 110

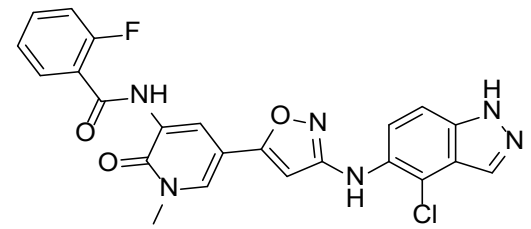
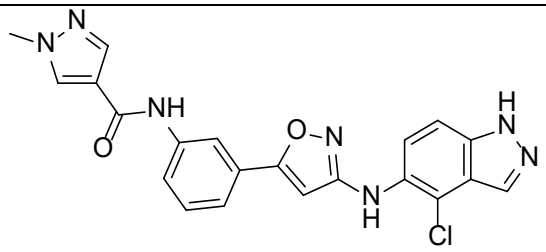
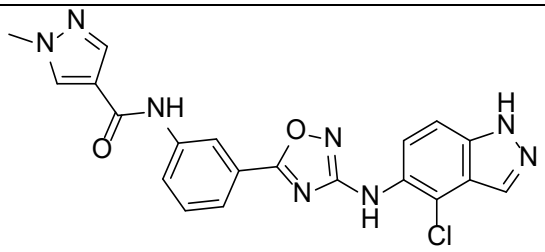
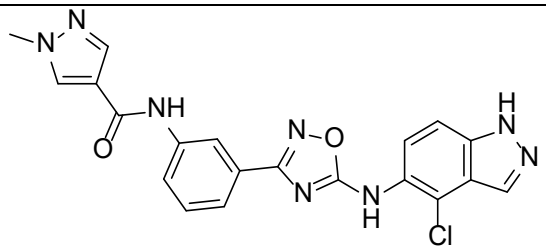
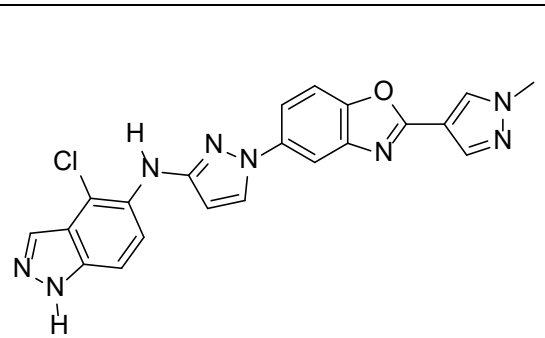
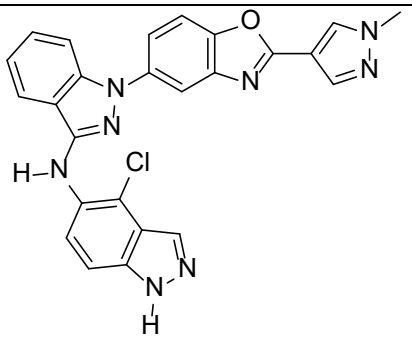
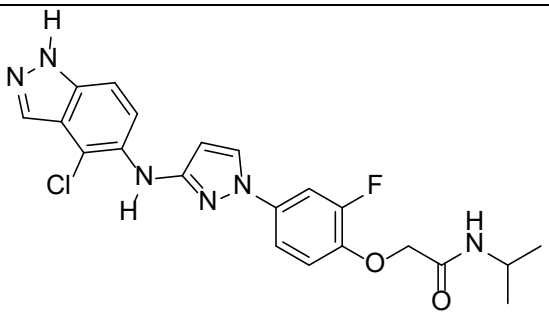
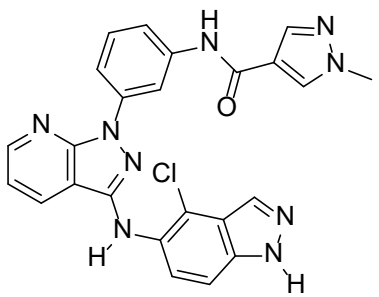
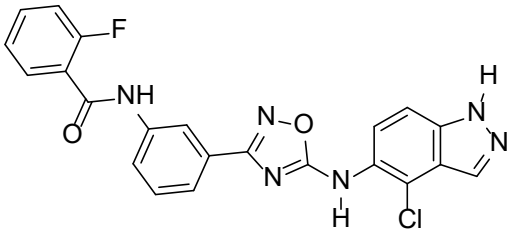
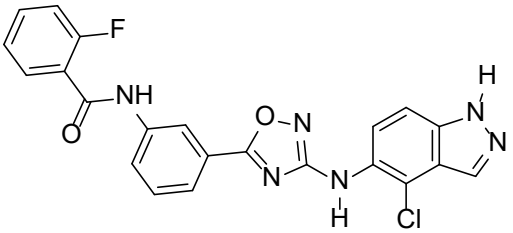
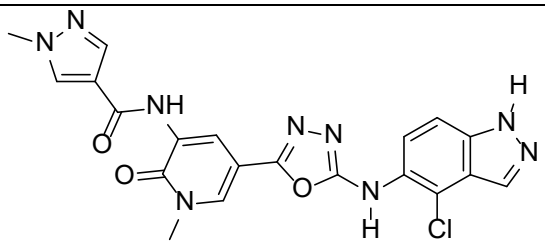
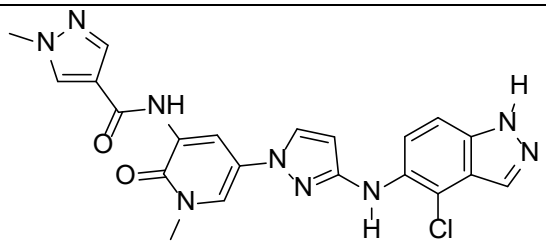
 111	 112
 113	 114
 115	 116
 117	 118

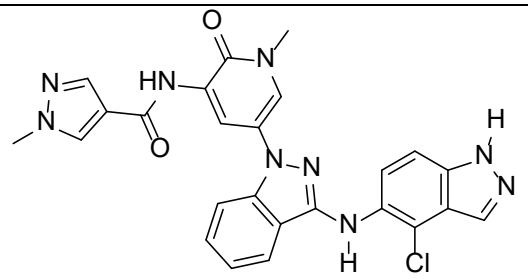
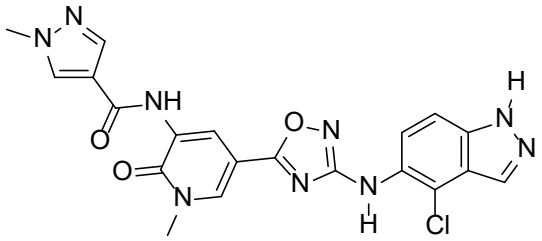
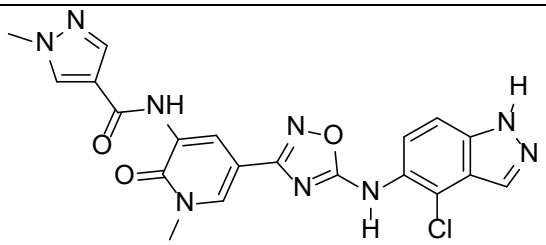
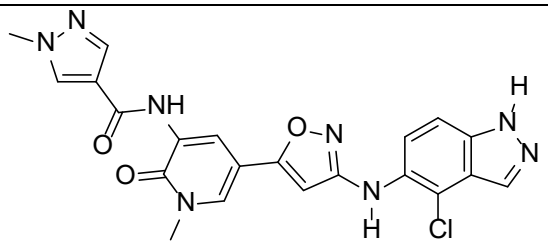
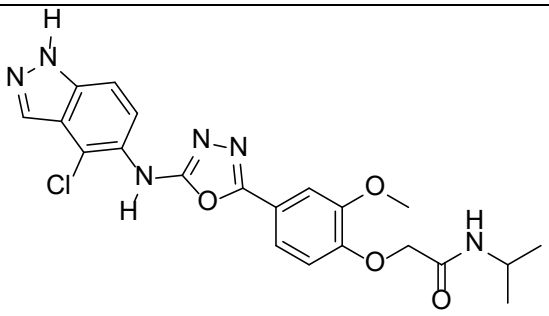
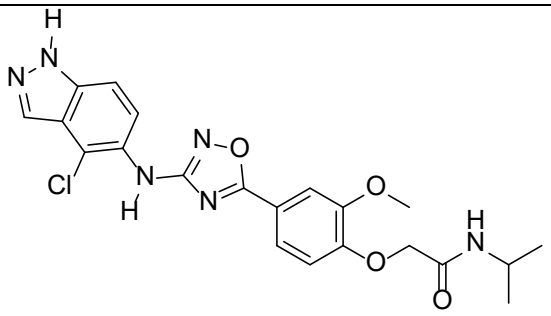
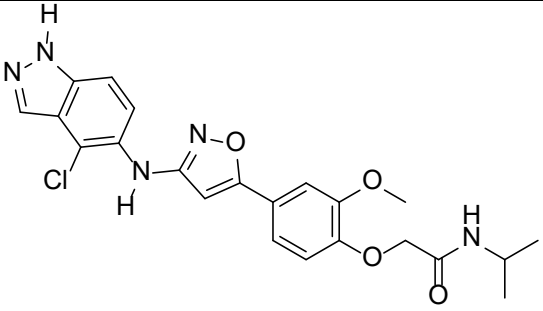
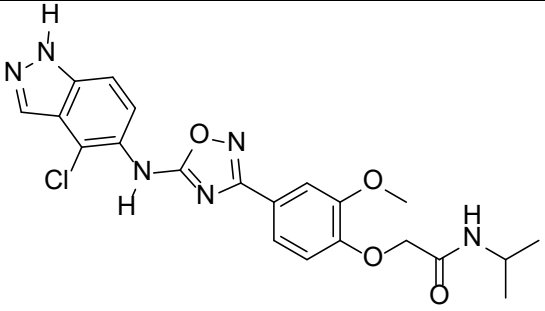
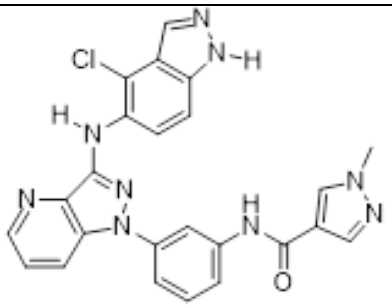
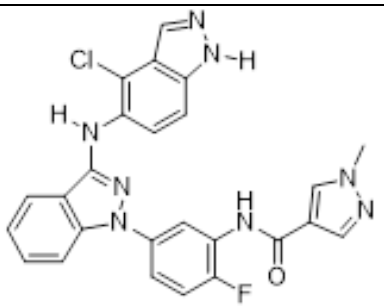
 119	 120
 122	
 123	 124
 125	
 135	 136

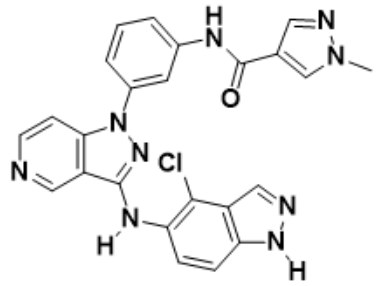
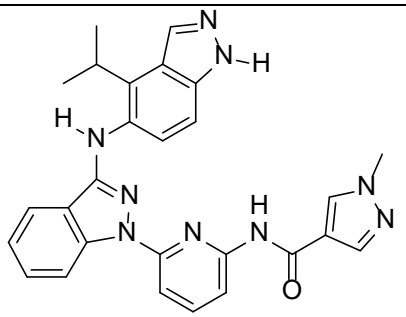
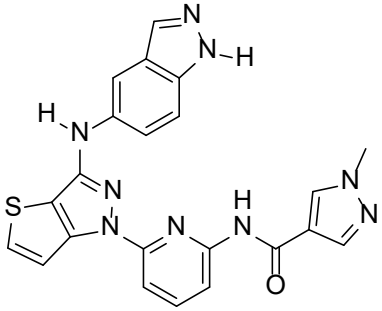
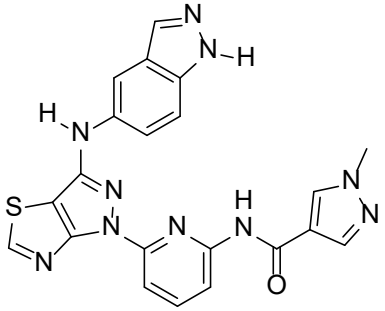
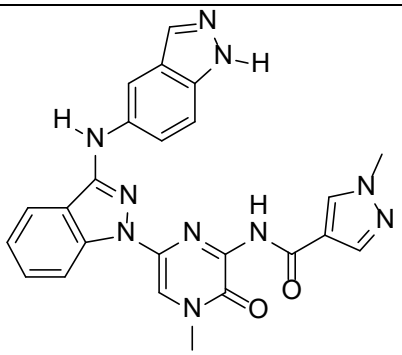
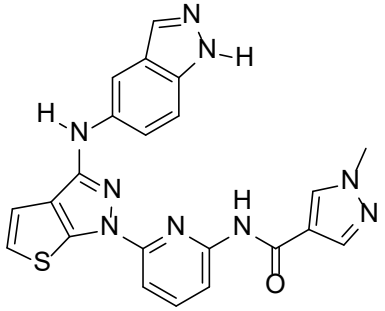
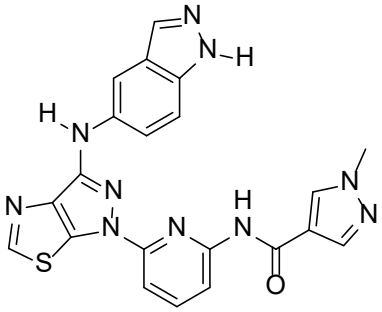
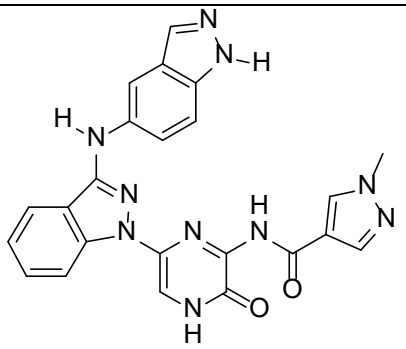
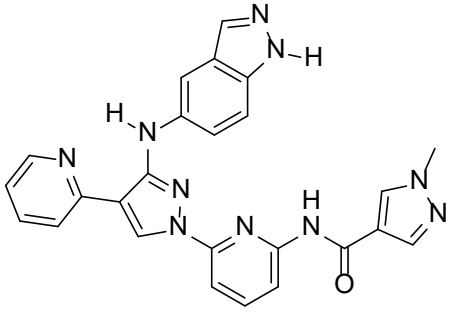
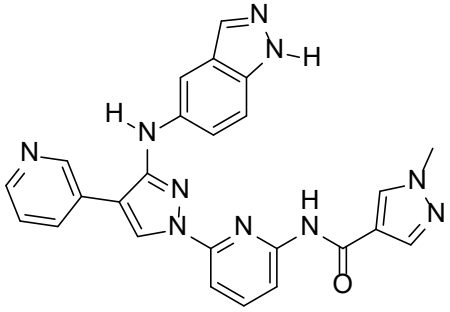
 137	 138
 139	 140
 141	 142
 143	 144
 145	 146

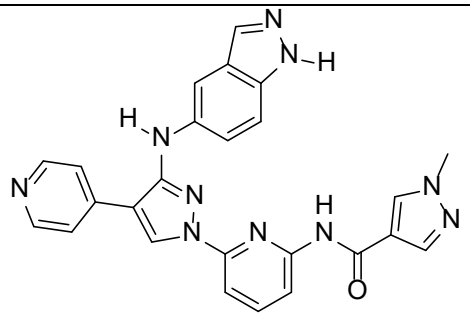
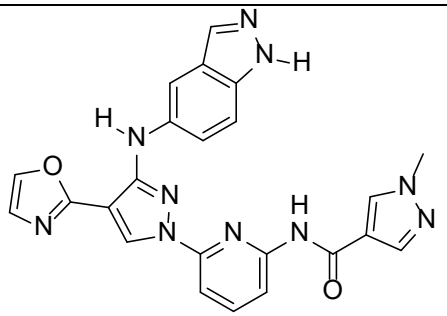
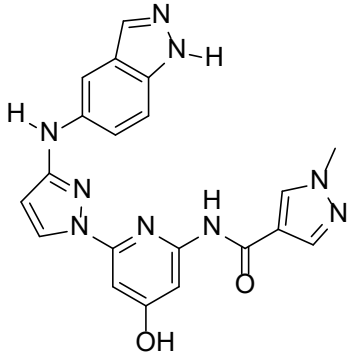
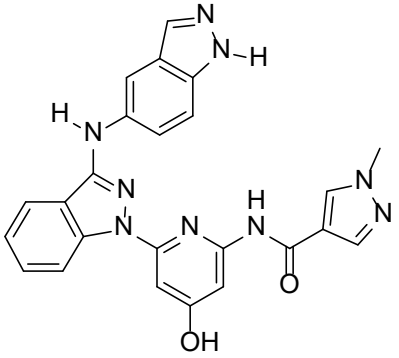
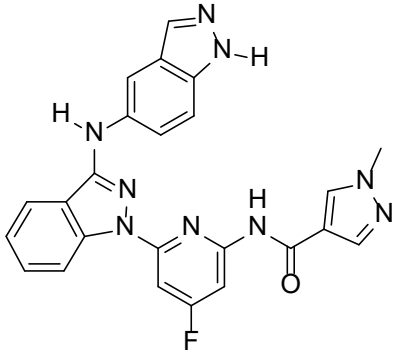
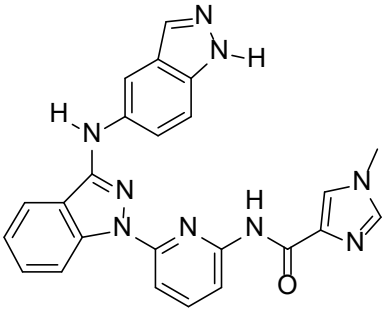
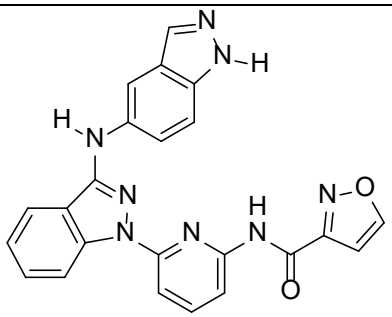
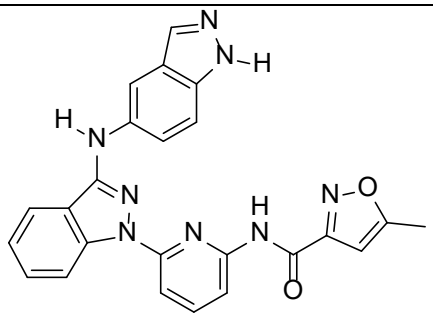
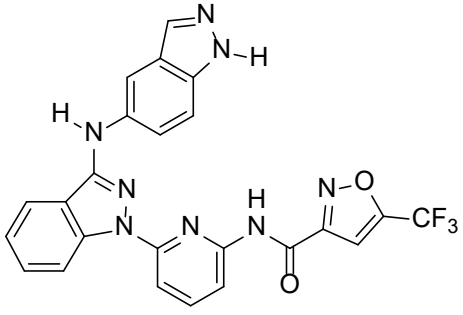
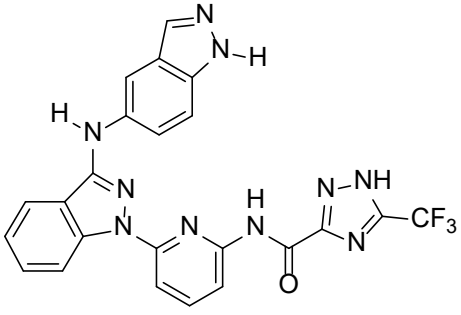
 147	 148
 149	 150
 151	 152
 153	 154
 155	 156
 157	 158

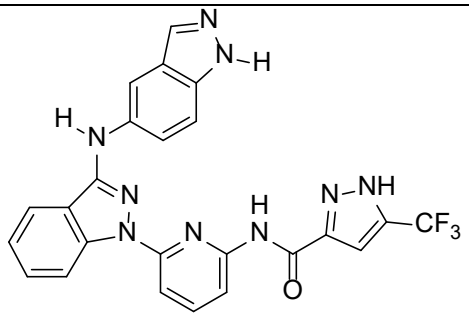
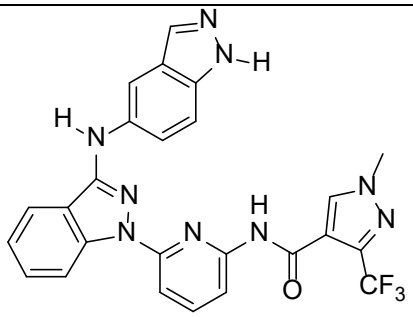
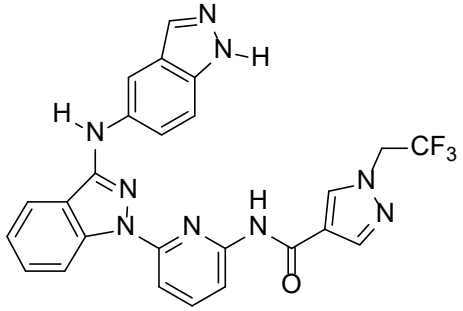
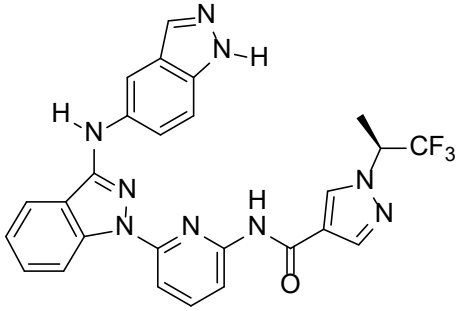
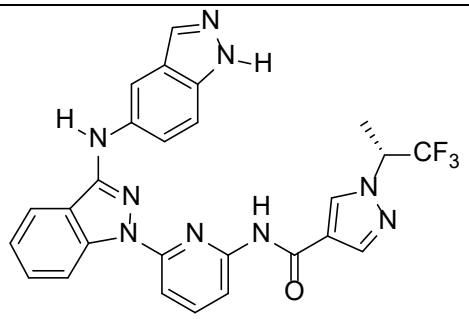
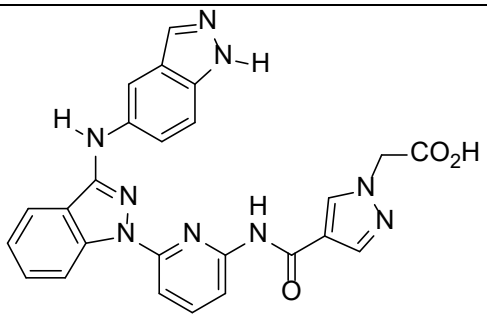
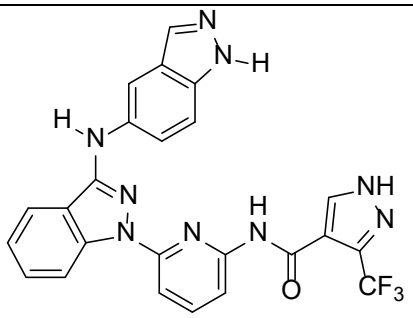
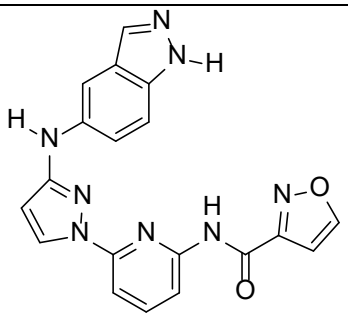
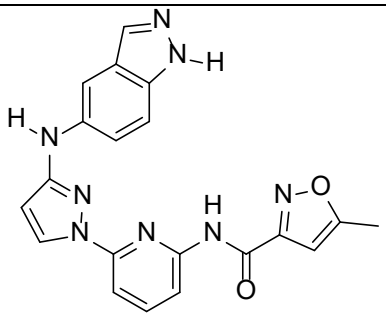
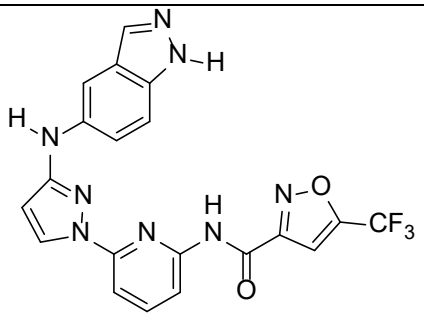
 159	 160
 161	 162
 163	 164
 165	 166
 167	 168
 169	 170

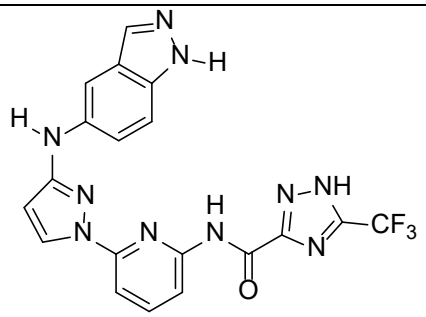
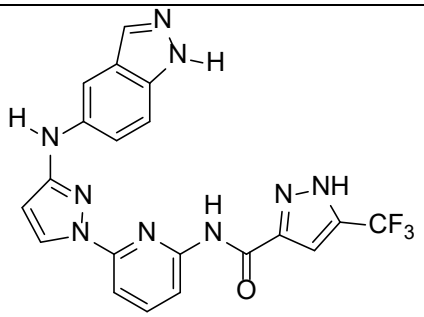
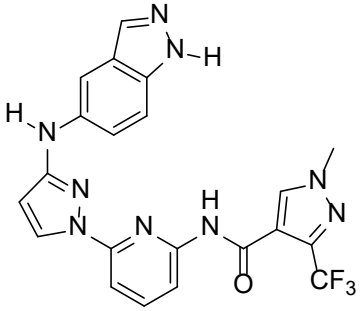
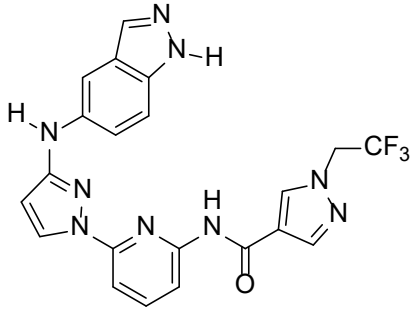
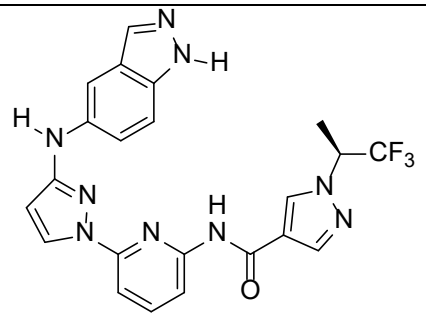
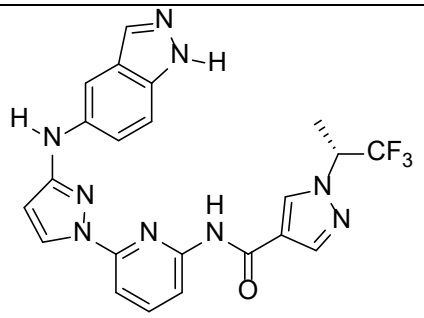
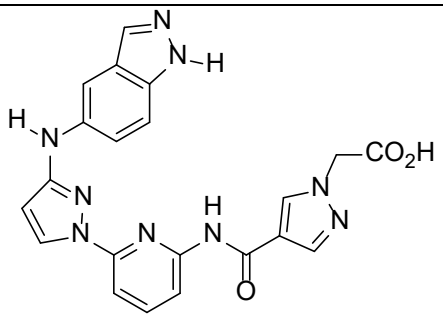
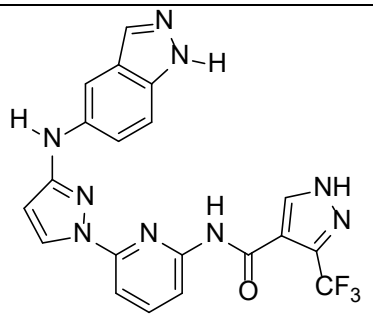
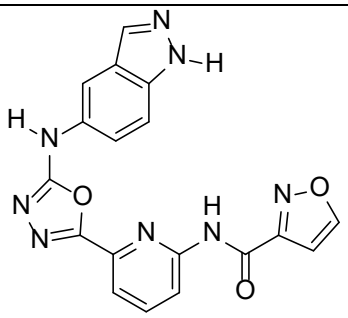
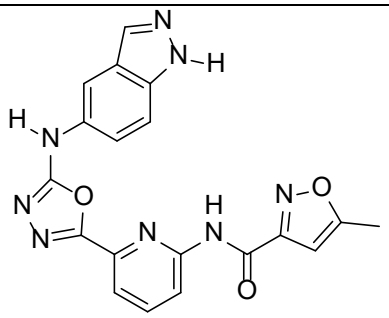
 171	 172
 173	 174
 175	 176
 177	 178
 179	 180
 181	 182

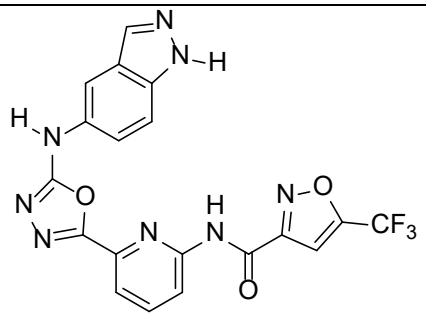
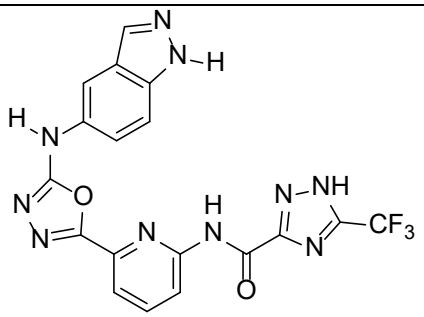
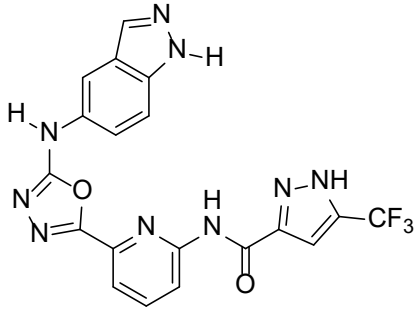
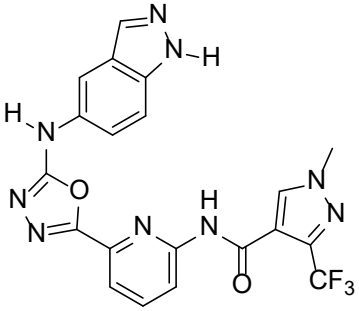
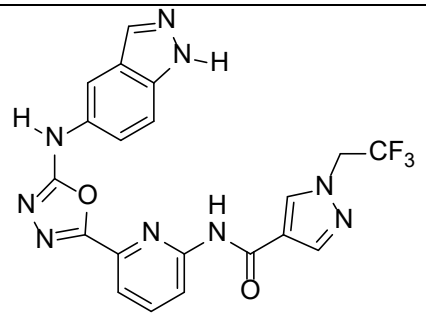
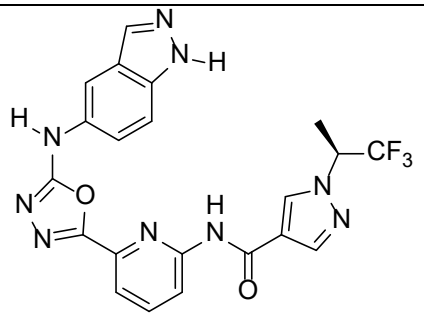
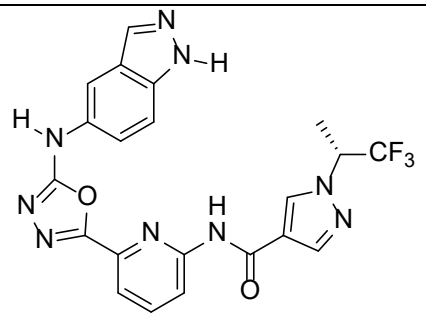
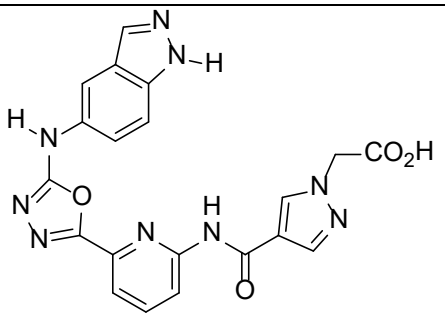
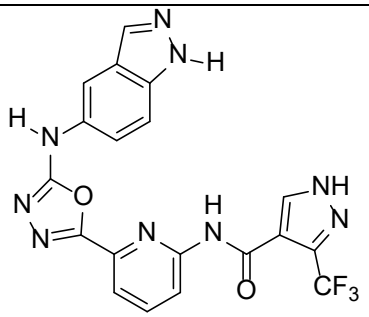
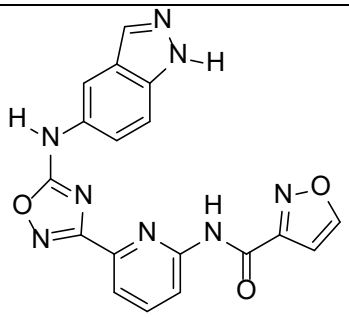
 183	 184
 185	 186
 187	 188
 189	 190
 191	 192

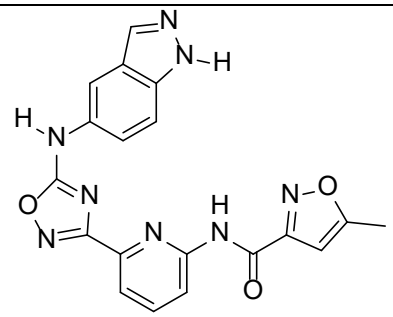
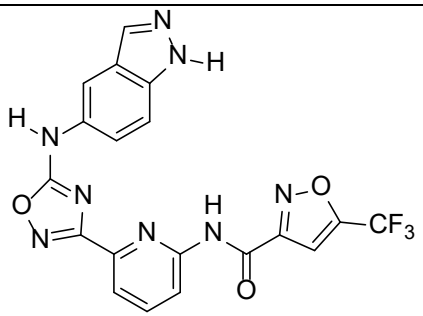
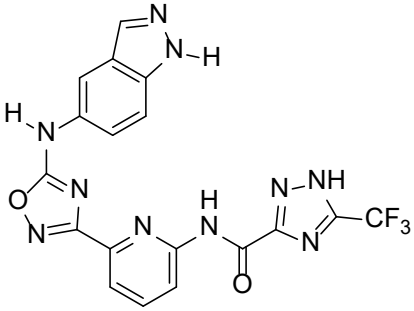
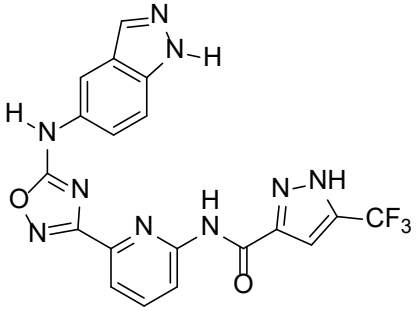
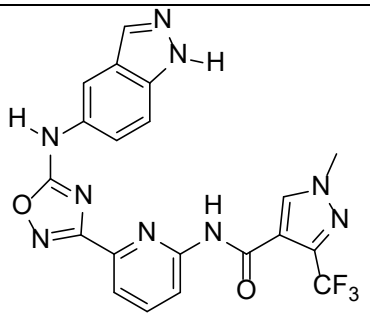
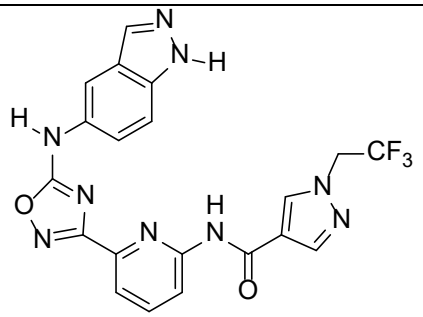
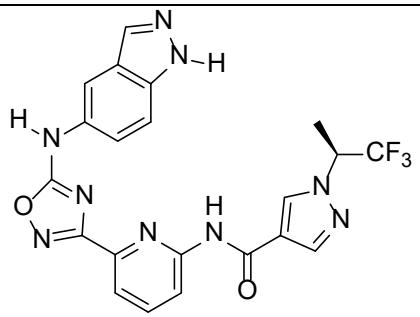
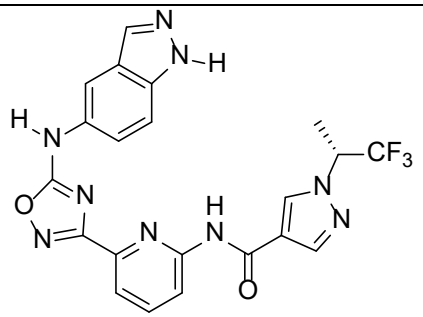
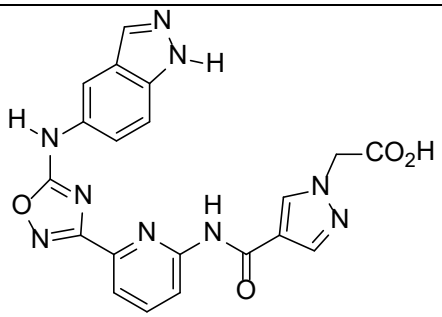
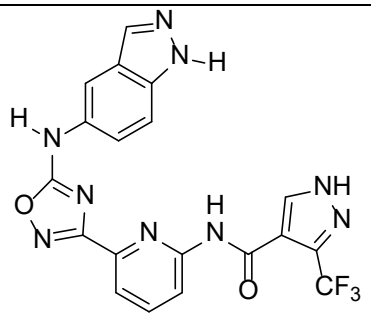
 193	 194
 195	 196
 197	 198
 199	 200
 201	 202

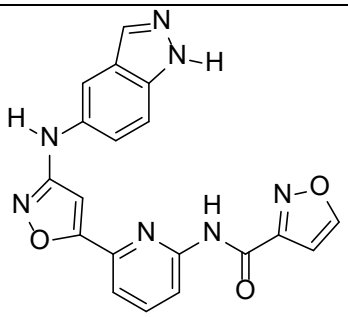
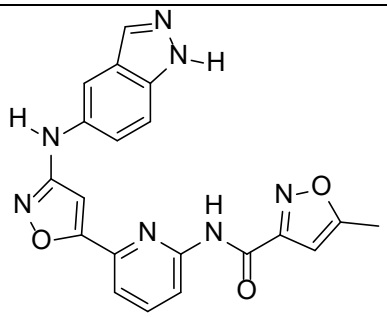
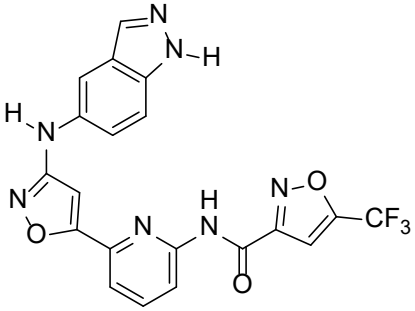
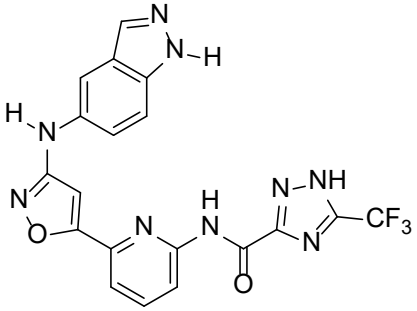
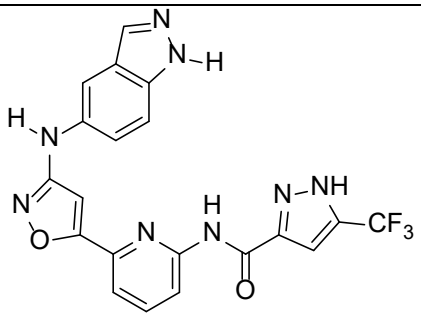
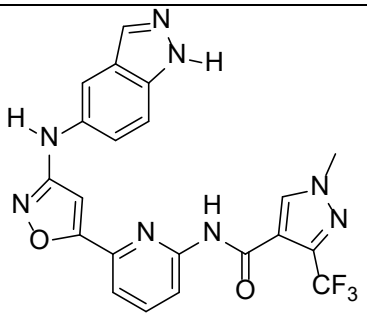
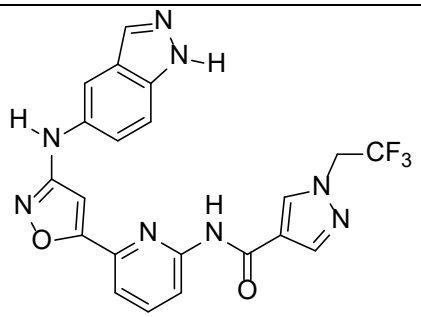
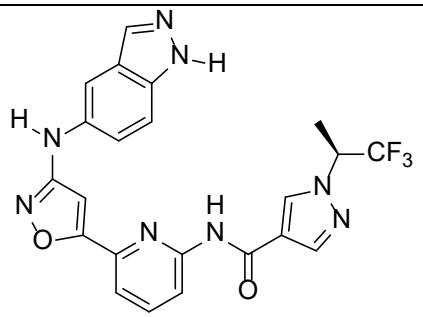
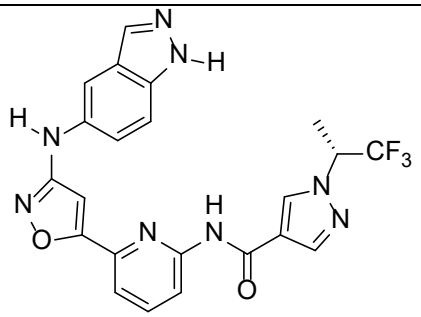
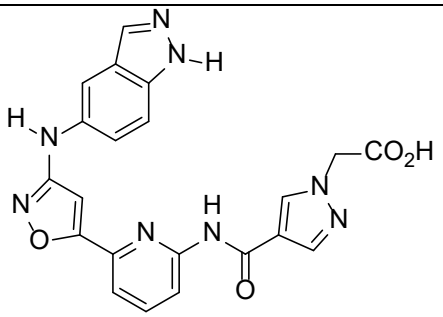
 203	 204
 205	 206
 207	 208
 209	 210
 211	 212

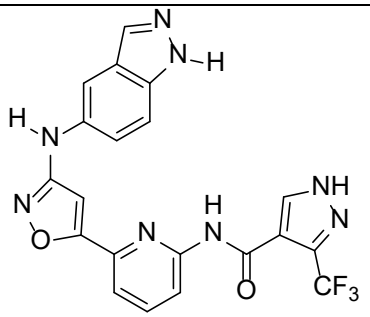
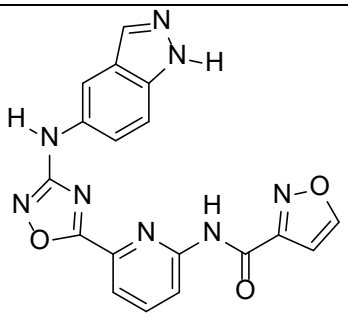
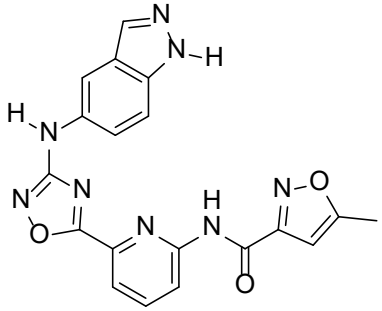
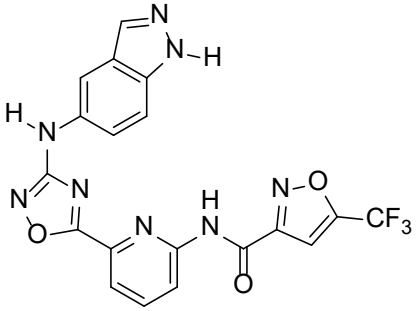
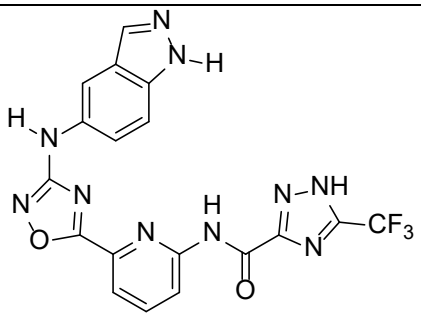
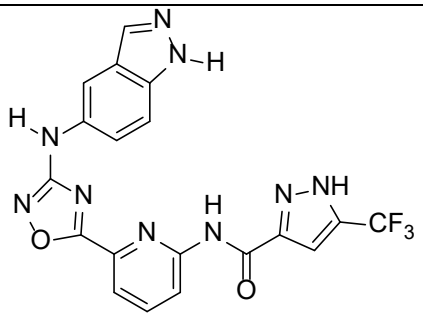
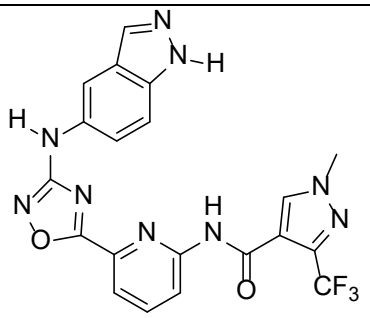
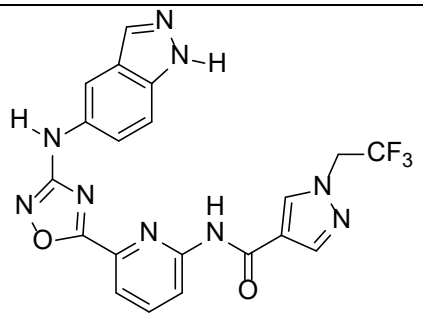
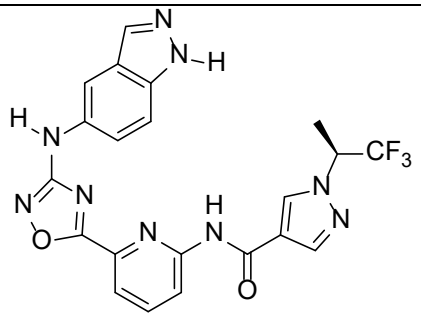
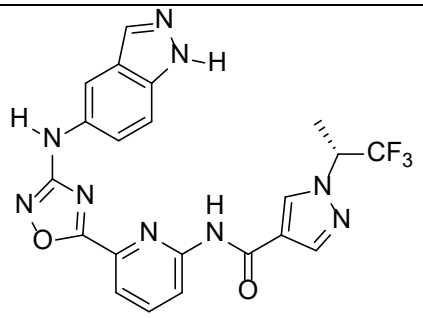
 213	 214
 215	 216
 217	 218
 219	 220
 221	 222

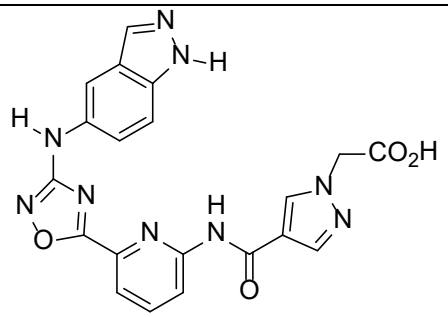
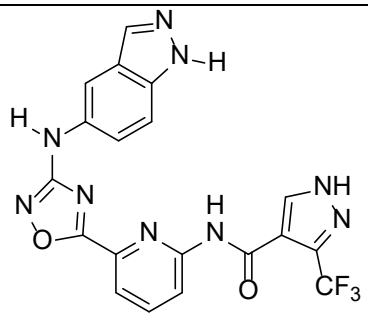
 223	 224
 225	 226
 227	 228
 229	 230
 231	 232

 233	 234
 235	 236
 237	 238
 239	 240
 241	 242

 243	 244
 245	 246
 247	 248
 249	 250
 251	 252

 253	 254
 255	 256
 257	 258
 259	 260
 261	 262

 263	 264
 265	 266
 267	 268
 269	 270
 271	 272

	
273	274

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

61. The compound of any of claims 1-60, or a pharmaceutically acceptable salt or tautomer thereof.

62. A pharmaceutical composition comprising a compound of any of claims 1-60, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, and a pharmaceutically acceptable excipient.

63. Use of a compound of any of claims 1-60, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or a pharmaceutical composition of claim 62, in the manufacture of a medicament for treating a disease or disorder associated with ROCK2 in a subject in need thereof, wherein an effective amount of the compound, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or the pharmaceutical composition is to be administered to the subject.

64. Use of compound of any of claims 1-60, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or a pharmaceutical composition of claim 62, in the manufacture of a medicament for preventing a disease or disorder associated with ROCK2 in a subject in need thereof, wherein an effective amount of the compound, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or the pharmaceutical composition is to be administered to the subject.

65. A compound of any one of claims 1-60, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or a pharmaceutical composition of claim 62, for use as a medicament.

66. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is a fibrotic disorder, autoimmune disease, inflammatory condition, edema, opthalmic disease, cardiovascular disease, central nervous system disorder, or cancer.

67. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is pulmonary fibrosis, cystic pulmonary fibrosis, idiopathic pulmonary fibrosis, radiation induced lung injury, liver fibrosis including cirrhosis, cardiac fibrosis including arterial fibrosis, endomyocardial fibrosis, old myocardial infraction, arterial stiffness, atherosclerosis, restenosis, arthrofibrosis, Crohns disease, myelofibrosis, Peyronie’s diseases, nephrogenic systemic fibrosis, progressive massive fibrosis, retroperitoneal cavity fibrosis, schleroderma/systemic sclerosis, mediastinal fibrosis, Keloids and hypertrophic scars, glial scaring, or renal fibrosis.

68. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is Huntington’s disease, Parkinson’s disease, Alzheimer’s disease, Amyotrophic lateral sclerosis (ALS), Batten disease, dementia, spinal muscular atrophy, motor neurone diseases, spinocerebellar ataxia, acute or chronic pain, dementia, neuronal degeneration, spinal cord injury, or cerebral vasospasm.

69. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is glaucoma.

70. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is asthma, cardiovascular inflammation, renal inflammation, or arteriosclerosis.

71. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is hypertension, atherosclerosis, angina, arterial obstruction, peripheral arterial disease, peripheral circulatory disorder, cerebral cavernous malformation, restenosis, cardiac hypertrophy, ocular hypertension, cerebral ischemia, cerebral vasospasm, acute respiratory distress syndrome (ARDS), or erectile dysfunction.

72. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, psoriasis, Crohn's disease, atopic dermatitis, eczema, or graft-versus-host disease (GVHD).

73. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is cancer.

74. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is lymphedema.

75. The use of claim 74, wherein the lymphedema is caused at least by a parasitic disease.

76. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is angioedema, brain edema, CHAPLE syndrome, cardiac edema, hydrops fetalis, inflammatory edema, macular edema, myxedema, pulmonary edema, peripheral edema, periorbital edema, or cutaneous edema.

77. The use of claim 63 or 64, wherein the disease or disorder associated with ROCK2 is hereditary angioedema, cystoid macular edema, Irvine-Gass syndrome, diabetic macular edema, or pedal edema.

78. An *in vitro* or *ex-vivo* method of inhibiting ROCK2 comprising contacting ROCK2 with an effective amount of a compound of any of claims 1-60, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or a pharmaceutical composition of claim 62.

79. A method of screening a library of compounds comprising performing an assay on a compound of any of claims 1-60, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, and an additional compound, wherein the additional compound is different from the compound of any of claims 1-60, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof.

80. A kit comprising a compound of any of claims 1-60, or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or a pharmaceutical composition of claim 62 and instructions for using the compound, or pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched compound, or prodrug thereof, or pharmaceutical composition.