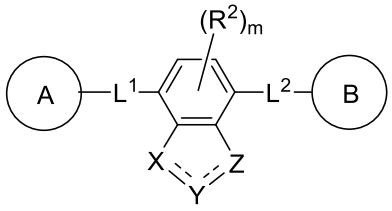
CLAIMS

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



(I-a)

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

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

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

X and Y are each independently $C(R^{3a})$, $C(R^{3a})(R^{3b})$, N, $N(R^{3c})$, or O;

Z is N, $N(R^{3c})$, or O;

and the bonds in the ring comprising X, Y, and Z may be single or double bonds as valency permits;

L^1 is absent;

L^2 is absent, C_1-C_6-alkylene, C_1-C_6-heteroalkylene, -O-, -C(O)-, $-N(R^4)C(O)-$, or $-C(O)N(R^4)-$, wherein each alkylene and heteroalkylene is optionally substituted with one or more R^5;

each R^1 is independently hydrogen, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkenylene-aryl, C_1-C_6 alkylene-heteroaryl, heteroaryl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, $–SR^E$, or $–S(O)_xR^D$, wherein each alkyl, alkylene, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^6; or

two R^1 groups, together with the atoms to which they are attached, form a 3-7-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^6;

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

$R^{3a}$and R^{3b} are each independently hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, $–OR^A$, $–NR^BR^C$, $–C(O)R^D$, or $–C(O)OR^D$; or

each of R^{3a} and R^{3b}, together with the carbon atom to which they are attached, form an oxo group;

R^{3c} is hydrogen or C_1-C_6-alkyl;

each R^4 is independently hydrogen, C_1-C_6-alkyl, or C_1-C_6-haloalkyl;

each R^5 is independently hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–C(O)R^D$, or $–C(O)OR^D$;

each R^6 is independently C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, $–SR^E$, or $–S(O)_xR^D$, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^{11};

each R^7 is C_1-C_6-alkyl, halo, cyano, oxo, or $–OR^{A1}$;

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

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

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

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

each R^D and R^E is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_6 alkylene-aryl, or C_1-C_6 alkylene-heteroaryl;

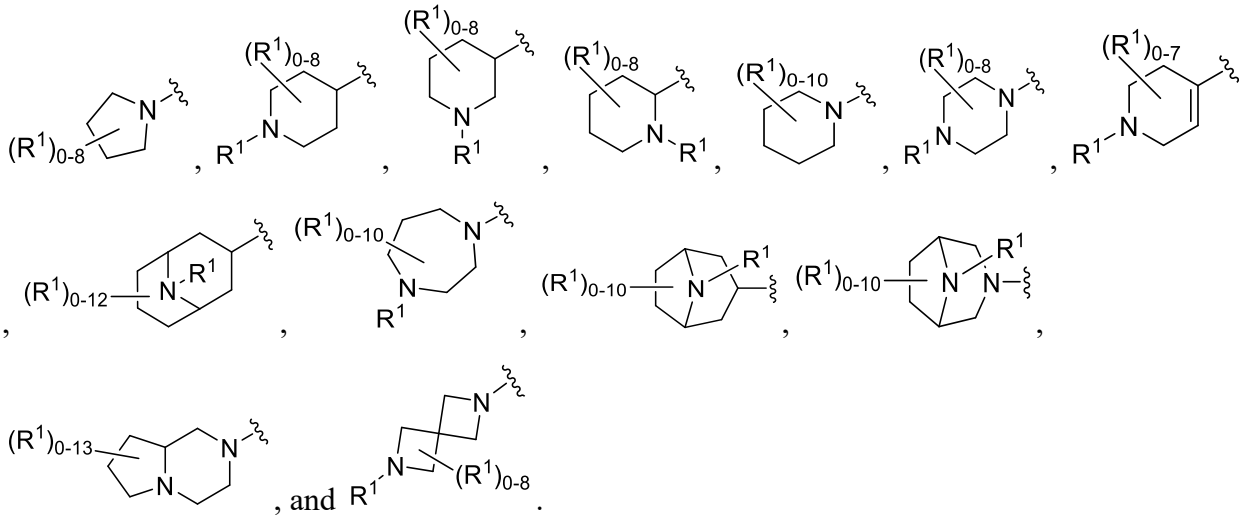
each R^{A1} is hydrogen or C_1-C_6-alkyl;

m is 0, 1, or 2; and

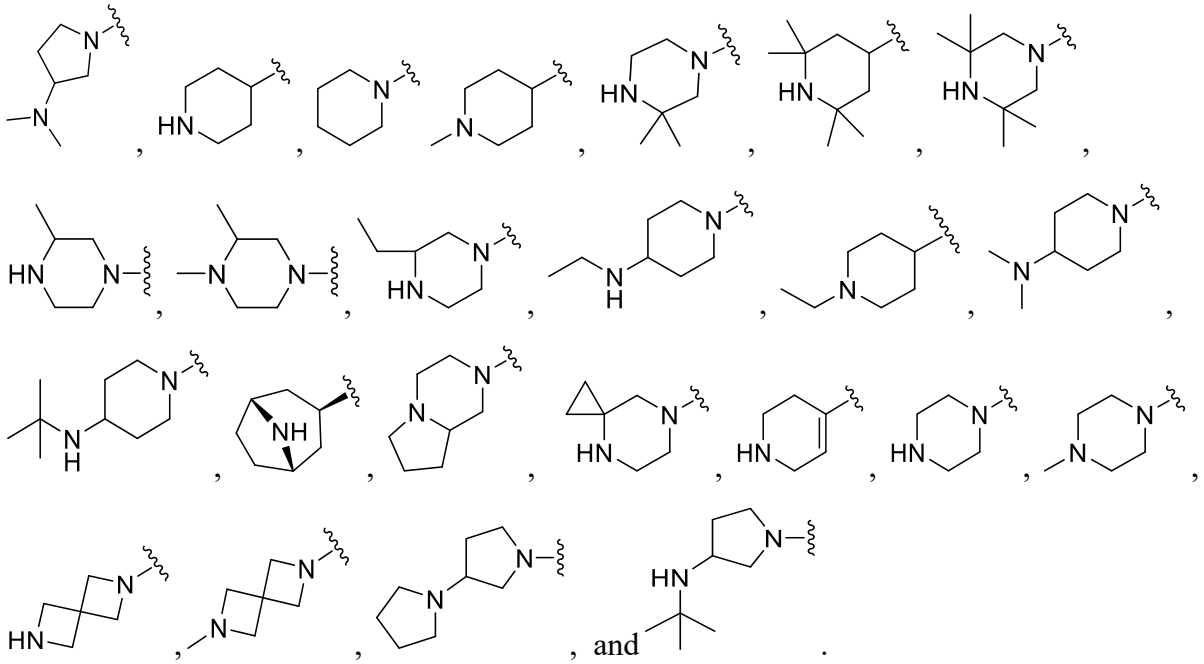
x is 0, 1, or 2.

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

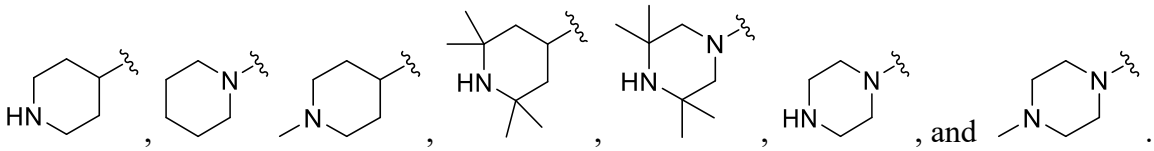
3. The compound of any one of the preceding claims, wherein A is selected from



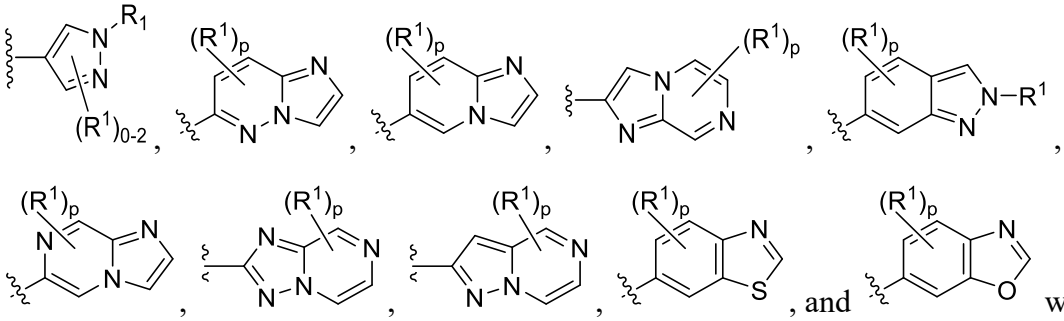
4. The compound of any one of the preceding claims, wherein A is selected from



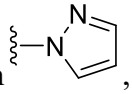
5. The compound of any one of the preceding claims, wherein A is selected from

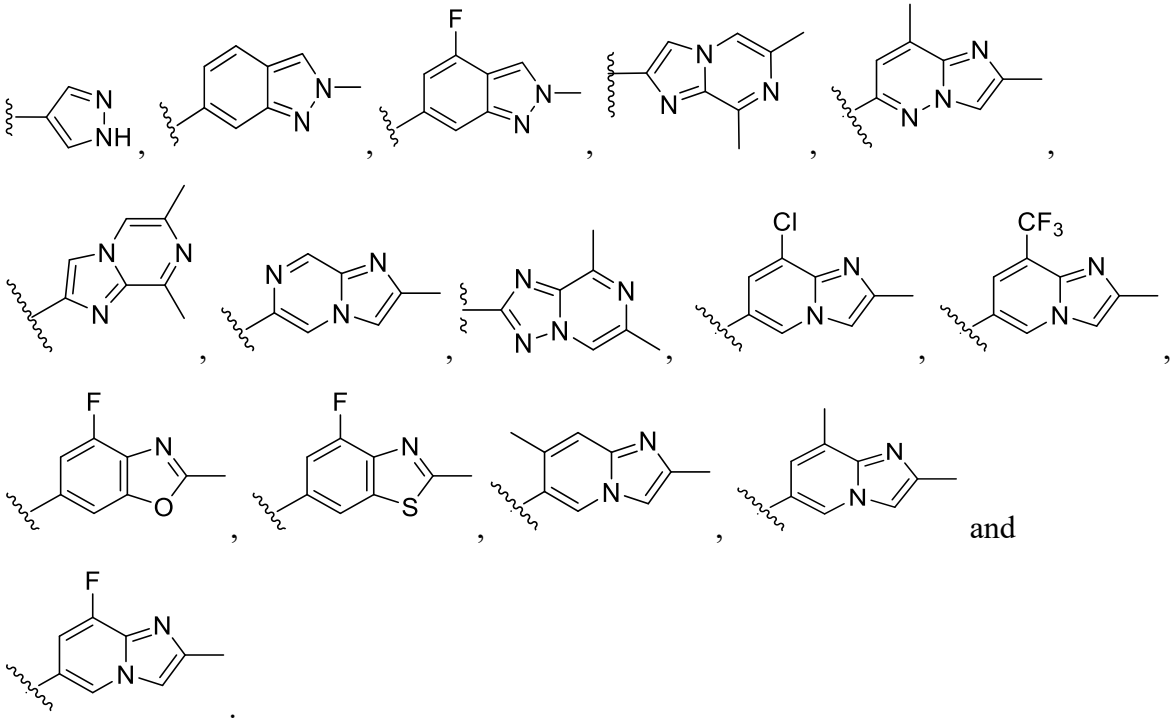


6. The compound of any one of the preceding claims, wherein B is selected from ,



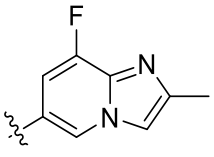
wherein p is 0, 1, 2, 3, or 4.

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



and

.

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

.

9. The compound of any one of the preceding claims, wherein L^2 is absent, -O-, -$N(R^4)C(O)$-, or -$C(O)N(R^4)$-.

10. The compound of any one of the preceding claims, wherein L^2 is -$C(O)N(R^4)$-.

11. The compound of any one of the preceding claims, wherein at least one of X, Y, and Z is N or $N(R^{3c})$.

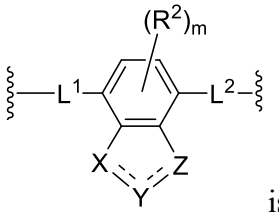
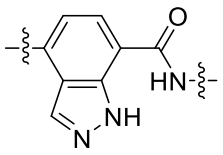
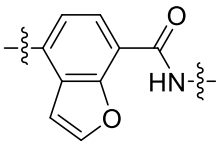
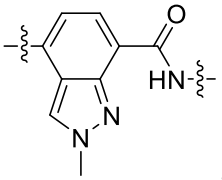
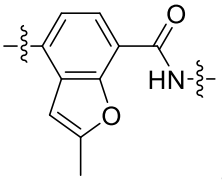
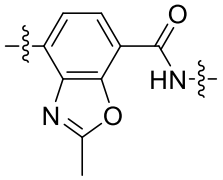
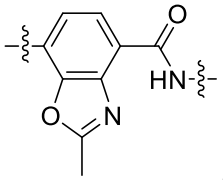
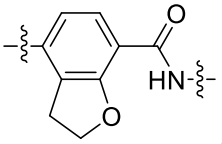
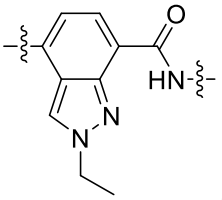
12. The compound of any one of claims 1 to 10, wherein one of X, and Y, is $C(R^{3a})$, and the others of X, Y, and Z are each independently O, N or $N(R^{3c})$.

13. The compound of any one of claims 1 to 10, wherein at least one of X, Y, and Z is O.

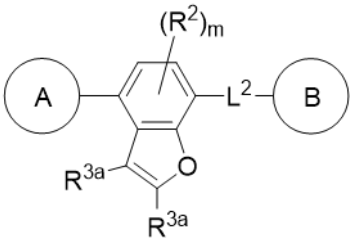
14. The compound of any one of claims 1 to 10, wherein Z and Y are each independently N or $N(R^{3c})$, and X is $C(R^{3a})$.

15. The compound of any one of claims 1 to 10, wherein X is $C(R^{3a})$, and Y and Z are each independently N or $N(R^{3c})$.

16. The compound of any one of claims 1 to 10, wherein X is $C(R^{3a})$, Y is $C(R^{3a})$, and Z is O.

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

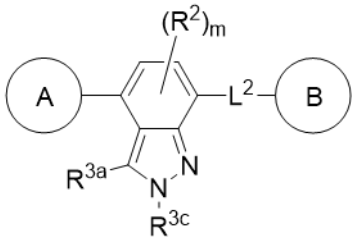
18. The compound of claim 1, wherein the compound of Formula (I-a) is a compound of Formula (I-c):



(I-c)

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

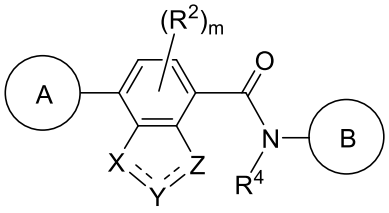
19. The compound of claim 1, wherein the compound of Formula (I-a) is a compound of Formula (I-d):



(I-d)

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

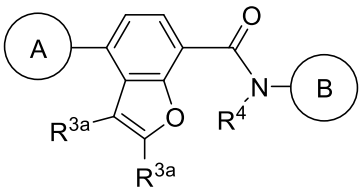
20. The compound of claim 1, wherein the compound of Formula (I-a) is a compound of Formula (I-e):



(I-e)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B, X, Y, Z, L^2, R^2, R^4, m, and subvariables thereof are defined as in claim 1.

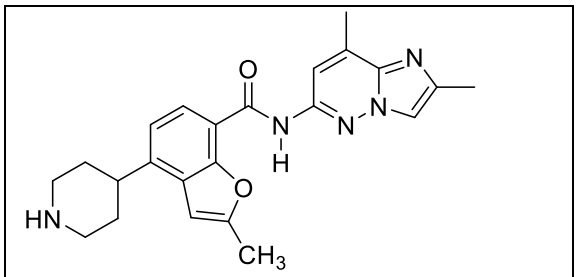
21. The compound of claim 1, wherein the compound of Formula (I-a) is a compound of Formula (I-h):

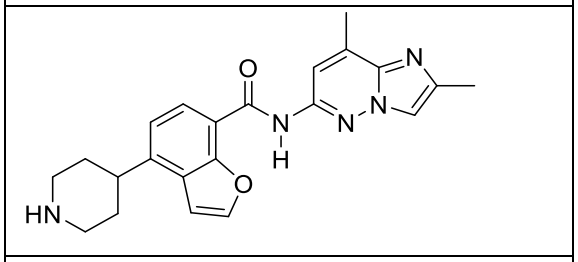


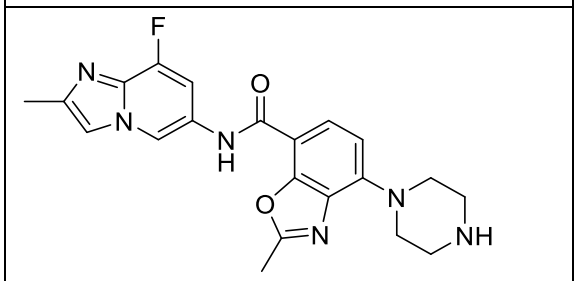
(I-h)

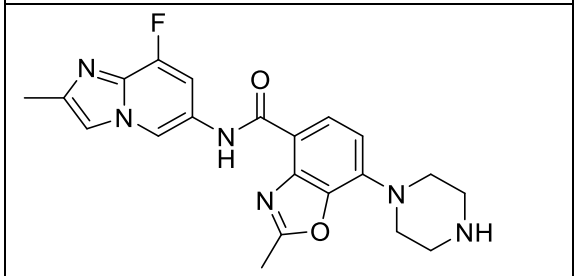
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B, L^2, R^{3a}, R^4, m, and subvariables thereof are defined as in claim 1.

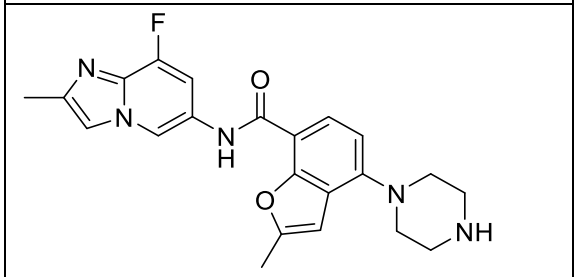
22. The compound of claim 1, wherein the compound is selected from:

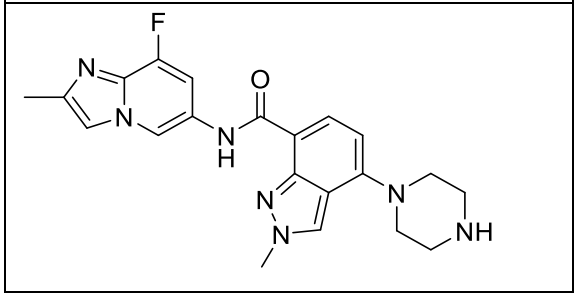


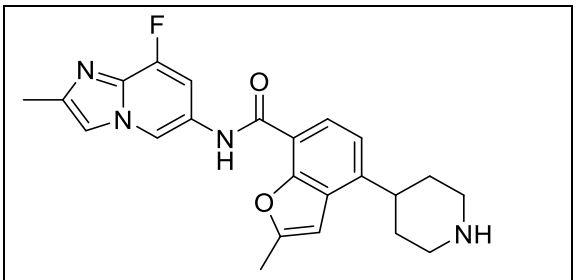


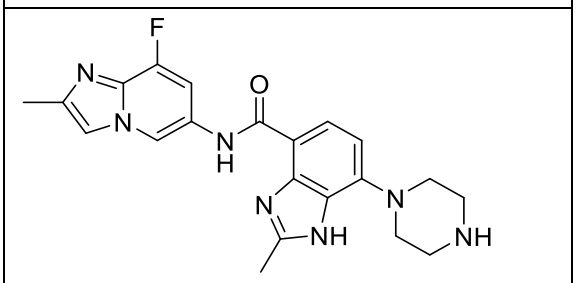


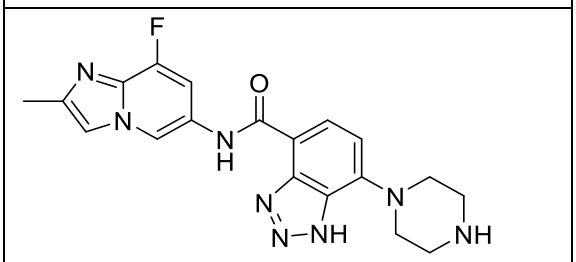


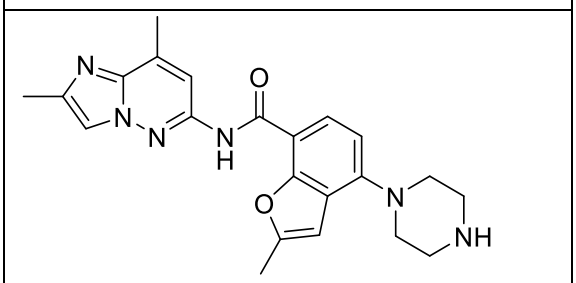


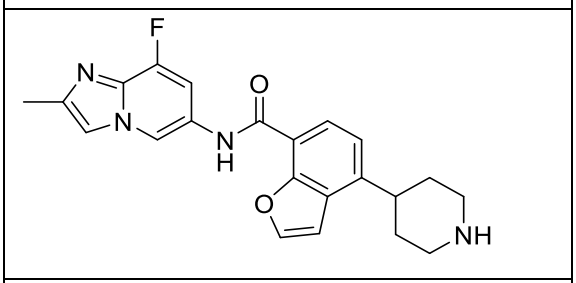


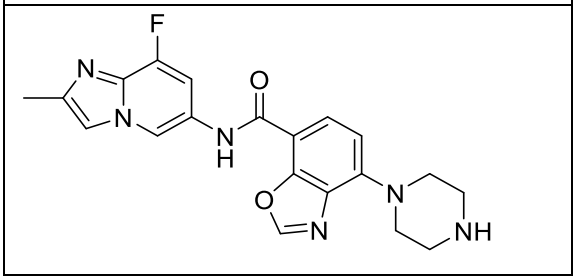


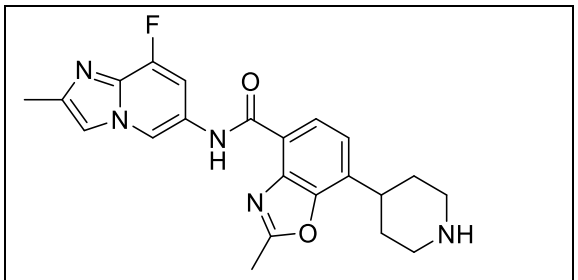


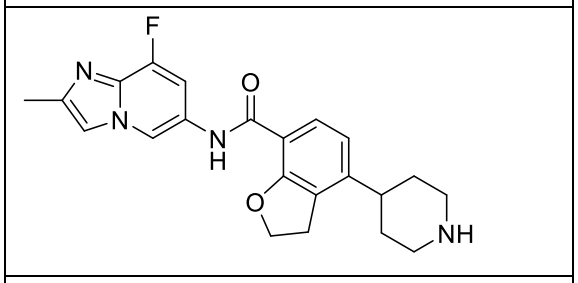


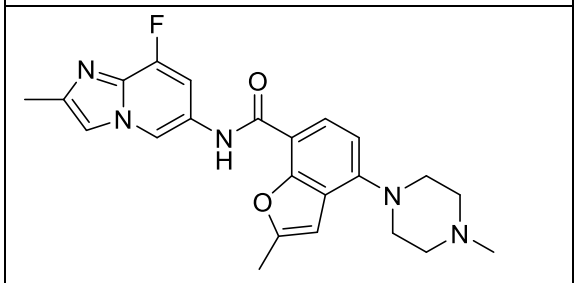


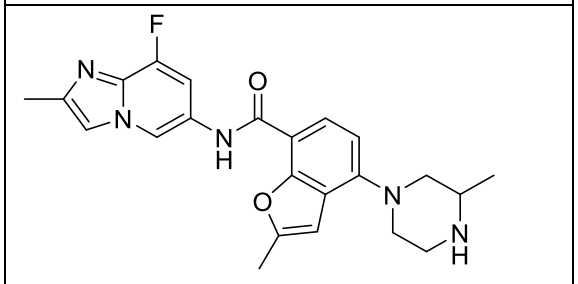


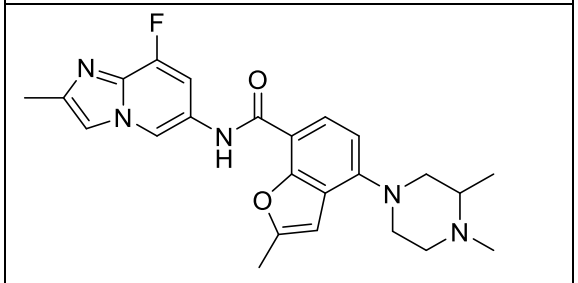


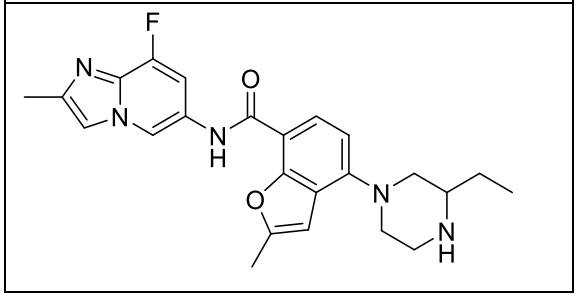


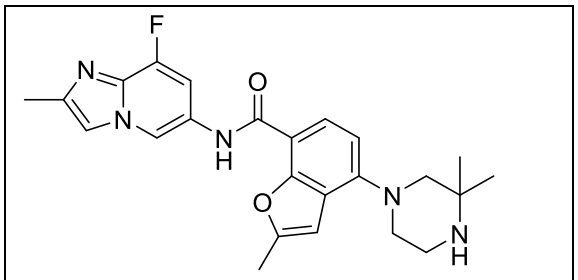


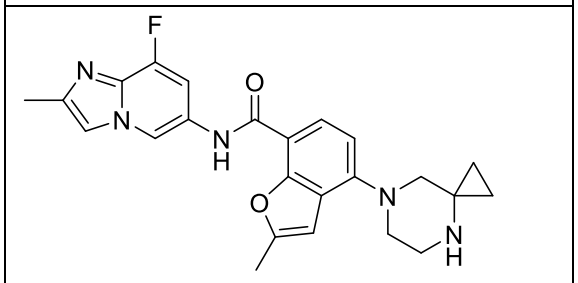


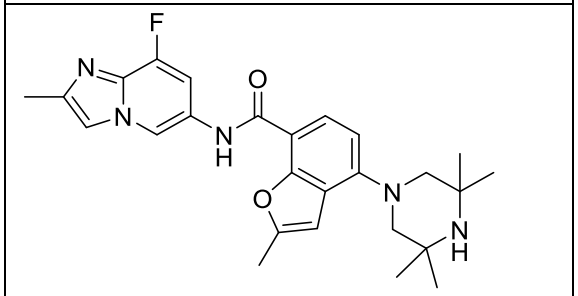


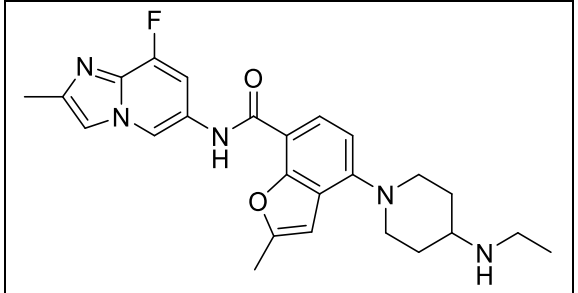


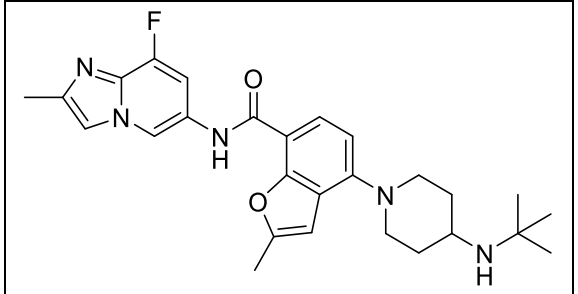


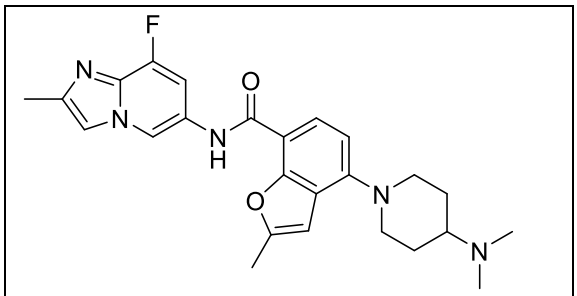


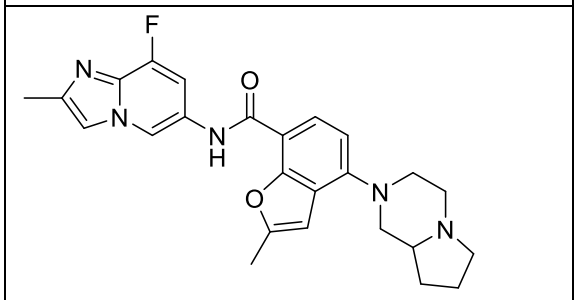


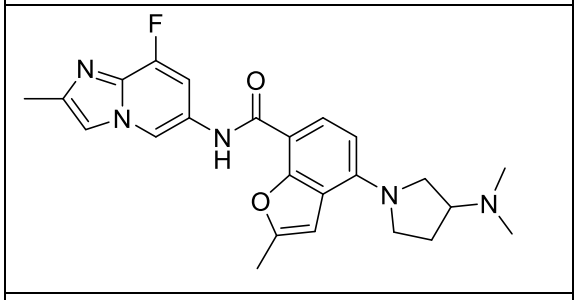


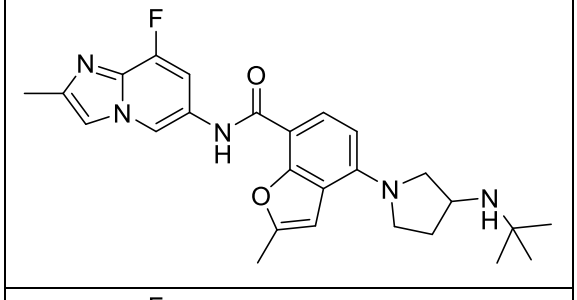


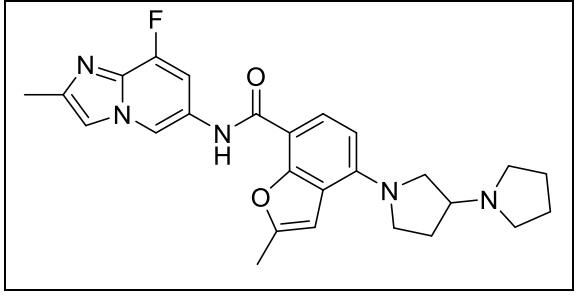


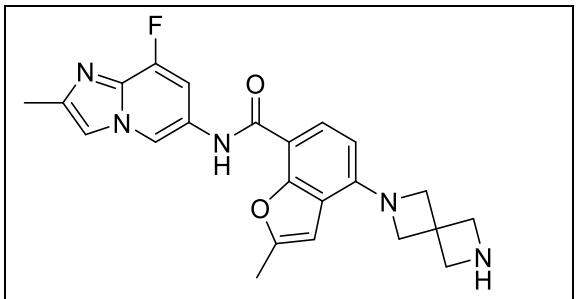


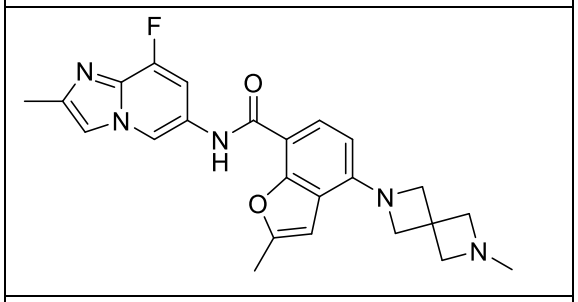


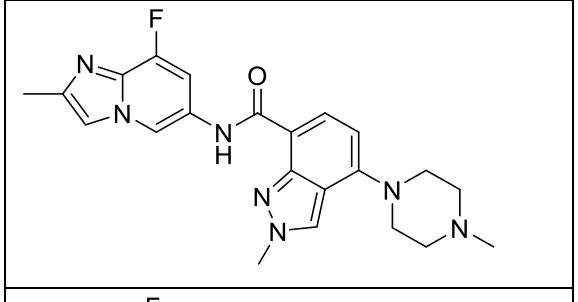


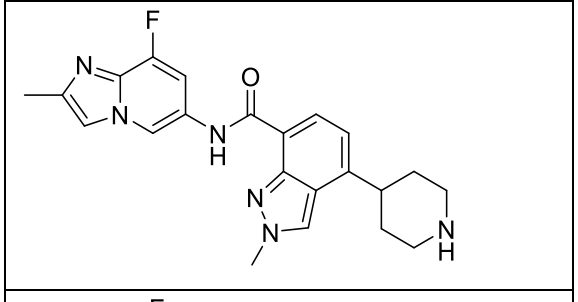


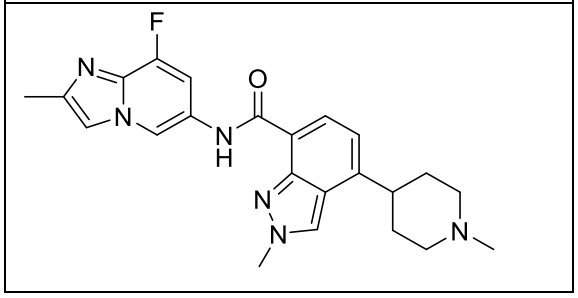


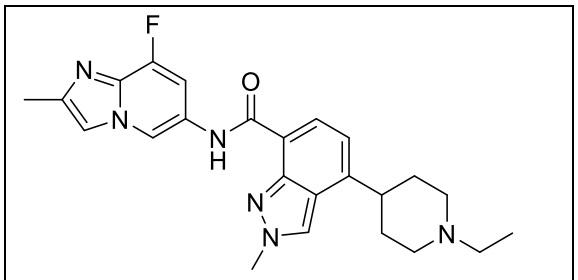


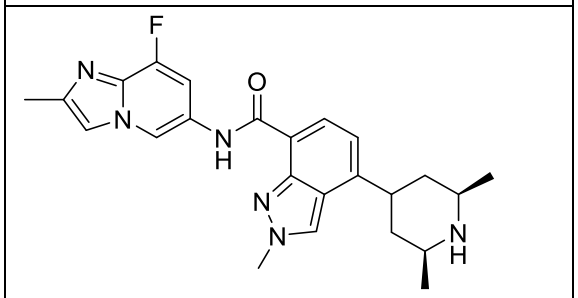


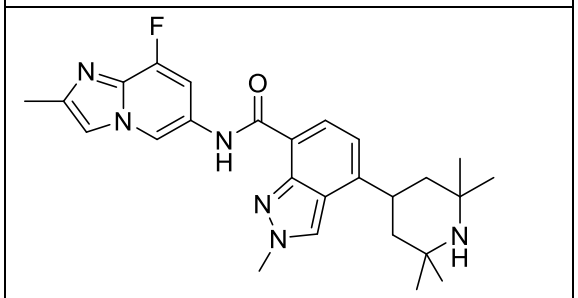


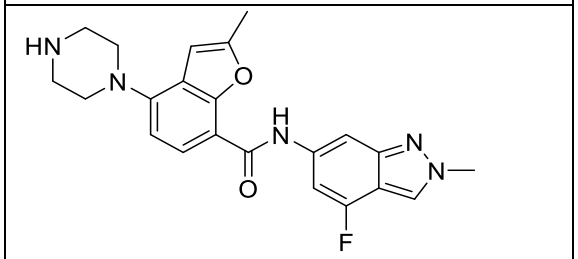


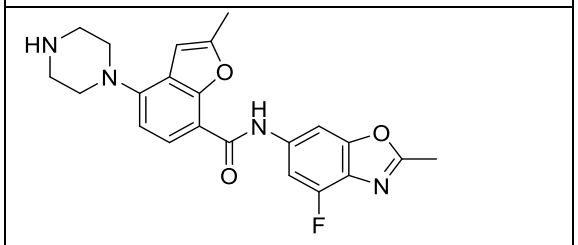


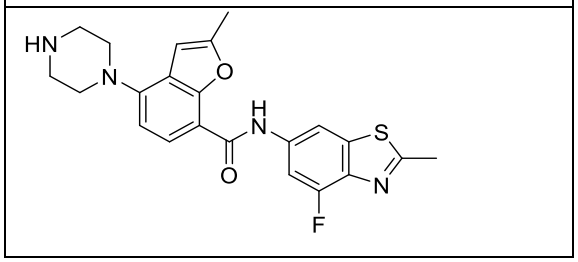


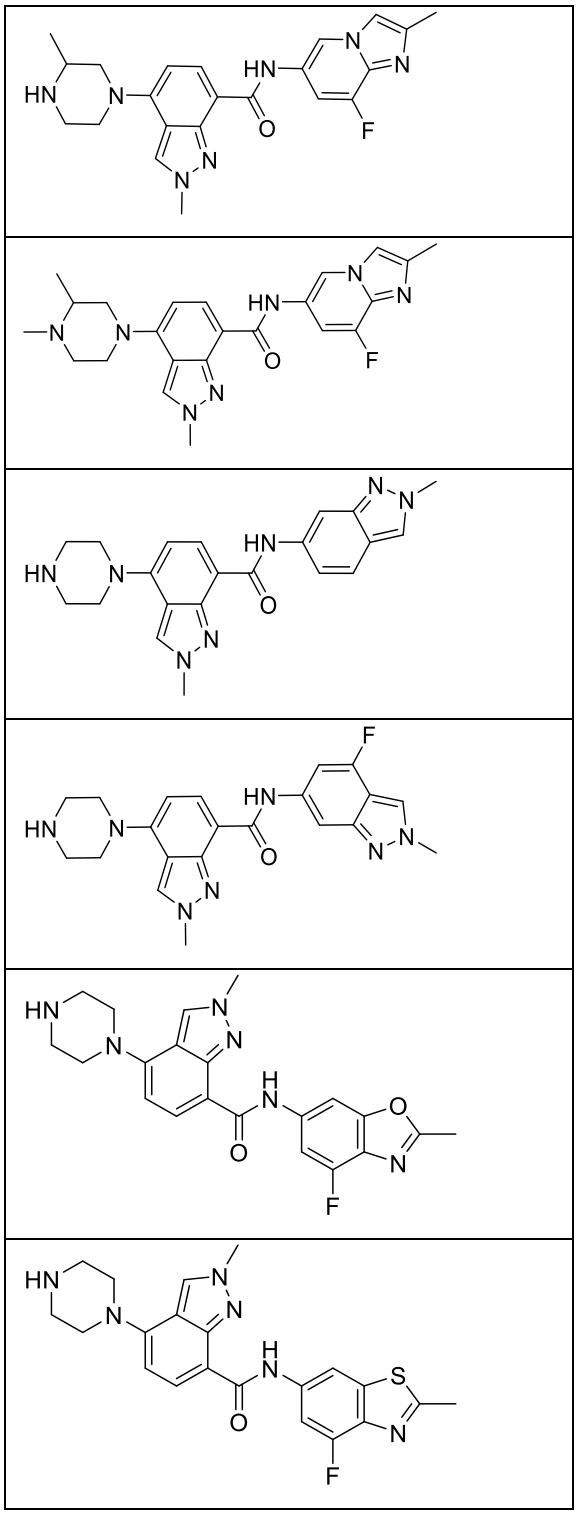


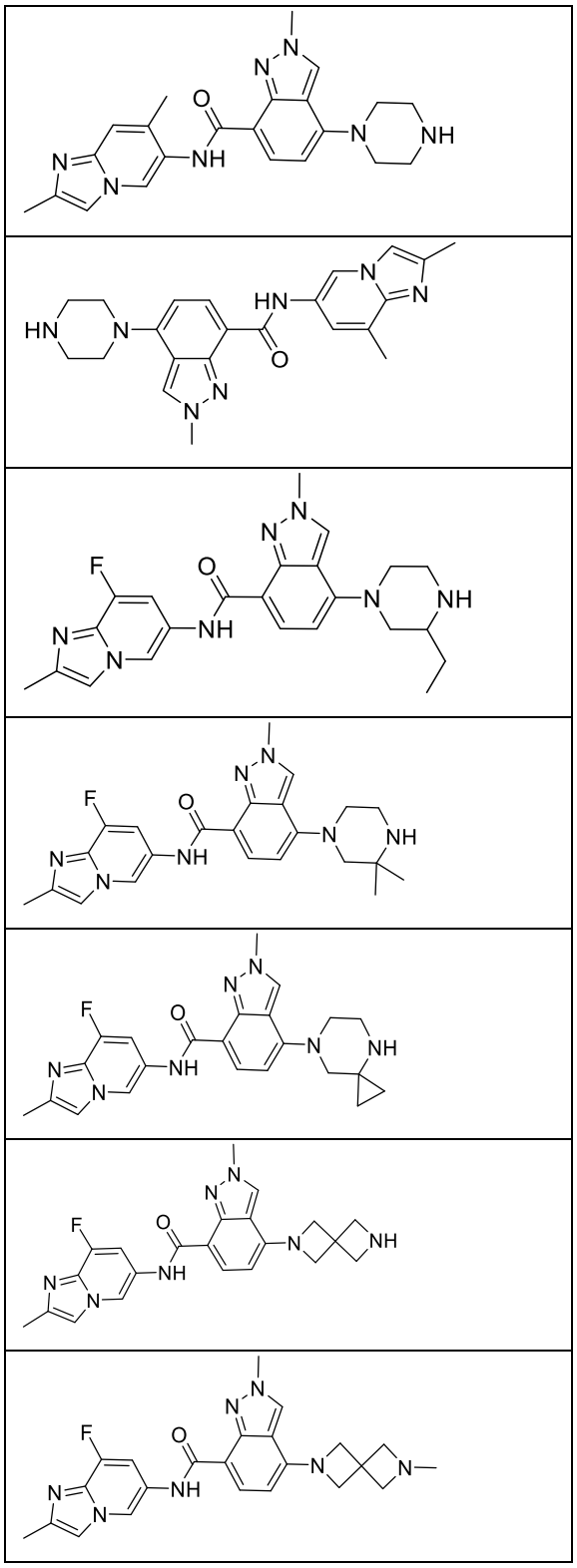


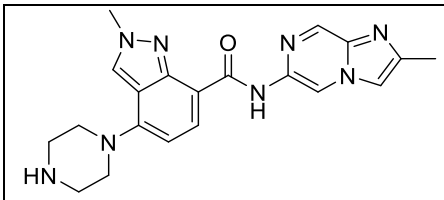
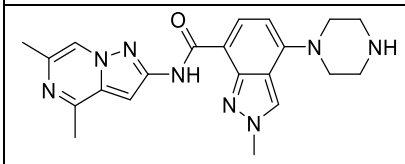
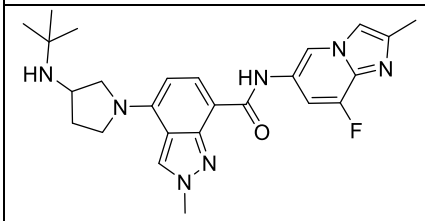
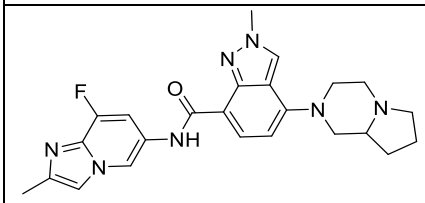
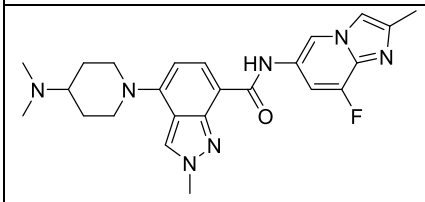
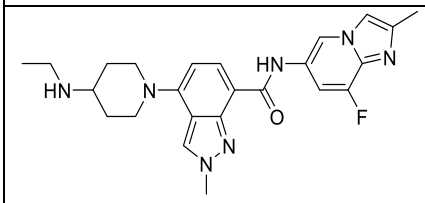
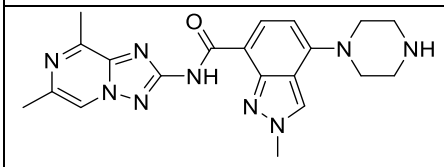
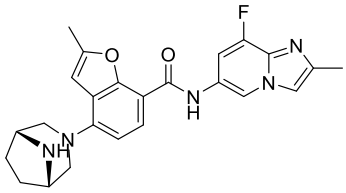


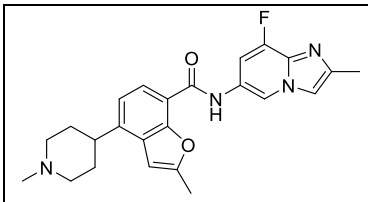
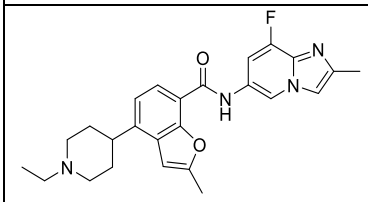
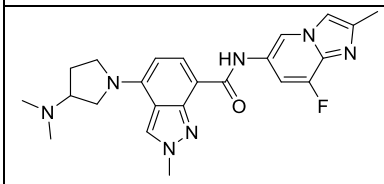
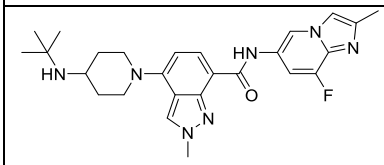
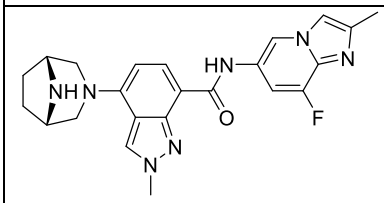
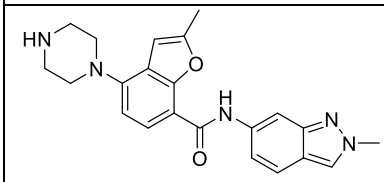
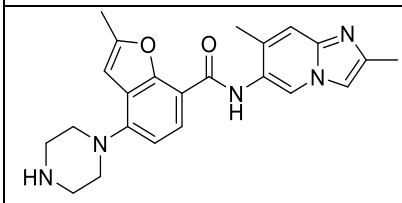
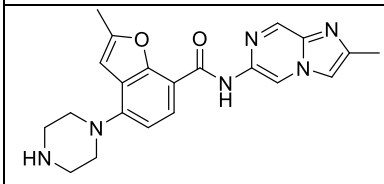


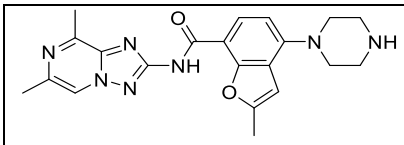
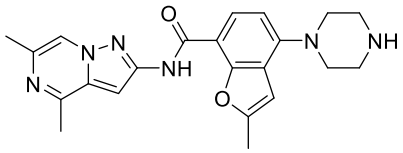
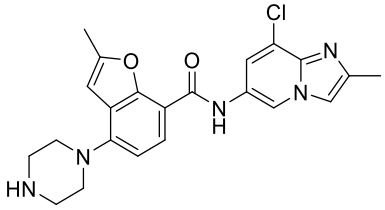
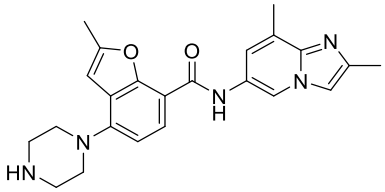
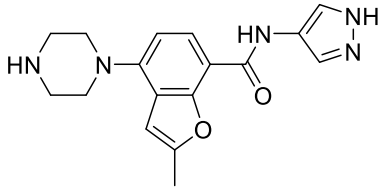
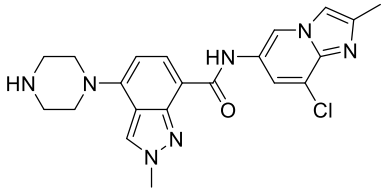
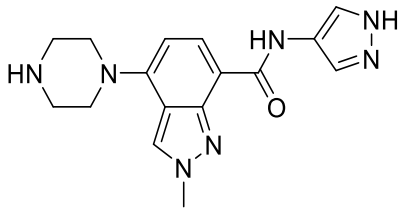
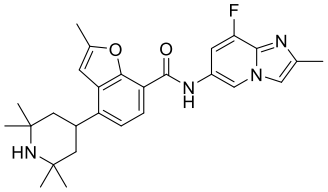


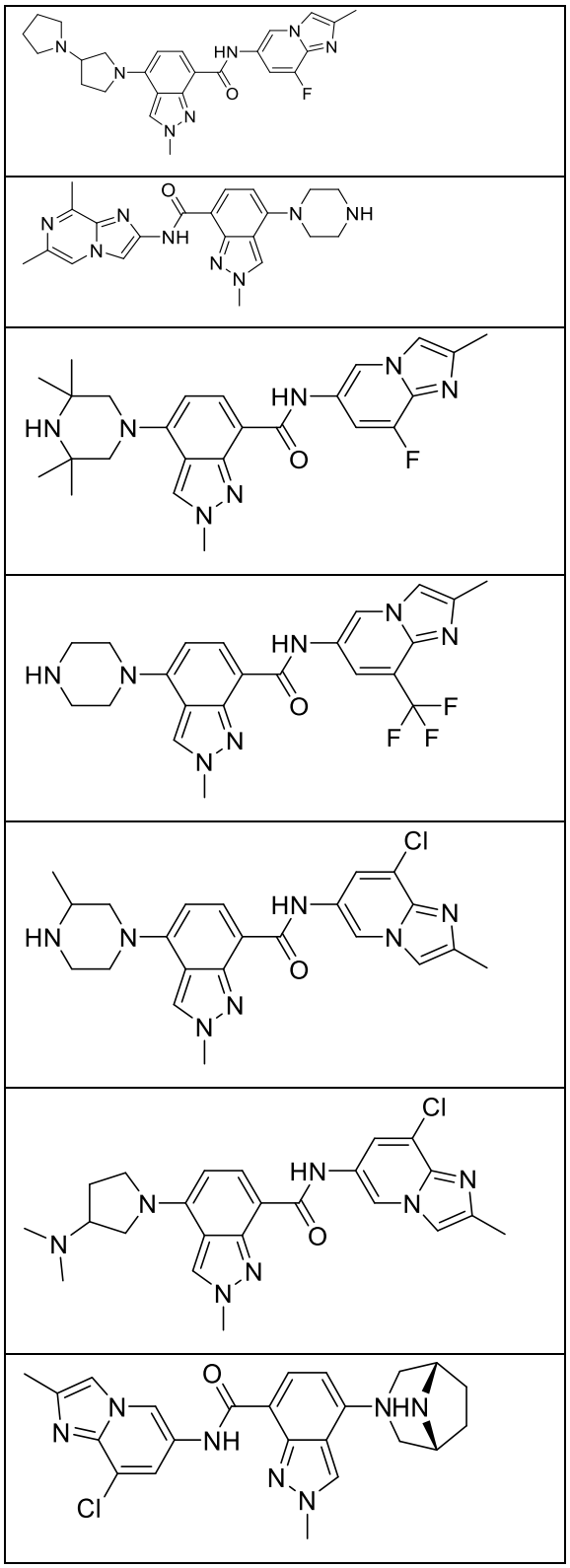


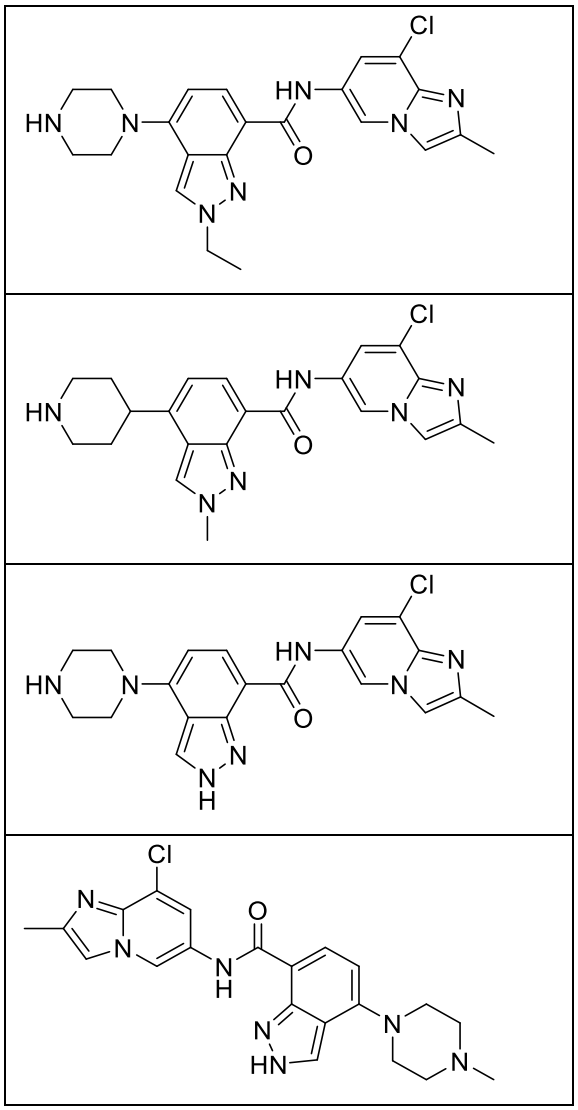






or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof.

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

24. The compound of any one of claims 1-22, or the pharmaceutical composition of claim 23, wherein the compound alters a target nucleic acid.

25. The compound of any one of claims 1-22, or the pharmaceutical composition of claim 23, wherein the compound binds to a target nucleic acid.

26. The compound of any one of claims 1-22, or the pharmaceutical composition of claim 23, wherein the compound stabilizes a target nucleic acid.

27. The compound of any one of claims 1-22, or the pharmaceutical composition of claim 23, wherein the compound increases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more, as determined by qPCR.

28. The compound of any one of claims 1-22, or the pharmaceutical composition of claim 23, wherein the compound decreases splicing at splice site on a target nucleic acid, by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more, as determined by qPCR %.

29. A method of forming a complex comprising a component of a spliceosome, a nucleic acid, and a compound of Formula (I-a) according to any one of claims 1-22 or a composition thereof according to claim 23:

comprising contacting the nucleic acid with a compound of Formula (I-a).

30. The method of claim 29, wherein the component of a spliceosome is recruited to the nucleic acid in the presence of the compound of Formula (I-a).

31. A method of altering the conformation of a nucleic acid comprising contacting the nucleic acid with a compound of Formula (I-a) according to any one of claims 1-22, or the pharmaceutical composition of claim 23.

32. The method of claim 31, wherein the altering comprises forming a bulge in the nucleic acid.

33. The method of claim 31, wherein the altering comprises stabilizing a bulge in the nucleic acid.

34. The method of claim 31, wherein the altering comprises reducing a bulge in the nucleic acid.

35. The method of any one of any one of claims 31-34, wherein the nucleic acid comprises a splice site.

36. Use of a compound of Formula (I-a) according to any one of claims 1-22 or the pharmaceutical composition of claim 23 in the manufacture of a medicament for the treatment of a disease or disorder selected from: proliferative disease, neurological disease or disorder, autoimmune disease or disorder, immunodeficiency disease or disorder, lysosomal storage disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, respiratory disease or disorder, renal disease or disorder, or infectious disease.

37. The use of claim 36, wherein the disease or disorder comprises a proliferative disease.

38. The use of claim 36, wherein the disease or disorder comprises a neurological disease or disorder, autoimmune disease or disorder, immunodeficiency disease or disorder, lysosomal storage disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, respiratory disease or disorder, renal disease or disorder, or infectious disease.

39. The use of claim 36, wherein the disease or disorder comprises neurological disease or disorder.

40. The use of claim 36 or claim 39, wherein the disease or disorder comprises Huntington's disease.

41. A compound of Formula (I-a) according to any one of claims 1-22 or the pharmaceutical composition of claim 23 for use in therapy.