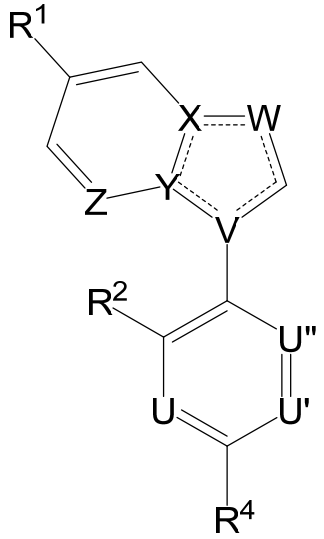
WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

V, W, X, Y, and Z are each independently C or N;

wherein at least two of V, W, X, Y, and Z are N, and the ring comprising V, W, X, Y, and Z forms a heteroaryl ring;

U is CR^3 or N;

U' is CR^5 or N;

U" is CR^6 or N;

R^1 is selected from C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl-, OR^{a1}, $C(O)R^{b1}$, $C(O)NR^{c1}R^{d1}$, $NR^{c1}C(O)R^{b1}$, $C(O)OR^{a1}$, $OC(O)R^{b1}$, $OC(O)NR^{c1}R^{d1}$, and $NR^{c1}C(O)OR^{a1}$, wherein the C_{6-10} aryl, C_{3-10} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (5-10 membered heteroaryl)-C_{1-6} alkyl-, and (4-10 membered heterocycloalkyl)-C_{1-6} alkyl- are each optionally substituted with 1, 2, 3, or 4 independently selected R^{1A} substituents;

R^{a1} , R^{b1}, R^{c1}, and R^{d1} are each independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl,

wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1, 2, 3, or 4 independently selected R^{1A} substituents;

or R^{c1} and R^{d1}, together with the nitrogen to which they are attached, come together to form a 10-14 membered heterocycloalkyl or 10-14 membered heteroaryl group, wherein the 10-14 membered heterocycloalkyl and 10-14 membered heteroaryl group are each optionally substituted with 1, 2, 3, or 4 independently selected R^{1A} substituents;

each R^{1A} is independently selected from halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, NO_2, CN, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted with C_{1-4} alkoxy;

R^2 is selected from H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

R^3 is selected from H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

R^4 is selected from H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, (5-10 membered heteroaryl)-C_{1-6} alkyl, NO_2, CN, OR^{a4}, $C(O)R^{b4}$, $C(O)NR^{c4}R^{d4}$, $C(O)N(R^{c4})NR^{c4}R^{d4}$, $NR^{c4}C(O)R^{b4}$, $C(O)OR^{a4}$, $OC(O)R^{b4}$, $OC(O)NR^{c4}R^{d4}$, and $NR^{c4}C(O)OR^{a4}$, wherein the C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1, 2, 3, or 4 independently selected R^{4A} substituents;

R^{a4}, R^{b4}, R^{c4}, and R^{d4} are each independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

each R^{4A} is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

R^5 is selected from H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

or R^4 and R^5, together with the carbon atoms to which they are attached, come together to form a 5-6 membered aryl ring which is optionally substituted with 1, 2, 3, or 4 independently selected R^7 substituents;

R^6 is selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, and C_{1-6} alkoxy;

each R^7 is independently selected from C_{6-10} aryl, C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, (5-10 membered heteroaryl)-C_{1-6} alkyl, NO_2, CN, and OR^{a7}, wherein the C_{6-10} aryl, C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1, 2, 3, or 4 independently selected R^{7A} substituents;

each R^{a7} is independently selected from C_{6-10} aryl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{6-10} aryl-C_{1-6} alkyl-, C_{3-10} cycloalkyl-C_{1-6} alkyl-, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl; and

each R^{7A} is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, phenyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, and wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted with amino or C_{1-4} alkoxy.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

V, X, and Z are each C, and W and Y are each N; or

X, Y, and Z are each C, and V and W are each N; or

V, Y, and Z are each C, and W and X are each N; or

V and Y are each C, and W, X, and Z are each N.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from 5-10 membered heteroaryl, OR^{a1}, $C(O)NR^{c1}R^{d1}$, and $NR^{c1}C(O)R^{b1}$, wherein the 5-10 membered heteroaryl is optionally substituted with 1, 2, 3, or 4 independently selected R^{1A} substituents.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

R^{a1}, R^{b1}, R^{c1}, and R^{d1} are each independently selected from H, 4-10 membered heterocycloalkyl, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl, wherein the 4-10 membered heterocycloalkyl, (4-10 membered

heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1 or 2 independently selected R^{1A} substituents; or

R^{c1} and R^{d1}, together with the nitrogen to which they are attached, come together to form a 10-14 membered heterocycloalkyl or 10-14 membered heteroaryl group.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:

each R^{1A} is independently selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, and CN, wherein each C_{1-6} alkyl is optionally substituted with C_{1-4} alkoxy.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is selected from H and C_{1-6} alkoxy;

R^3 is selected from H, halo, and C_{1-6} alkoxy;

R^4 is selected from H, 5-10 membered heteroaryl, CN, and $C(O)NR^{c4}R^{d4}$, wherein the 5-10 membered heteroaryl is optionally substituted with 1, 2, 3, or 4 independently selected R^{4A} substituents;

R^5 is selected from H, halo, C_{1-6} alkyl, and C_{1-6} alkoxy; and

R^6 is selected from H and C_{1-6} alkoxy.

7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein:

R^4 and R^5 together with the carbon atoms to which they are attached, come together to form a 6-membered aryl ring which is optionally substituted with 1 or 2 independently selected R^7 substituents.

8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein:

each R^7 is independently selected from C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, 5-10 membered heteroaryl, and OR^{a7}, wherein the C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, and 5-10 membered heteroaryl are each optionally substituted with 1 or 2 independently selected R^{7A} substituents.

9. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

V, X, and Z are each C, and W and Y are each N; or

X, Y, and Z are each C, and V and W are each N; or

V, Y, and Z are each C, and W and X are each N; or

V and Y are each C, and W, X, and Z are each N;

R^1 is selected from 5-10 membered heteroaryl, OR^{a1}, $C(O)NR^{c1}R^{d1}$, and $NR^{c1}C(O)R^{b1}$, wherein the 5-10 membered heteroaryl is optionally substituted with 1, 2, 3, or 4 independently selected R^{1A} substituents;

R^{a1}, R^{b1}, R^{c1}, and R^{d1} are each independently selected from H, 4-10 membered heterocycloalkyl, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl, wherein the 4-10 membered heterocycloalkyl, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1 or 2 independently selected R^{1A} substituents;

or R^{c1} and R^{d1}, together with the nitrogen to which they are attached, come together to form a 10-14 membered heterocycloalkyl or 10-14 membered heteroaryl group;

each R^{1A} is independently selected from C_{1-6} alkyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, and CN, wherein each C_{1-6} alkyl is optionally substituted with C_{1-4} alkoxy;

R^2 is H or C_{1-6} alkoxy;

U is CR^3 or N;

U' is CR^5 or N;

U" is CR^6 or N;

R^3 is selected from H, halo, and C_{1-6} alkoxy;

R^4 is selected from H, 5-10 membered heteroaryl, CN, and $C(O)NR^{c4}R^{d4}$, wherein the 5-10 membered heteroaryl is optionally substituted with 1, 2, 3, or 4 independently selected R^{4A} substituents;

R^{c4} and R^{d4} are each independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl;

each R^{4A} is an independently selected C_{1-6} alkyl group;

R^5 is selected from H, halo, C_{1-6} alkyl, and C_{1-6} alkoxy;

or R^4 and R^5 together with the carbon atoms to which they are attached, come together to form a 5-6 membered aryl ring which is optionally substituted with 1, 2, 3, or 4 independently selected R^7 substituents;

R^6 is selected from H and C_{1-6} alkoxy;

each R^7 is independently selected from C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, 5-10 membered heteroaryl, and OR^{a7}, wherein the C_{3-10} cycloalkyl, 4-14

membered heterocycloalkyl, and 5-10 membered heteroaryl are each optionally substituted with 1 or 2 independently selected R^{7A} substituents;

each R^{a7} is an independently selected 4-10 membered heterocycloalkyl group; and

each R^{7A} is independently selected from C_{1-6} alkyl, amino, C_{3-6} cyclopropyl and 4-6 membered heterocycloalkyl, wherein each C_{1-6} alkyl is optionally substituted with amino or C_{1-4} alkoxy.

10. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

V, X, and Z are each C, and W and Y are each N; or

X, Y, and Z are each C, and V and W are each N; or

V, Y, and Z are each C, and W and X are each N; or

V and Y are each C, and W, X, and Z are each N;

R^1 is selected from 5-6 membered heteroaryl, OR^{a1}, $C(O)NR^{c1}R^{d1}$, and $NR^{c1}C(O)R^{b1}$, wherein the 5-6 membered heteroaryl is optionally substituted with 1 or 2 independently selected R^{1A} substituents;

R^{a1}, R^{b1}, R^{c1}, and R^{d1} are each independently selected from H, 4-10 membered heterocycloalkyl, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl, wherein the 4-10 membered heterocycloalkyl, (4-10 membered heterocycloalkyl)-C_{1-6} alkyl, and (5-10 membered heteroaryl)-C_{1-6} alkyl are each optionally substituted with 1 or 2 independently selected R^{1A} substituents;

or R^{c1} and R^{d1}, together with the nitrogen to which they are attached, come together to form a 10-14 membered heterocycloalkyl or 10-14 membered heteroaryl group;

each R^{1A} is independently selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and CN, wherein each C_{1-6} alkyl is optionally substituted with C_{1-4} alkoxy;

R^2 is H or C_{1-6} alkoxy;

U is CR^3 or N;

U' is CR^5 or N;

U" is CR^6 or N;

R^3 is selected from H, halo, and C_{1-6} alkoxy;

R^4 is selected from H, 5-6 membered heteroaryl, CN, and $C(O)NR^{c4}R^{d4}$, wherein the 5-6 membered heteroaryl is optionally substituted with 1 or 2 independently selected R^{4A} substituents;

R^{c4} and R^{d4} are each independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl;

each R^{4A} is an independently selected C_{1-6} alkyl group;

R^5 is selected from H, halo, C_{1-6} alkyl, and C_{1-6} alkoxy;

or R^4 and R^5 together with the carbon atoms to which they are attached, come together to form a 6-membered aryl ring which is optionally substituted with 1 or 2 independently selected R^7 substituents;

each R^7 is independently selected from C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, 5-10 membered heteroaryl, and OR^{a7}, wherein the C_{3-10} cycloalkyl, 4-14 membered heterocycloalkyl, and 5-10 membered heteroaryl are each optionally substituted with 1 or 2 independently selected R^{7A} substituents;

each R^{a7} is an independently selected 4-10 membered heterocycloalkyl group; and each R^{7A} is independently selected from C_{1-6} alkyl, amino, C_{3-6} cyclopropyl and 4-6 membered heterocycloalkyl, wherein each C_{1-6} alkyl is optionally substituted with amino or C_{1-4} alkoxy.

11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

V, X, and Z are each C, and W and Y are each N; or

X, Y, and Z are each C, and V and W are each N; or

V, Y, and Z are each C, and W and X are each N; or

V and Y are each C, and W, X, and Z are each N;

R^1 is selected from 5-6 membered heteroaryl, OR^{a1}, $C(O)NR^{c1}R^{d1}$, and $NR^{c1}C(O)R^{b1}$, wherein the 5-6 membered heteroaryl is optionally substituted with 1 or 2 independently selected R^{1A} substituents;

R^{a1}, R^{b1}, R^{c1}, and R^{d1} are each independently selected from H, methyl, pyrazolyl, pyridinylmethyl, pyridinylethyl, imidazo[1,2-a]pyridinylmethyl, benzoimidazolylmethyl, imidazo[4,5-c]pyridinylmethyl, benzoxazolylmethyl, oxetanylmethyl, oxetanylethyl, thietanyl-(1,1-dioxide)methyl, 2-oxaspiro[3.3]heptanyl, and 2-oxaspiro[3.5]nonanyl, wherein the methyl, pyrazolyl, pyridinylmethyl, pyridinylethyl, imidazo[1,2-a]pyridinylmethyl, benzoimidazolylmethyl, imidazo[4,5-c]pyridinylmethyl, benzoxazolylmethyl, oxetanylmethyl, oxetanylethyl, thietanyl-(1,1-dioxide)methyl, 2-oxaspiro[3.3]heptanyl, and 2-oxaspiro[3.5]nonanyl are each optionally substituted with 1 or 2 independently selected R^{1A} substituents;

or R^{c1} and R^{d1}, together with the nitrogen to which they are attached, come together to form 1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyrazinyl;

each R^{1A} is independently selected from methyl, ethyl, methoxymethyl, and CN;

R^2 is H or C_{1-6} alkoxy;

U is CR^3 or N;

U' is CR^5 or N;

U" is CR^6 or N;

R^3 is selected from H, halo, and C_{1-6} alkoxy;

R^4 is selected from H, 5-6 membered heteroaryl, CN, and $C(O)NR^{c4}R^{d4}$, wherein the 5-6 membered heteroaryl is optionally substituted with 1 or 2 independently selected R^{4A} substituents;

R^{c4} and R^{d4} are each independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl;

each R^{4A} is an independently selected C_{1-6} alkyl group;

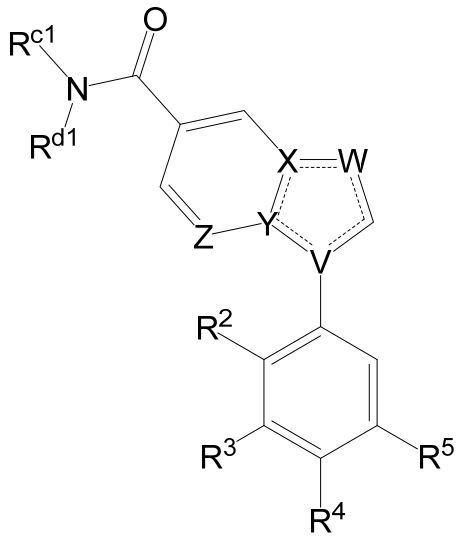
R^5 is selected from H, halo, C_{1-6} alkyl, and C_{1-6} alkoxy;

or R^4 and R^5 together with the carbon atoms to which they are attached, come together to form a 6-membered aryl ring which is optionally substituted with 1 or 2 independently selected R^7 substituents;

each R^7 is independently selected from bicyclo[1.1.1]pentanyl, azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, imidazolyl, azaspiro[3.3]heptanyl, diazaspiro[3.5]nonanyl, oxadiazaspiro[5.5]undecanyl, diazaspiro[4.4]nonanyl, and azetidinyloxy, wherein the bicyclo[1.1.1]pentanyl, azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, imidazolyl, azaspiro[3.3]heptanyl, diazaspiro[3.5]nonanyl, oxadiazaspiro[5.5]undecanyl, and diazaspiro[4.4]nonanyl are each optionally substituted with 1 or 2 R^{7A} substituents; and

each R^{7A} is independently selected from methyl, methoxyethyl, aminomethyl, amino, cyclopropyl, and oxetanyl.

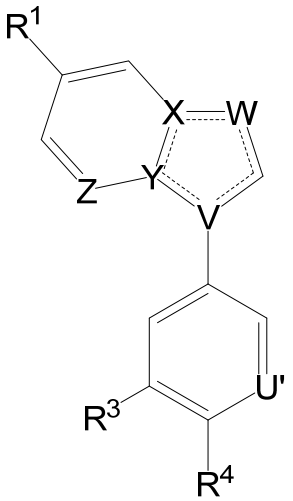
12. The compound of claim 1, wherein the compound of Formula I is a compound of Formula II:



II

or a pharmaceutically acceptable salt thereof; or,

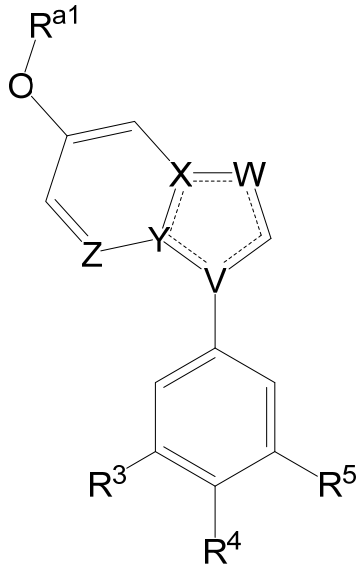
wherein the compound of Formula I is a compound of Formula III:



III

or a pharmaceutically acceptable salt thereof; or,

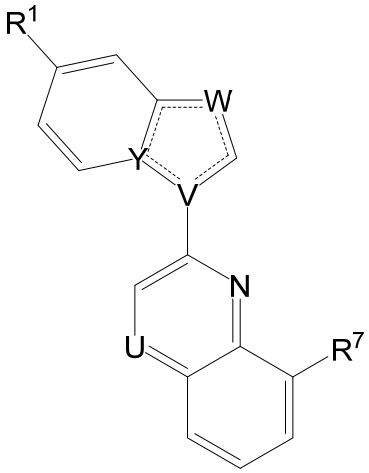
wherein the compound of Formula I is a compound of Formula IV:



IV

or a pharmaceutically acceptable salt thereof; or,

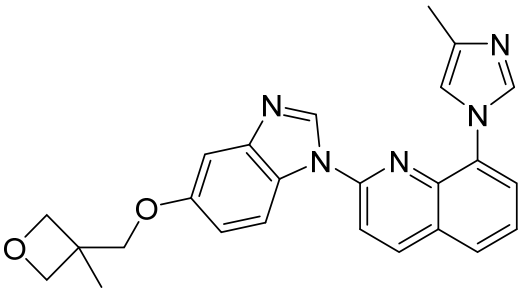
wherein the compound of Formula I is a compound of Formula V:

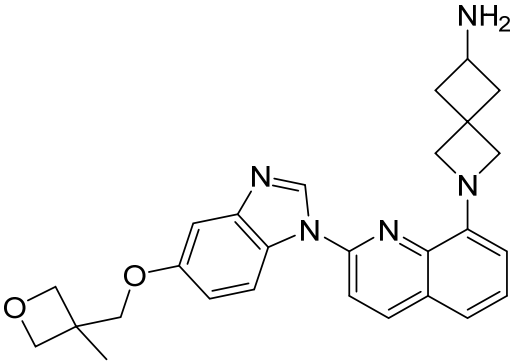


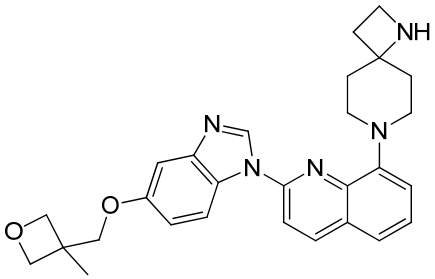
V

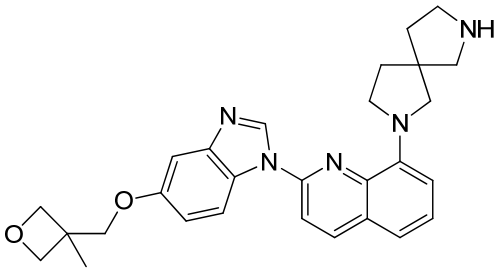
or a pharmaceutically acceptable salt thereof; or,

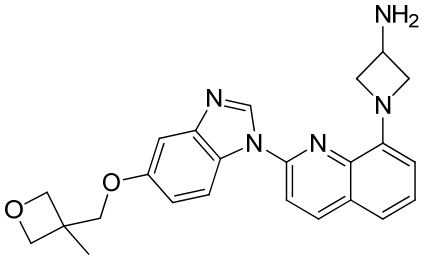
wherein the compound is selected from:

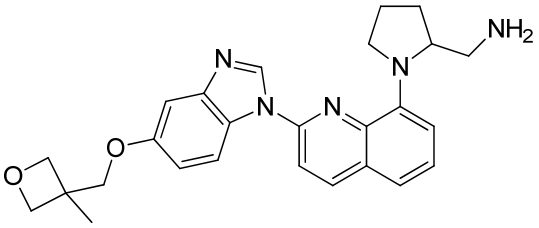


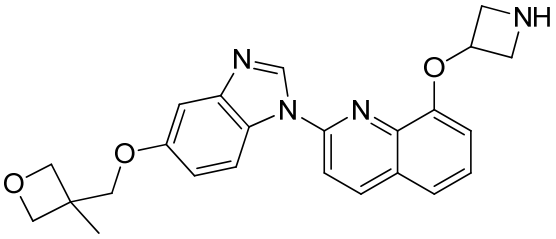


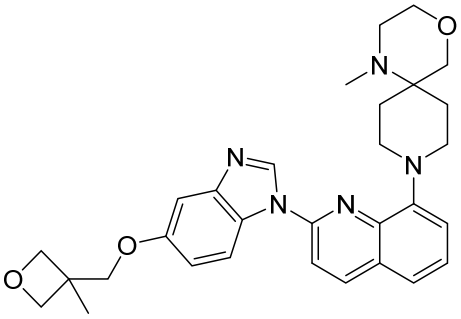


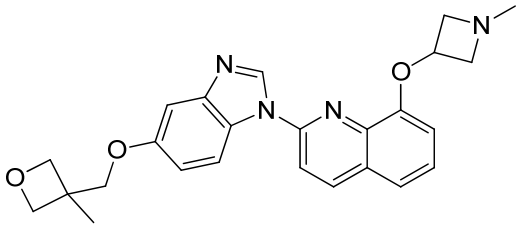


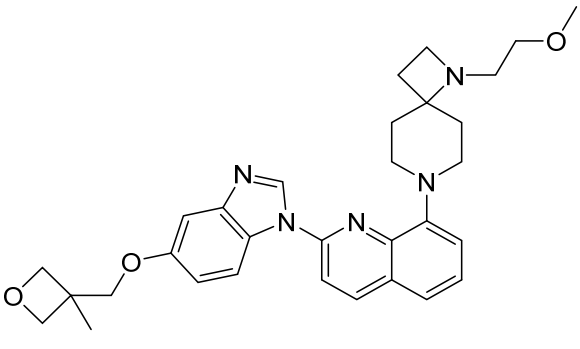


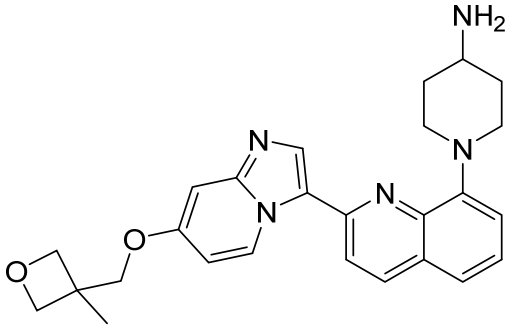


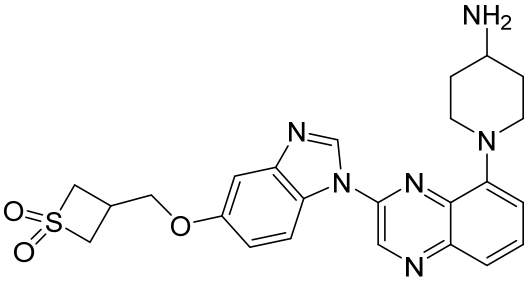


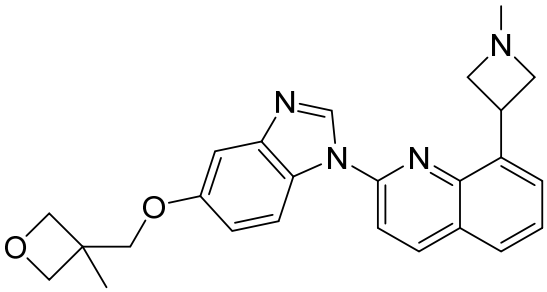


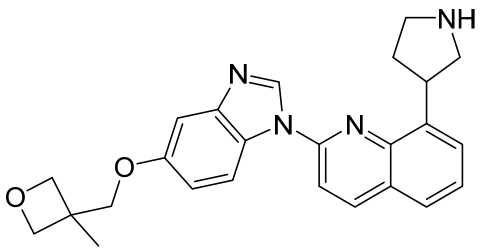


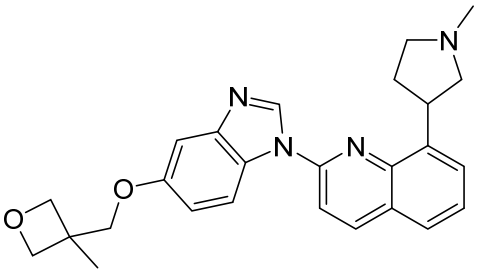


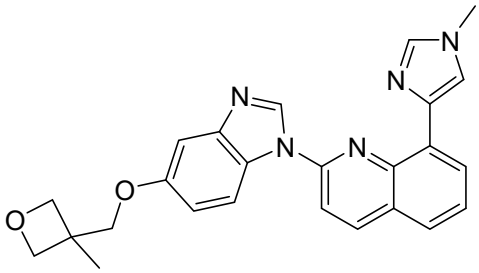


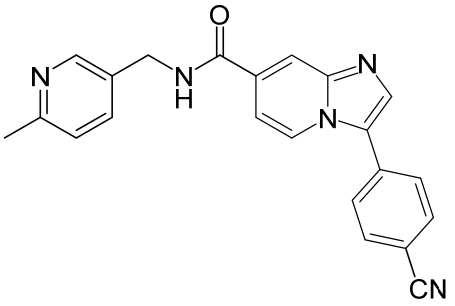


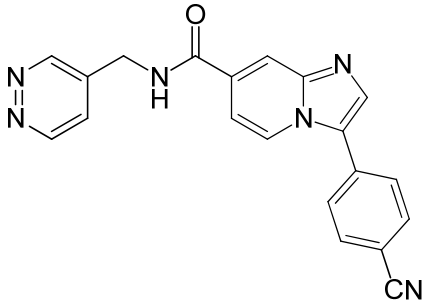


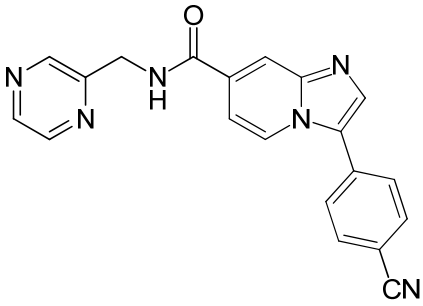


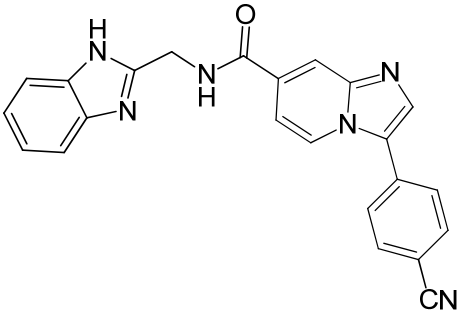


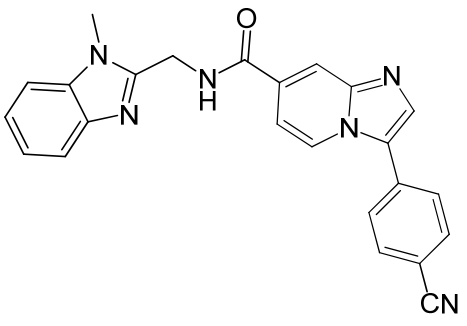


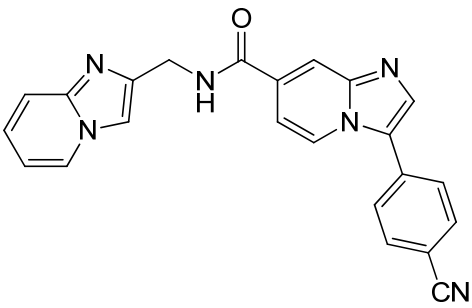


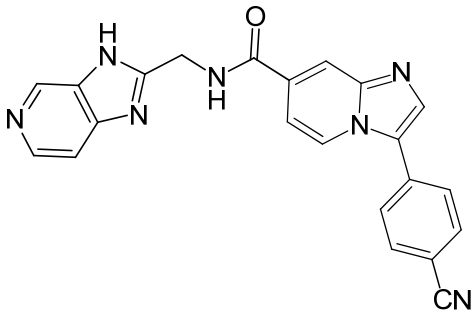
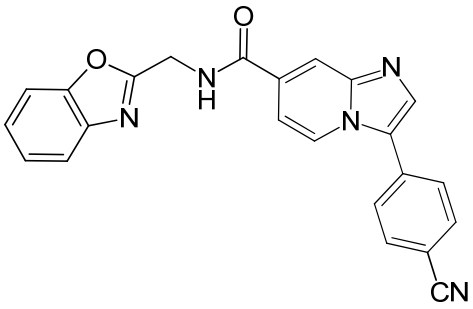
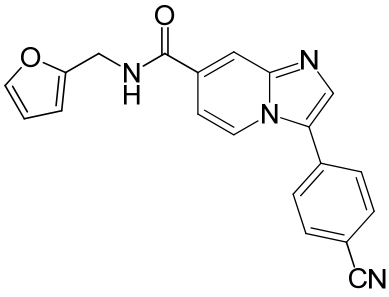
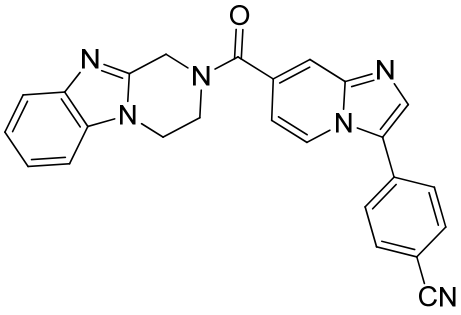
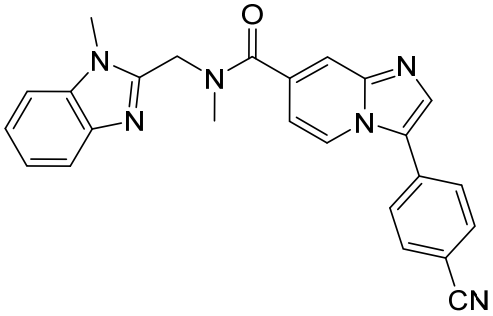
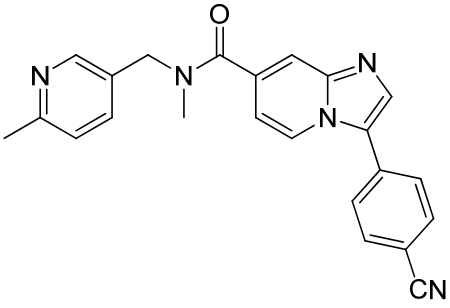
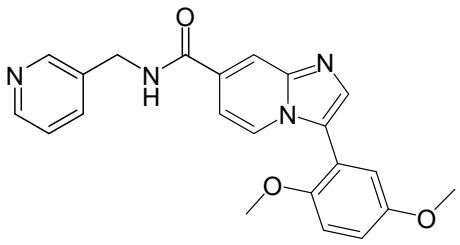
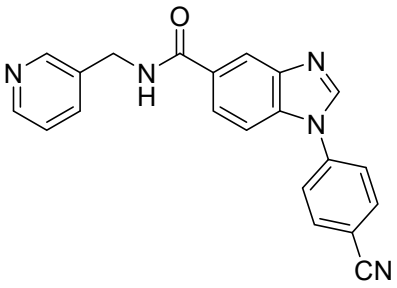
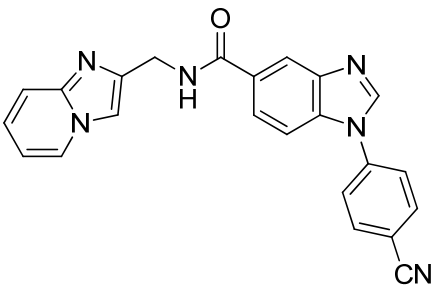
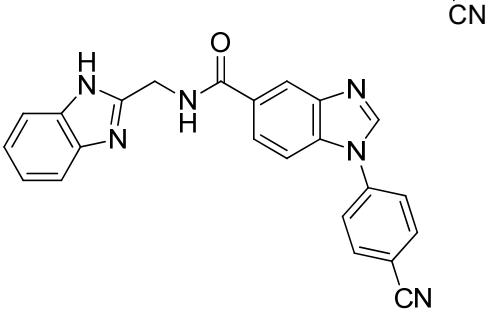
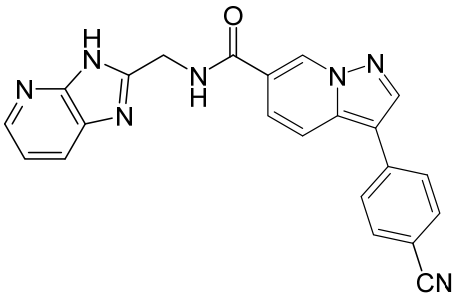
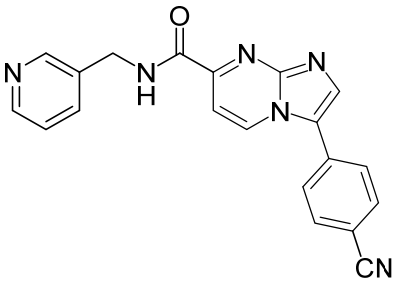


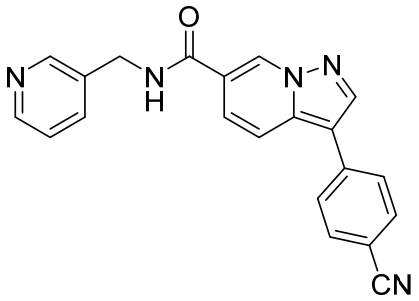


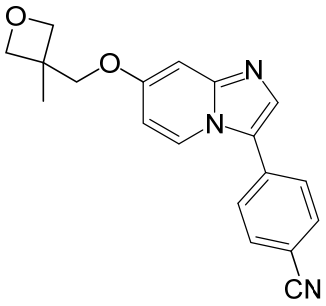


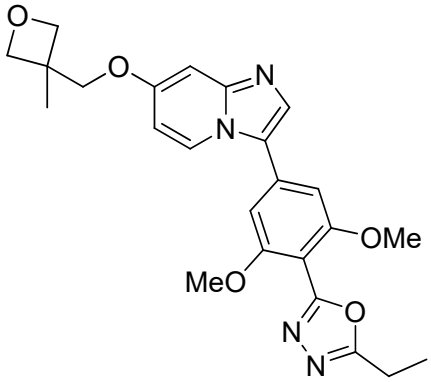


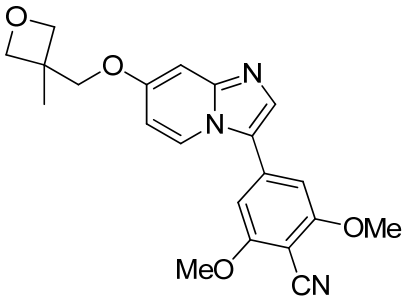


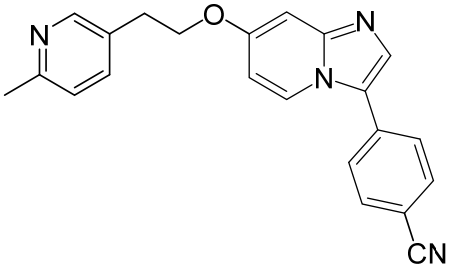













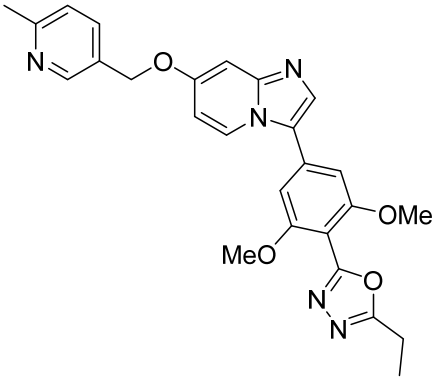



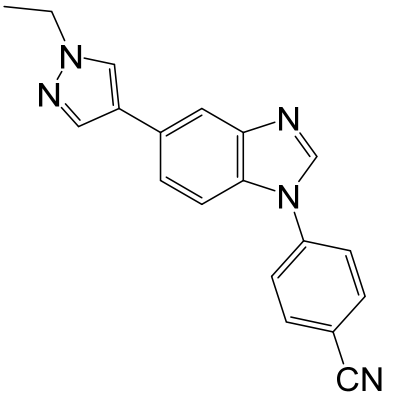


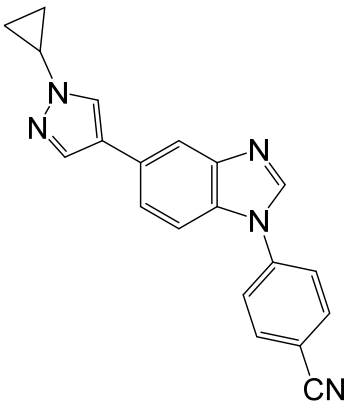


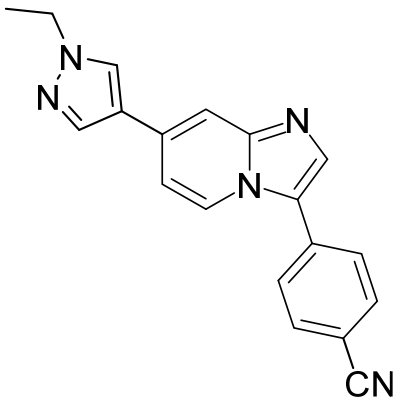


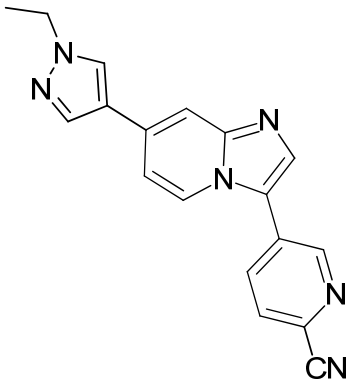


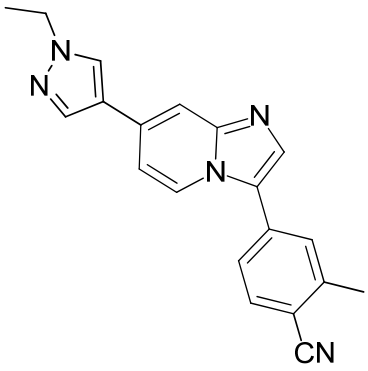


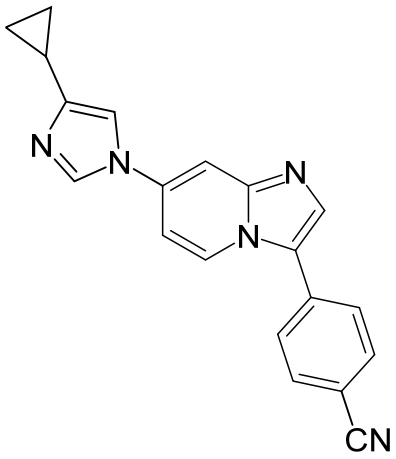


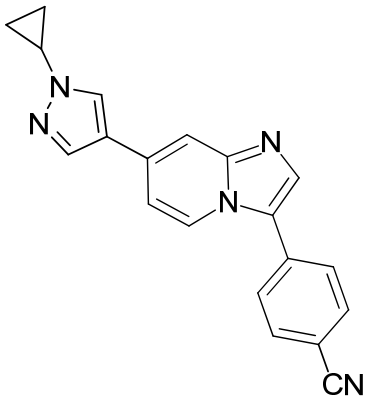


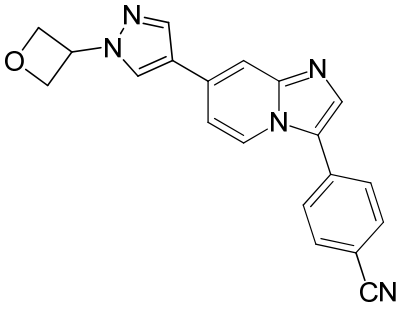


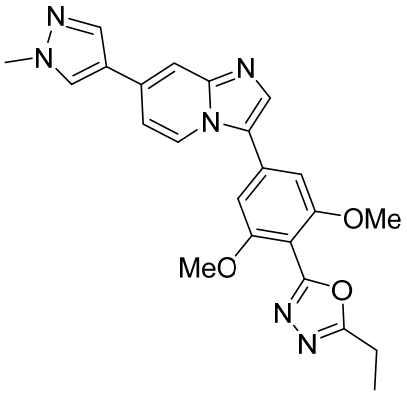


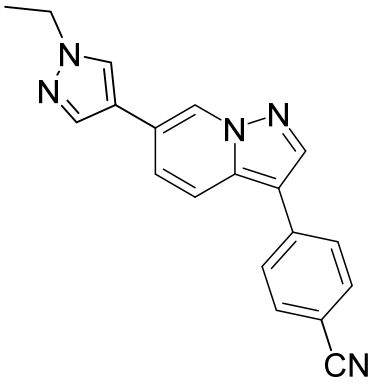


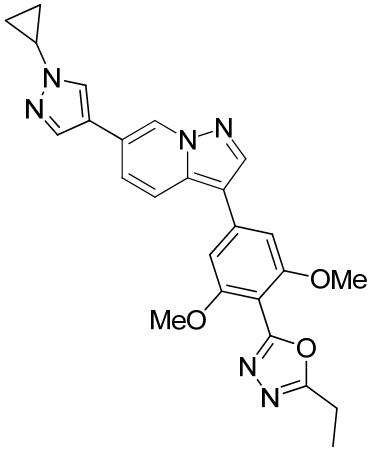
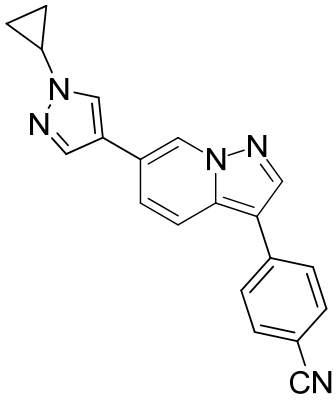
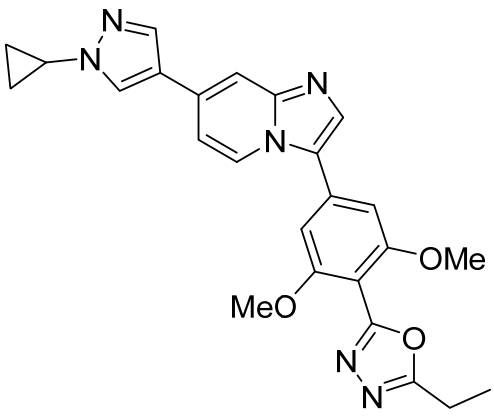
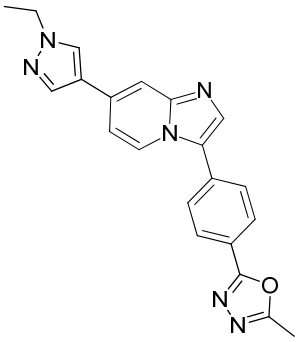
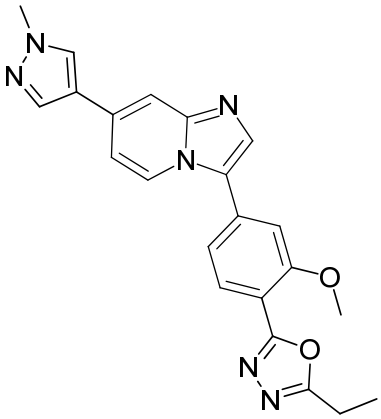
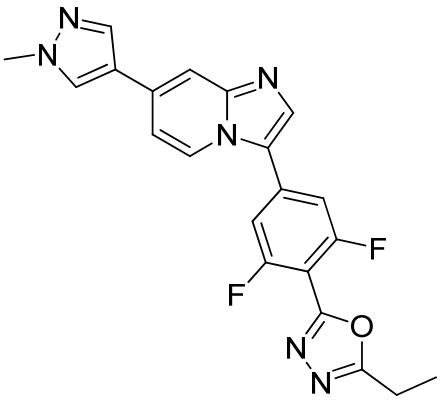
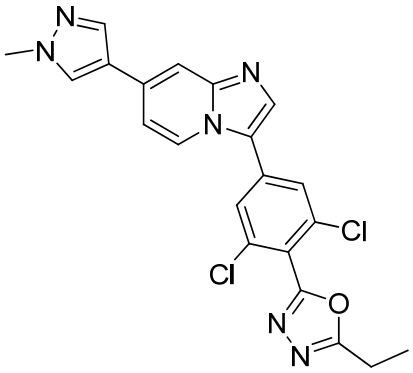
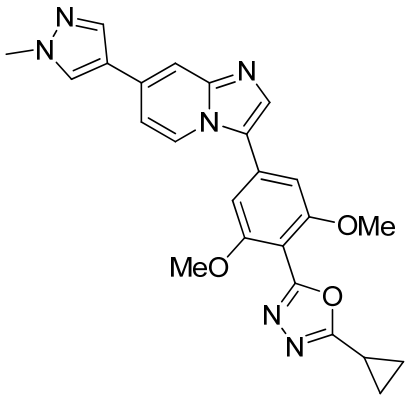


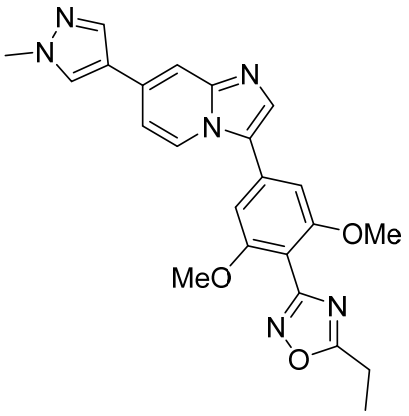
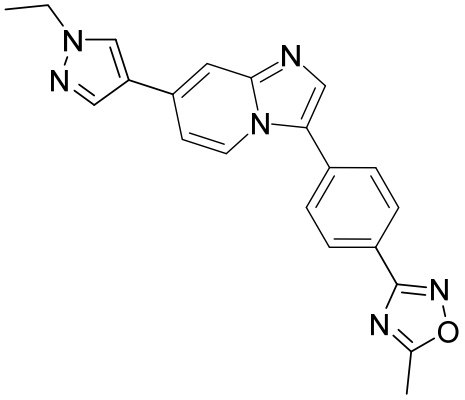
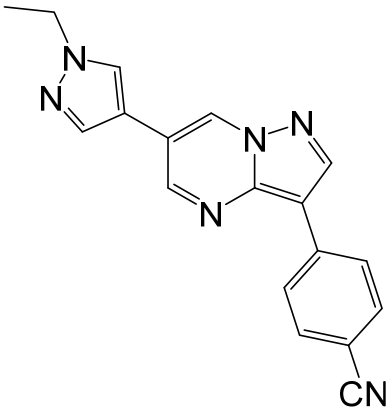
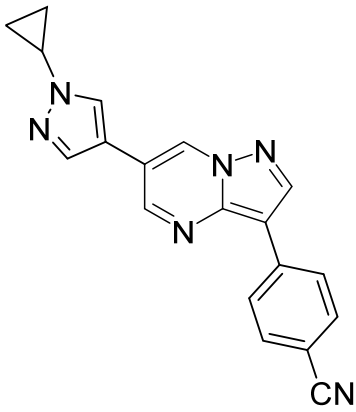
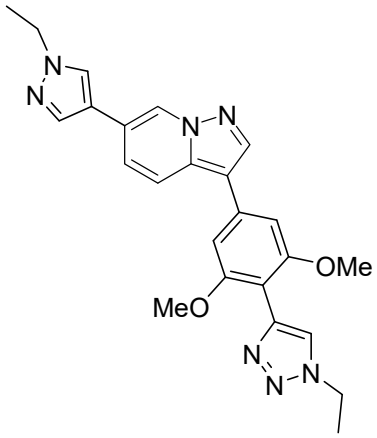
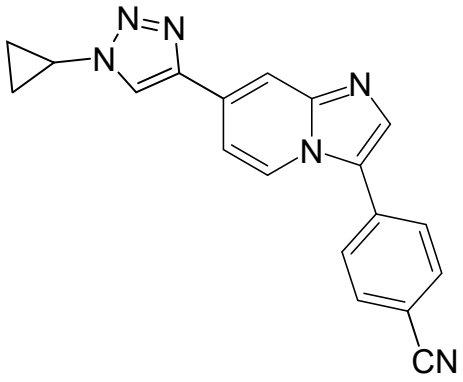
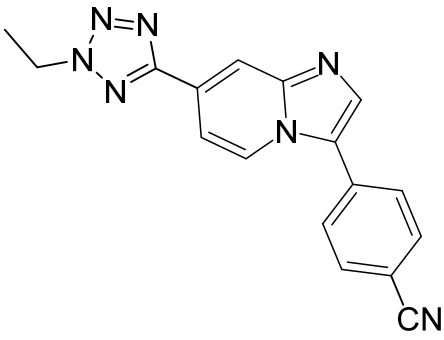
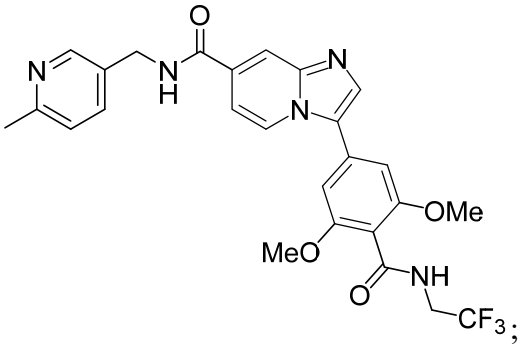








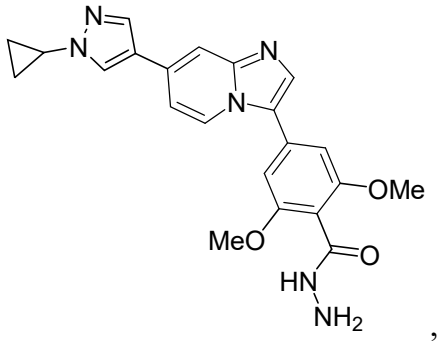









and

or a pharmaceutically acceptable salt thereof.

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



,

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. Use of the compound of any one of claims 1 to 13, or the pharmaceutically acceptable salt thereof for treating a disease in a patient, wherein the disease is associated with abnormal expression or activity of a salt inducible kinase (SIK), wherein a therapeutically effective amount of the compound of any one of claims 1 to 13, or the pharmaceutically acceptable salt thereof is to be administered to the patient in need thereof.

16. The compound of any one of claims 1 to 13, or the pharmaceutically acceptable salt thereof for use as a medicament.