3H-IMIDAZO[4,5-B]PYRIDINE COMPOUNDS AS NON-COVALENT MODIFIERS OF AKT1 AND USES THEREOF

CROSS-REFERENCE

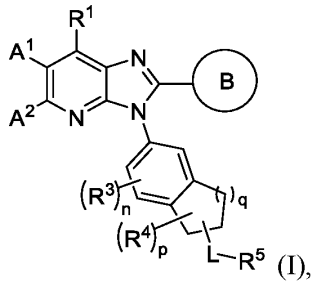
[0001] This application claims the benefit of U.S. Provisional Application No. 63/517,760 filed August 4, 2023 and U.S. Provisional Application No. 63/650,658 filed May 22, 2024, each of which application is hereby incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] The AKT or Protein Kinase B (PKB) family of serine/threonine protein kinases is comprised of 3 highly homologous members, AKT1, AKT2 and AKT3. The family of AKT proteins are involved in signal transduction pathways that regulate cellular processes including apoptosis, proliferation, differentiation, and metabolism. The AKT1 pathway is the most frequently dysregulated signaling pathways in human cancers. Enhanced activation of all the isoforms can be implicated in tumor development and progression, and has been demonstrated in breast, ovarian, pancreatic, and prostate cancers among others (Song et al., 2019). In cancer cells, AKT1 is involved in proliferation and growth, promoting tumor initiation, and suppressing apoptosis, whereas AKT2 regulates cytoskeleton dynamics, favoring local tissue invasion and metastasis. The role of AKT3 hyperactivation in cancer is hypothesized to be involved with possible stimulation of cell proliferation (Hinz et al., *Cell Commun Signal* 2019, 17(1), 154; Pascual et al., *Ann. Oncol.* 2019, 30(7), 1051-1060). Expression of these AKT family members is altered in many human malignant carcinomas including gastric, breast, prostate, ovarian, and pancreatic. AKT family members are rarely mutated however, the most common mutation is AKT1 E17K which has been reported in 6-8% of breast cancers, 2-6% of colorectal cancers, and in 6% of meningiomas, in humans (Yu et al., *PLoS One* 2015, 10 (10), No. e0140479). Thus, there is a need to develop new treatments for the modulation of AKT1 and mutants thereof.

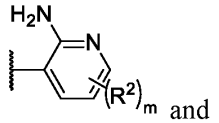
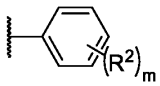
SUMMARY OF THE INVENTION

[0003] In one aspect, the present disclosure provides a compound represented by the structure of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

Ring B is selected from:  and ;

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{3-8} carbocycle which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN, 4- to 8-membered heterocycle, which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$,- $S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-SR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$,

$-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NS(O)_2N(R^{11})_2$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-6} alkynyl, C_{3-8} carbocycle, or 4- to 8-membered heterocycle, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, -OR^{14}, -SR^{14}, -$N(R^{14})_2$, -$C(O)R^{14}$, -$C(O)N(R^{14})_2$, -$N(R^{14})C(O)R^{14}$, -$C(O)OR^{14}$, -$OC(O)R^{14}$, -NO_2, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{14}, -SR^{14}, -$N(R^{14})_2$, -$C(O)R^{14}$, -$C(O)N(R^{14})_2$, -$N(R^{14})C(O)R^{14}$, -$C(O)OR^{14}$, -$OC(O)R^{14}$, -NO_2, =O, =S, =$N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and =$N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{14}, -SR^{14}, -$N(R^{14})_2$, -NO_2, and -CN;

L is represented by -L^1-L^2-L^3-L^4-, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -$N(R^{15})$-, -S-, -S(O)-, -$S(O)_2$-, -$S(O)(NR^{15})$-, -$N(R^{15})C(O)$-, -$N(R^{15})C(O)O$-, -$N(R^{15})S(O)_2$-, -$N(R^{15})S(O)_2N(R^{15})$-, -$S(O)(NR^{15})N(R^{15})$-, -$N(R^{15})N(R^{15})$-, -$(R^{15})NC(O)N(R^{15})$-, and -$(R^{15})NC(O)N(R^{15})N(R^{15})$-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, -SR^{15}, =O, =S, and -CN;

wherein L^1, L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -$C(O)N(R^{16})_2$, -$C(O)OR^{16}$, -$OC(O)R^{16}$, -$N(R^{16})C(O)R^{16}$, -$N(R^{16})S(O)_2R^{16}$, -$S(O)_2N(R^{16})_2$, -$N(R^{16})C(O)N(R^{16})_2$, -$N(R^{16})C(O)OR^{16}$, -$OC(O)N(R^{16})_2$, -$S(O)R^{16}$, -$S(O)_2R^{16}$, -NO_2, =O, =S, =$N(R^{16})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -NO_2, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally

substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN;

R^{10}, R^{11}, R^{11A}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 3- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

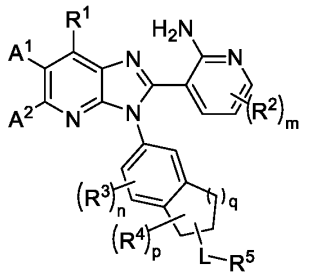
halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 3- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, -CN, and C_{3-8} carbocycle or 4- to 8-membered heterocycle, either of which is optionally further substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

[0004] In one other aspect, the present disclosure provides a compound represented by the structure of Formula (II):



(II),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$,$-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, -

$C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN;

L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, -

$N(R^{15})N(R^{15})$-, -$(R^{15})NC(O)N(R^{15})$-, and -$(R^{15})NC(O)N(R^{15})N(R^{15})$-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, -SR^{15}, =O, =S, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -$C(O)N(R^{16})_2$, -$C(O)OR^{16}$, -$OC(O)R^{16}$, -$N(R^{16})C(O)R^{16}$, -$N(R^{16})S(O)_2R^{16}$, -$S(O)_2N(R^{16})_2$, -$N(R^{16})C(O)N(R^{16})_2$, -$N(R^{16})C(O)OR^{16}$, -$OC(O)N(R^{16})_2$, -$S(O)R^{16}$, -$S(O)_2R^{16}$, -NO_2, =O, =S, =$N(R^{16})$, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -NO_2, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -NO_2, and -CN;

R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{20}, -SR^{20}, -$N(R^{20})_2$, -$C(O)R^{20}$, -$C(O)OR^{20}$, -$OC(O)R^{20}$, -$C(O)N(R^{20})_2$, -$N(R^{20})C(O)R^{20}$, -$N(R^{20})C(O)N(R^{20})_2$, -$N(R^{20})C(O)OR^{20}$, -$OC(O)N(R^{20})_2$, -$S(O)R^{20}$, -$S(O)_2R^{20}$, -$N(R^{20})S(O)_2R^{20}$, -$S(O)_2N(R^{20})_2$, -NO_2, and -CN;

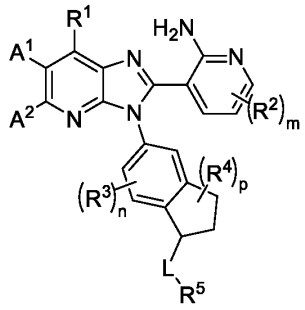
C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{20}, -SR^{20}, -$N(R^{20})_2$, -$C(O)R^{20}$, -$C(O)OR^{20}$, -$OC(O)R^{20}$, -$C(O)N(R^{20})_2$, -$N(R^{20})C(O)R^{20}$, -$N(R^{20})C(O)N(R^{20})_2$, -$N(R^{20})C(O)OR^{20}$, -

$OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

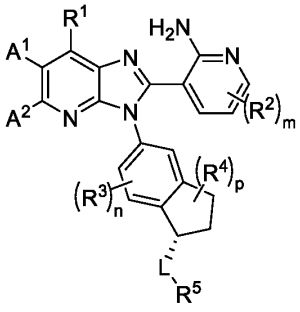
[0005] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (III):



(III);

or a pharmaceutically acceptable salt thereof.

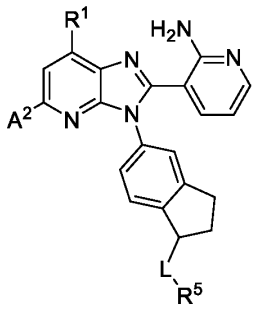
[0006] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (III-A):



(III-A);

or a pharmaceutically acceptable salt thereof.

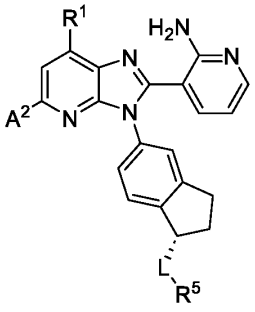
[0007] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (IV):



(IV);

or a pharmaceutically acceptable salt thereof.

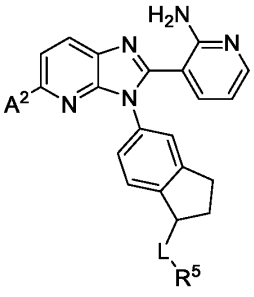
[0008] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (IV-A):



(IV-A);

or a pharmaceutically acceptable salt thereof.

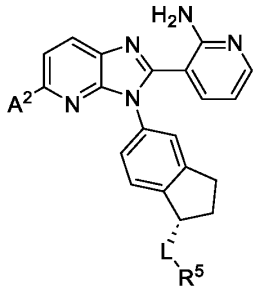
[0009] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (V):



(V);

or a pharmaceutically acceptable salt thereof.

[0010] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (V-A):



(V-A);

or a pharmaceutically acceptable salt thereof.

[0011] In one aspect, the present disclosure provides a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof.

[0012] In one aspect, the present disclosure provides a method of modulating activity of wild-type AKT1 comprising, administering to a subject in need thereof a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof. In one aspect, the present disclosure provides a method of modulating activity of a mutant AKT1 comprising, administering to a subject in need thereof a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof. In some embodiments, the mutant AKT1 is AKT1 E17K.

[0013] In one aspect, the present disclosure provides a method of selectively modulating activity of wild-type AKT1 over wild-type AKT2 comprising administering to a subject in need thereof a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof.

[0014] In one aspect, the present disclosure provides a method of selectively modulating activity of a mutant AKT1 over wild-type AKT2 comprising administering to a subject in need thereof a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV),

(IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof. In some embodiments, the mutant AKT1 is AKT1 E17K.

[0015] In one aspect, the present disclosure provides a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure comprising a pharmaceutically acceptable excipient and a compound of Formula (I), (II), (III), (III-A), (IV), (IV-A), (V), (V-A), or a pharmaceutically acceptable salt thereof. In some embodiments, the cancer is selected from breast cancer, colorectal cancer, and meningioma. In some embodiments, the administration modulates activity of wild-type AKT1. In some embodiments, the administration modulates activity of a mutant AKT1. In some embodiments, the mutant AKT1 is AKT1 E17K.

INCORPORATION BY REFERENCE

[0016] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference for the specific purposes identified herein.

DETAILED DESCRIPTION OF THE INVENTION

[0017] The AKT or Protein Kinase B (PKB) family of serine/threonine protein kinases regulate a myriad of key cellular functions, including apoptosis, proliferation, differentiation and metabolism. The AKT family is comprised of 3 highly homologous members, AKT1, AKT2 and AKT3, and each member possesses a unique tissue distribution and may perform a unique set of biological functions. Aberrant expression and/or activation of all AKT isoforms has been implicated in tumor development, including breast, ovarian, pancreatic, and prostate cancers among others.

[0018] Inhibitors of AKT proteins have been developed for the treatment of cancer, including the two major classes of small-molecule AKT inhibitors being investigated in the clinic: allosteric and ATP-competitive inhibitors. First, allosteric inhibitors (such as miransertib (ARQ 092) and MK-2206) interfere with PH-domain mediated membrane recruitment (the first step in AKT activation) and inhibit AKT kinase activation and AKT phosphorylation. Second, ATP-competitive inhibitors of AKT (such as ipatasertib and capivasertib) bind to the active kinase, in which the PH-domain has shifted from the kinase domain and exposed the ATP-binding pocket site, thus inhibiting ATP binding.

[0019] Provided herein are compounds for modulating (e.g., inhibiting) AKT1 function, as well as methods and compositions for using compounds of the present disclosure in the treatment of

cancer. In some embodiments, the compounds selectively inhibit (e.g., 2x, 5x, 10x, 50x, 100x, etc.) an AKT1 protein over an AKT2 and/or AKT3 protein.

Definitions

[0020] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs. All patents and publications referred to herein are incorporated by reference.

[0021] As used in the specification and claims, the singular form "a," "an," and "the" includes plural references unless the context clearly dictates otherwise.

[0022] "Alkyl" refers to a straight or branched hydrocarbon chain monovalent radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, and preferably having from one to twelve carbon atoms (i.e., C_{1-12} alkyl). The alkyl is attached to the remainder of the molecule through a single bond. An alkyl chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkyl comprises one to twelve carbon atoms (i.e., C_{1-12} alkyl). In certain embodiments, an alkyl comprises one to eight carbon atoms (i.e., C_{1-8} alkyl). In other embodiments, an alkyl comprises one to five carbon atoms (i.e., C_{1-5} alkyl). In other embodiments, an alkyl comprises one to four carbon atoms (i.e., C_{1-4} alkyl). In other embodiments, an alkyl comprises one to three carbon atoms (i.e., C_{1-3} alkyl). In other embodiments, an alkyl comprises one to two carbon atoms (i.e., C_{1-2} alkyl). In other embodiments, an alkyl comprises one carbon atom (i.e., C_1 alkyl). In other embodiments, an alkyl comprises five to fifteen carbon atoms (i.e., C_{5-15} alkyl). In other embodiments, an alkyl comprises five to eight carbon atoms (i.e., C_{5-8} alkyl). In other embodiments, an alkyl comprises two to five carbon atoms (i.e., C_{2-5} alkyl). In other embodiments, an alkyl comprises three to five carbon atoms (i.e., C_{3-5} alkyl). For example, the alkyl group may be attached to the rest of the molecule by a single bond, such as, methyl, ethyl, 1-propyl (*n*-propyl), 1-methylethyl (*iso*-propyl), 1-butyl (*n*-butyl), 1-methylpropyl (*sec*-butyl), 2-methylpropyl (*iso*-butyl), 1,1-dimethylethyl (*tert*-butyl), 1-pentyl (*n*-pentyl), and the like.

[0023] "Alkenyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one carbon-carbon double bond, and preferably having from two to twelve carbon atoms (i.e., C_{2-12} alkenyl). An alkenyl chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkenyl comprises two to eight carbon atoms (i.e., C_{2-8} alkenyl). In certain embodiments, an alkenyl comprises two to six carbon atoms (i.e., C_{2-6} alkenyl). In other embodiments, an alkenyl comprises two to four carbon atoms (i.e., C_{2-4} alkenyl). The alkenyl is

attached to the rest of the molecule by a single bond, for example, ethenyl (i.e., vinyl), prop-1-enyl (i.e., allyl), but-1-enyl, pent-1-enyl, penta-1,4-dienyl, and the like.

[0024] "Alkynyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one carbon--carbon triple bond, and preferably having from two to twelve carbon atoms (i.e., C_{2-12} alkynyl). An alkylnyl chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkynyl comprises two to eight carbon atoms (i.e., C_{2-8} alkynyl). In other embodiments, an alkynyl comprises two to six carbon atoms (i.e., C_{2-6} alkynyl). In other embodiments, an alkynyl comprises two to four carbon atoms (i.e., C_{2-4} alkynyl). The alkynyl is attached to the rest of the molecule by a single bond, for example, ethynyl, propynyl, butynyl, pentynyl, hexynyl, and the like.

[0025] "Alkylene" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing no unsaturation, and preferably having from one to twelve carbon atoms, for example, methylene, ethylene, propylene, (methyl)ethylene, butylene, and the like. The alkylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. An alkylene chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkylene comprises one to ten carbon atoms (i.e., C_{1-10} alkylene). In certain embodiments, an alkylene comprises one to eight carbon atoms (i.e., C_{1-8} alkylene). In other embodiments, an alkylene comprises one to five carbon atoms (i.e., C_{1-5} alkylene). In other embodiments, an alkylene comprises one to four carbon atoms (i.e., C_{1-4} alkylene). In other embodiments, an alkylene comprises one to three carbon atoms (i.e., C_{1-3} alkylene). In other embodiments, an alkylene comprises one to two carbon atoms (i.e., C_{1-2} alkylene). In other embodiments, an alkylene comprises one carbon atom (i.e., C_1 alkylene). In other embodiments, an alkylene comprises five to eight carbon atoms (i.e., C_{5-8} alkylene). In other embodiments, an alkylene comprises two to five carbon atoms (i.e., C_{2-5} alkylene). In other embodiments, an alkylene comprises three to five carbon atoms (i.e., C_{3-5} alkylene).

[0026] "Alkenylene" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing at least one carbon-carbon double bond, and preferably having from two to twelve carbon atoms. The alkenylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. An alkenylene chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkenylene comprises two to ten carbon atoms (i.e., C_{2-10} alkenylene). In certain embodiments, an

alkenylene comprises two to eight carbon atoms (i.e., C_{2-8} alkenylene). In other embodiments, an alkenylene comprises two to five carbon atoms (i.e., C_{2-5} alkenylene). In other embodiments, an alkenylene comprises two to four carbon atoms (i.e., C_{2-4} alkenylene). In other embodiments, an alkenylene comprises two to three carbon atoms (i.e., C_{2-3} alkenylene). In other embodiments, an alkenylene comprises two carbon atoms (i.e., C_2 alkenylene). In other embodiments, an alkenylene comprises five to eight carbon atoms (i.e., C_{5-8} alkenylene). In other embodiments, an alkenylene comprises three to five carbon atoms (i.e., C_{3-5} alkenylene).

[0027] "Alkynylene" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing at least one carbon-carbon triple bond, and preferably having from two to twelve carbon atoms. The alkynylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. An alkynylene chain may be optionally substituted by one or more substituents such as those substituents described herein. In certain embodiments, an alkynylene comprises two to ten carbon atoms (i.e., C_{2-10} alkynylene). In certain embodiments, an alkynylene comprises two to eight carbon atoms (i.e., C_{2-8} alkynylene). In other embodiments, an alkynylene comprises two to five carbon atoms (i.e., C_{2-5} alkynylene). In other embodiments, an alkynylene comprises two to four carbon atoms (i.e., C_{2-4} alkynylene). In other embodiments, an alkynylene comprises two to three carbon atoms (i.e., C_{2-3} alkynylene). In other embodiments, an alkynylene comprises two carbon atoms (i.e., C_2 alkynylene). In other embodiments, an alkynylene comprises five to eight carbon atoms (i.e., C_{5-8} alkynylene). In other embodiments, an alkynylene comprises three to five carbon atoms (i.e., C_{3-5} alkynylene).

[0028] The term "C_{x-y}" when used in conjunction with a chemical moiety, such as alkyl, alkenyl, or alkynyl is meant to include groups that contain from x to y carbons in the chain. For example, the term "C_{1-6} alkyl" refers to saturated hydrocarbon groups, including straight-chain alkyl and branched-chain alkyl groups that contain from 1 to 6 carbons. The term -C_{x-y} alkylene- refers to an alkylene chain with from x to y carbons in the alkylene chain. For example, -C_{1-6} alkylene- may be selected from methylene, ethylene, propylene, butylene, pentylene, and hexylene, any one of which may be optionally substituted.

[0029] The terms "C_{x-y} alkenyl" and "C_{x-y} alkynyl" refer to unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double or triple bond, respectively. The term -C_{x-y} alkenylene- refers to a alkenylene chain with from x to y carbons in the alkenylene chain. For example, -C_{2-6} alkenylene- may be selected from ethenylene, propenylene, butenylene, pentenylene, and hexenylene, any one of which may be optionally substituted. An alkenylene chain may have one double bond or more than one double bond in the alkenylene chain. The term -C_{x-y} alkynylene- refers to a alkynylene

chain with from x to y carbons in the alkynylene chain. For example, -C_{2-6} alkynylene- may be selected from ethynylene, propynylene, butynylene, pentynylene, and hexynylene, any one of which may be optionally substituted. An alkynylene chain may have one triple bond or more than one triple bond in the alkynylene chain.

[0030] The term "carbocycle" as used herein refers to a saturated, unsaturated or aromatic ring in which each atom of the ring is carbon. Carbocycle includes 3- to 10-membered monocyclic rings and polycyclic rings (e.g., 6- to 12-membered bicyclic rings). Each ring of a polycyclic carbocycle may be selected from saturated, unsaturated, and aromatic rings. Polycyclic carbocycles may be fused, bridged or spiro-ring systems. Each ring of a bicyclic carbocycle may be selected from saturated, unsaturated, and aromatic rings. Bicyclic carbocycles may be fused, bridged or spiro-ring systems. In some embodiments, the carbocycle is an aryl. In some embodiments, the carbocycle is a cycloalkyl. In some embodiments, the carbocycle is a cycloalkenyl. In an exemplary embodiment, an aromatic ring, e.g., phenyl, may be fused to a saturated or unsaturated ring, e.g., cyclohexane, cyclopentane, or cyclohexene. Any combination of saturated, unsaturated and aromatic bicyclic rings, as valence permits, are included in the definition of carbocyclic. Exemplary carbocycles include cyclopentyl, cyclohexyl, cyclohexenyl, adamantyl, phenyl, indanyl, and naphthyl. Carbocycle may be optionally substituted by one or more substituents such as those substituents described herein.

[0031] The term "carbocyclene" as used herein refers to a divalent saturated, unsaturated or aromatic ring in which each atom of the ring is carbon. The carbocyclene is attached to the rest of the molecule through a single bond and to the radical group through a single bond. A carbocyclene may be optionally substituted by one or more substituents such as those substituents described herein. Carbocyclene includes divalent 3- to 10-membered monocyclic rings and divalent polycyclic rings (e.g., 6- to 12-membered bicyclic rings). Each ring of a polycyclic carbocyclene may be selected from saturated, unsaturated, and aromatic rings. Polycyclic carbocyclenes may be fused, bridged or spiro-ring systems. Polycyclic carbocyclenes may be fused, bridged or spiro-ring systems. The single bond connecting the carbocyclene to the rest of the molecule and the single bond connecting the carbocyclene to the radical group may be located on the same ring or different rings of a polycyclic carbocyclene. In some embodiments, the carbocycle is an arylene, for example, a phenylene. A "phenylene" as used herein refers to a divalent benzene group. The phenylene is attached to the rest of the molecule through a single bond and to the radical group through a single bond. A phenylene may be optionally substituted by one or more substituents such as those substituents described herein.

[0032] "Cycloalkyl" refers to a stable fully saturated monocyclic or polycyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, which includes fused, bridged, or spiro-

ring systems, and preferably having from three to twelve carbon atoms (i.e., C_{3-12} cycloalkyl). In certain embodiments, a cycloalkyl comprises three to ten carbon atoms (i.e., C_{3-10} cycloalkyl). In other embodiments, a cycloalkyl comprises five to seven carbon atoms (i.e., C_{5-7} cycloalkyl). The cycloalkyl may be attached to the rest of the molecule by a single bond. Examples of monocyclic cycloalkyls include, e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic cycloalkyl radicals include, for example, adamantyl, norbornyl (i.e., bicyclo[2.2.1]heptanyl), norbornenyl, decalinyl, 7,7-dimethyl-bicyclo[2.2.1]heptanyl, and the like. Cycloalkyl may be optionally substituted by one or more substituents such as those substituents described herein.

[0033] "Aryl" refers to a radical derived from an aromatic monocyclic or aromatic polycyclic hydrocarbon ring system by removing a hydrogen atom from a ring carbon atom. The aromatic monocyclic or aromatic multicyclic hydrocarbon ring system contains only hydrogen and carbon and from five to eighteen carbon atoms, where at least one of the rings in the ring system is aromatic, i.e., it contains a cyclic, delocalized (4n+2) p–electron system in accordance with the Hückel theory. The ring system from which aryl groups are derived include, but are not limited to, groups such as benzene, fluorene, indane, indene, tetralin and naphthalene. Aryl may be optionally substituted by one or more substituents such as those substituents described herein.

[0034] A "C_{x-y} carbocycle" is meant to include groups that contain from x to y carbons in a ring. For example, the term "C_{3-6} carbocycle" can be a saturated, unsaturated or aromatic ring system that contains from 3 to 6 carbon atoms—any one of which may be optionally substituted as provided herein.

[0035] The term "heterocycle" as used herein refers to a saturated, unsaturated, non-aromatic or aromatic ring comprising one or more heteroatoms. Exemplary heteroatoms include N, O, Si, P, B, and S atoms. Heterocycles include 3- to 10-membered monocyclic rings and polycyclic rings (e.g., 6- to 12-membered bicyclic rings). Polycyclic heterocycles may be fused, bridged or spiro-ring systems. Each ring of a polycyclic heterocycle may be selected from saturated, unsaturated, and aromatic rings. In some embodiments, the heterocycle comprises at least one heteroatom selected from oxygen, nitrogen, sulfur, or any combination thereof. In some embodiments, the heterocycle comprises at least one heteroatom selected from oxygen, nitrogen, or any combination thereof. In some embodiments, the heterocycle comprises at least one heteroatom selected from oxygen, sulfur, or any combination thereof. In some embodiments, the heterocycle comprises at least one heteroatom selected from nitrogen, sulfur, or any combination thereof. The heterocycle may be attached to the rest of the molecule through any atom of the heterocycle, valence permitting, such as a carbon or nitrogen atom of the heterocycle. In some embodiments, the heterocycle is a heteroaryl. In some embodiments, the heterocycle is a

heterocycloalkyl. Exemplary heterocycles include pyrrolidinyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, piperidinyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, thiophenyl, oxazolyl, thiazolyl, morpholinyl, indazolyl, indolyl, and quinolinyl. Heterocycle may be optionally substituted by one or more substituents such as those substituents described herein. Bicyclic heterocycles may be fused, bridged or spiro-ring systems. In an exemplary embodiment, a heterocycle, e.g., pyridyl, may be fused to a saturated or unsaturated ring, e.g., cyclohexane, cyclopentane, or cyclohexene. Heterocycle may be optionally substituted by one or more substituents such as those substituents described herein.

[0036] The term "heterocyclene" as used herein refers to a divalent saturated, unsaturated, non-aromatic or aromatic ring comprising one or more heteroatoms. Exemplary heteroatoms include N, O, Si, P, B, and S atoms. The heterocyclene is attached to the rest of the molecule through a single bond and to the radical group through a single bond. The single bond attaching the heterocyclene group to the rest of the molecule and the single bond attaching the heterocyclene group to the radical group may be each independently connected through any atom of the heterocyclene as valency permits, including a carbon atom in the heterocyclene ring or a heteroatom in the heterocyclene ring. A heterocyclene may be optionally substituted by one or more substituents such as those substituents described herein. Heterocyclenes include 3- to 10-membered monocyclic rings and polycyclic rings (e.g., 6- to 12-membered bicyclic rings). Each ring of a polycyclic heterocyclene may be selected from saturated, unsaturated, and aromatic rings. Polycyclic heterocyclenes may be fused, bridged or spiro-ring systems. The single bond connecting the heterocyclene to the rest of the molecule and the single bond connecting the heterocyclene to the radical group may be located on the same ring or different rings of a polycyclic heterocyclene and may be attached to the rest of the molecule or the radical group through any atom of the heterocyclene, valence permitting, such as a carbon or nitrogen atom of the heterocycle. In some embodiments, the heterocyclene comprises at least one heteroatom selected from oxygen, nitrogen, sulfur, or any combination thereof. In some embodiments, the heterocyclene comprises at least one heteroatom selected from oxygen, nitrogen, or any combination thereof. In some embodiments, the heterocyclene comprises at least one heteroatom selected from oxygen, sulfur, or any combination thereof. In some embodiments, the heterocyclene comprises at least one heteroatom selected from nitrogen, sulfur, or any combination thereof. In some embodiments, the heterocyclene is a heteroarylene. In some embodiments, the heterocyclene is a heterocycloalkylene.

[0037] "Heterocycloalkyl" refers to a stable 3 to 12 membered non-aromatic ring radical that comprises two to twelve carbon atoms and at least one heteroatom wherein each heteroatom may be selected from N, O, Si, P, B, and S atoms. In some embodiments, the heterocycloalkyl

comprises at least one heteroatom selected from oxygen, nitrogen, sulfur, or any combination thereof. In some embodiments, the heterocycloalkyl comprises at least one heteroatom selected from oxygen, nitrogen, or any combination thereof. In some embodiments, the heterocycloalkyl comprises at least one heteroatom selected from oxygen, sulfur, or any combination thereof. In some embodiments, the heterocycloalkyl comprises at least one heteroatom selected from nitrogen, sulfur, or any combination thereof. The heterocycloalkyl may be selected from monocyclic or bicyclic, and fused, bridged, or spiro-ring systems. The heteroatoms in the heterocycloalkyl radical are optionally oxidized. One or more nitrogen atoms, if present, are optionally quaternized. The heterocycloalkyl radical is partially or fully saturated. The heterocycloalkyl is attached to the rest of the molecule through any atom of the heterocycloalkyl, valence permitting, such as any carbon or nitrogen atoms of the heterocycloalkyl. Examples of heterocycloalkyl radicals include, but are not limited to, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolinyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, quinuclidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranyl, thiomorpholinyl, thiamorpholinyl, 1-oxothiomorpholinyl, and 1,1-dioxothiomorpholinyl. Heterocycloalkyl may be optionally substituted by one or more substituents such as those substituents described herein.

[0038] The term “heteroaryl” refers to a radical derived from a 5- to 12-membered aromatic ring radical whose ring structure comprise at least one heteroatom, preferably between one to four heteroatoms. In some embodiments, the heteroaryl comprises at least one heteroatom selected from oxygen, nitrogen, sulfur, or any combination thereof. In some embodiments, the heteroaryl comprises at least one heteroatom selected from oxygen, nitrogen, or any combination thereof. In some embodiments, the heteroaryl comprises at least one heteroatom selected from oxygen, sulfur, or any combination thereof. In some embodiments, the heteroaryl comprises at least one heteroatom selected from nitrogen, sulfur, or any combination thereof. As used herein, the heteroaryl ring may be selected from monocyclic or bicyclic and fused or bridged ring systems wherein at least one of the rings in the ring system is aromatic, i.e., it contains a cyclic, delocalized (4n+2) p–electron system in accordance with the Hückel theory. The heteroatom(s) in the heteroaryl radical may be optionally oxidized. One or more nitrogen atoms, if present, are optionally quaternized. The heteroaryl may be attached to the rest of the molecule through any atom of the heteroaryl, valence permitting, such as a carbon or nitrogen atom of the heteroaryl. Heteroaryl includes aromatic single ring structures, preferably 5- to 6-membered rings, whose ring structures include at least one heteroatom, preferably one to four heteroatoms, more

preferably one or two heteroatoms. Heteroaryl groups include, for example, pyrrole, furan, thiophene, imidazole, oxazole, thiazole, pyrazole, pyridine, pyrazine, pyridazine, and pyrimidine, and the like. Heteroaryl may be optionally substituted by one or more substituents such as those substituents described herein. Heteroaryl also includes polycyclic ring systems having two or more rings in which two or more atoms are common to two adjoining rings wherein at least one of the rings is heteroaromatic, e.g., the other rings can be aromatic or non-aromatic carbocyclic, or heterocyclic. Heteroaryl may be optionally substituted by one or more substituents such as those substituents described herein.

[0039] An "X-membered heterocycle" refers to the number of endocyclic atoms, i.e., X, in the ring. For example, a 5-membered heteroaryl ring or 5-membered aromatic heterocycle has 5 endocyclic atoms, e.g., triazole, oxazole, thiophene, etc.

[0040] "Alkoxy" refers to a radical bonded through an oxygen atom of the formula: –O-alkyl, where alkyl is an alkyl chain as defined above.

[0041] "Halo" or "halogen" refers to halogen substituents such as bromo, chloro, fluoro, and iodo substituents.

[0042] As used herein, the term "haloalkyl" or "haloalkane" refers to an alkyl radical, as defined above, that is substituted by one or more halogen radicals, for example, trifluoromethyl, dichloromethyl, bromomethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl, and the like. In some embodiments, the alkyl part of the fluoroalkyl radical is optionally further substituted. Examples of halogen substituted alkanes ("haloalkanes") include halomethane (e.g., chloromethane, bromomethane, fluoromethane, iodomethane), di-and trihalomethane (e.g., trichloromethane, tribromomethane, trifluoromethane, triiodomethane), 1-haloethane, 2-haloethane, 1,2-dihaloethane, 1-halopropane, 2-halopropane, 3-halopropane, 1,2-dihalopropane, 1,3-dihalopropane, 2,3-dihalopropane, 1,2,3-trihalopropane, and any other suitable combinations of alkanes (or substituted alkanes) and halogens (e.g., Cl, Br, F, and I). When an alkyl group is substituted with more than one halogen radical, each halogen may be independently selected for example, 1-chloro,2-fluoroethane.

[0043] The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more carbons or substitutable heteroatoms, e.g., an NH or NH_2 of a compound. Unless specified otherwise (e.g., by using the terms "substituted" or "optionally substituted," or by the inclusion of an "-R" group), chemical groups described herein are unsubstituted. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, i.e., a compound which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. In

certain embodiments, substituted refers to moieties having substituents replacing two hydrogen atoms on the same carbon atom, such as substituting the two hydrogen atoms on a single carbon with an oxo, imino, or thioxo group. As used herein, the term "substituted" is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, and aromatic and non-aromatic substituents of organic compounds. The permissible substituents can be one or more and the same or different for appropriate organic compounds.

[0044] In some embodiments, substituents may include any substituents described herein, for example: halogen, hydroxy, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo (=N-OH), hydrazino ($=N-NH_2$), $-R^b-OR^a$, $-R^b-OC(O)R^a$, $-R^b-OC(O)OR^a$, $-R^b-OC(O)N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 0, 1, or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2), and $-P(O)(R^a)_2$; and alkyl, alkenyl, alkynyl, aryl, aralkyl, aralkenyl, aralkynyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, and heteroarylalkyl any one of which may be optionally substituted by alkyl, alkenyl, alkynyl, halogen, haloalkyl, haloalkenyl, haloalkynyl, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo(=N-OH), hydrazine($=N-NH_2$), $-R^b-OR^a$, $-R^b-OC(O)R^a$, $-R^b-OC(O)OR^a$, $-R^b-OC(O)N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 0, 1, or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2), and $-P(O)(R^a)_2$; wherein each R^a is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^a, valence permitting, may be optionally substituted with alkyl, alkenyl, alkynyl, halogen, haloalkyl, haloalkenyl, haloalkynyl, oxo (=O), thioxo (=S), cyano (-CN), nitro ($-NO_2$), imino (=N-H), oximo (=N-OH), hydrazine ($=N-NH_2$), $-R^b-OR^a$, $-R^b-OC(O)-R^a$, $-R^b-OC(O)-OR^a$, $-R^b-OC(O)-N(R^a)_2$, $-R^b-N(R^a)_2$, $-R^b-C(O)R^a$, $-R^b-C(O)OR^a$, $-R^b-C(O)N(R^a)_2$, $-R^b-O-R^c-C(O)N(R^a)_2$, $-R^b-N(R^a)C(O)OR^a$, $-R^b-N(R^a)C(O)R^a$, $-R^b-N(R^a)S(O)_tR^a$ (where t is 1 or 2), $-R^b-S(O)_tR^a$ (where t is 0, 1, or 2), $-R^b-S(O)_tOR^a$ (where t is 1 or 2), $-R^b-S(O)_tN(R^a)_2$ (where t is 1 or 2) , and $-P(O)(R^a)_2$; and wherein each R^b is independently selected from a direct bond or a straight or branched alkylene, alkenylene, or alkynylene chain, and each R^c is a straight or branched alkylene, alkenylene or alkynylene chain. It will be understood by those skilled in the art that substituents can themselves be substituted, if appropriate.

[0045] The term "salt" or "pharmaceutically acceptable salt" refers to salts derived from a variety of organic and inorganic counter ions well known in the art. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases.

[0046] The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0047] The phrase "pharmaceutically acceptable excipient" or "pharmaceutically acceptable carrier" as used herein means a pharmaceutically acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient.

[0048] The terms "subject," "individual," and "patient" may be used interchangeably and refer to humans as well as non-human mammals (e.g., non-human primates, canines, equines, felines, porcines, bovines, ungulates, lagomorphs, and the like). In various embodiments, the subject can be a human (e.g., adult male, adult female, adolescent male, adolescent female, male child, female child) under the care of a physician or other health worker in a hospital, as an outpatient, or other clinical context. In certain embodiments, the subject may not be under the care or prescription of a physician or other health worker.

[0049] As used herein, the phrase "a subject in need thereof" refers to a subject, as described infra, that suffers from, or is at risk for, a pathology to be prophylactically or therapeutically treated with a compound or salt described herein.

[0050] The terms "administer," "administered," "administers," and "administering" are defined as providing a composition to a subject via a route known in the art, including but not limited to intravenous, intraarterial, oral, parenteral, buccal, topical, transdermal, rectal, intramuscular, subcutaneous, intraosseous, transmucosal, or intraperitoneal routes of administration. In certain embodiments, oral routes of administering a composition can be used. The terms "administer," "administered," "administers," and "administering" a compound should be understood to mean providing a compound or salt of the invention or a prodrug of a compound or salt of the invention to the individual in need.

[0051] As used herein, "treatment" or "treating" refers to an approach for obtaining beneficial or desired results with respect to a disease, disorder, or medical condition including, but not limited to, a therapeutic benefit and/or a prophylactic benefit. In certain embodiments, treatment or

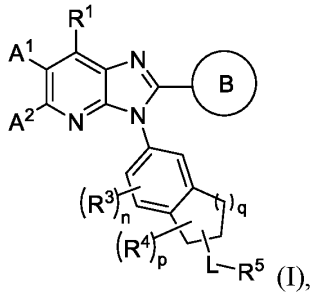
treating involves administering a compound or composition disclosed herein to a subject. A therapeutic benefit may include the eradication or amelioration of the underlying disorder being treated. Also, a therapeutic benefit may be achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disorder, such as observing an improvement in the subject, notwithstanding that the subject may still be afflicted with the underlying disorder. In certain embodiments, for prophylactic benefit, the compositions are administered to a subject at risk of developing a particular disease, or to a subject reporting one or more of the physiological symptoms of a disease, even though a diagnosis of this disease may not have been made. Treating can include, for example, reducing, delaying or alleviating the severity of one or more symptoms of the disease or condition, or it can include reducing the frequency with which symptoms of a disease, defect, disorder, or adverse condition, and the like, are experienced by a patient. Treating can be used herein to refer to a method that results in some level of treatment or amelioration of the disease or condition and can contemplate a range of results directed to that end, including but not restricted to prevention of the condition entirely.

[0052] In certain embodiments, the term "prevent" or "preventing" as related to a disease or disorder may refer to a compound that, in a statistical sample, reduces the occurrence of the disorder or condition in the treated sample relative to an untreated control sample, or delays the onset or reduces the severity of one or more symptoms of the disorder or condition relative to the untreated control sample.

[0053] A "therapeutic effect," as that term is used herein, encompasses a therapeutic benefit and/or a prophylactic benefit as described above. A prophylactic effect includes delaying or eliminating the appearance of a disease or condition, delaying or eliminating the onset of symptoms of a disease or condition, slowing, halting, or reversing the progression of a disease or condition, or any combination thereof.

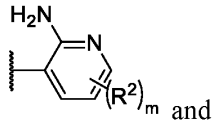
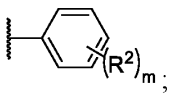
Compounds

[0054] In some aspects, the present disclosure provides compounds represented by the structure of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

Ring B is selected from:  and ;

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-SR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN;

L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

wherein L^1, L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN;

R^{10}, R^{11}, R^{11A}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

[0055] In some embodiments, for the compound or salt of Formula (II), A^2 is selected from C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, =O, and $-NO_2$, -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-NO_2$, =O, and -CN.

[0056] In some embodiments, for the compound or salt of Formula (I), A^2 is selected from C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-NO_2$, =O, and -CN.

[0057] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$,-CN; C_{3-10} carbocycle and 4- to 10-membered heterocycle, the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, and -CN.

[0058] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from C_{3-6} carbocycle and 4- to 6-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$,=O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$,=O, and -CN.

[0059] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0060] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0061] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0062] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, C_{1-6} alkyl and C_{1-6} haloalkyl.

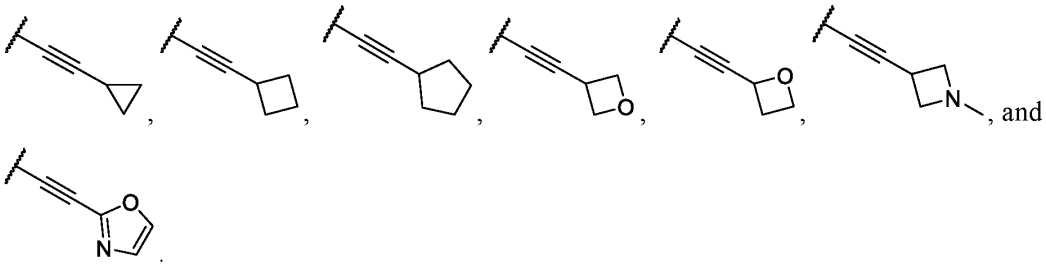
[0063] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl and C_{1-6} haloalkyl.

[0064] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with cyclopropyl, cyclopentyl, oxetanyl, azetidinyl, and oxazolyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0065] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with cyclopropyl, cyclopentyl, oxetanyl, azetidinyl, and oxazolyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0066] In some embodiments, for the compound or salt of Formula (I), A^2 is C_{2-6} alkynyl optionally substituted with cyclopropyl, cyclopentyl, oxetanyl, azetidinyl, and oxazolyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

[0067] In some embodiments, for the compound or salt of Formula (I), A^2 is selected from



, and

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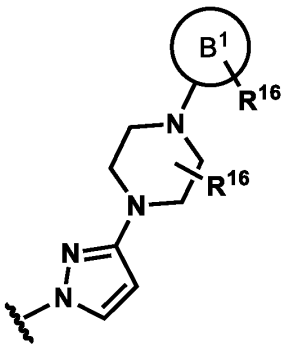
[0068] In some embodiments, for the compound or salt of Formula (I), A^2 is



, wherein ring B^1 is C_{3-8} carbocycle or 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN.

[0069] In some embodiments, for the compound or salt of Formula (I), L^1, L^2, L^3, and L^4 are all absent.

[0070] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0071] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0072] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0073] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0074] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, =O, and -CN; and

C_{1-4} alkyl optionally substituted with one or more substituents independently selected

from: halogen, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0075] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, and $-N(R^{16})_2$; and

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, and $-N(R^{16})_2$.

[0076] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0077] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0078] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[0079] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, -$N(R^{16})_2$, -NO_2, =O, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, -$N(R^{16})_2$, -NO_2, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{16}, -$N(R^{16})_2$, -NO_2, and -CN.

[0080] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, -$N(R^{16})_2$, -NO_2, =O, and -CN; and

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, -$N(R^{16})_2$, -NO_2, and -CN.

[0081] In some embodiments, for the compound or salt of Formula (I), R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, and -$N(R^{16})_2$; and

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, and -$N(R^{16})_2$.

[0082] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from azetidinyl, cyclopentyl, cyclohexyl, imidazolyl, pyrazolyl, 1H-1,2,3-triazolyl, 4H-1,2,4-triazolyl, 1,4-dihydropyridinyl, 3,4-dihydropyrido[3,4-d]pyrimidinyl, 1H-benzo[d][1,2,3]triazolyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -$C(O)N(R^{16})_2$, -$C(O)OR^{16}$, -$OC(O)R^{16}$, -$N(R^{16})C(O)R^{16}$, -$N(R^{16})S(O)_2R^{16}$, -$S(O)_2N(R^{16})_2$, -$N(R^{16})C(O)N(R^{16})_2$, -$N(R^{16})C(O)OR^{16}$, -$OC(O)N(R^{16})_2$, -$S(O)R^{16}$, -$S(O)_2R^{16}$, -NO_2, =O, =S, =$N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OR^{16}, -SR^{16}, -$N(R^{16})_2$, -NO_2, and -CN.

[0083] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from azetidinyl, cyclopentyl, cyclohexyl, imidazolyl, pyrazolyl, 1H-1,2,3-triazolyl, 4H-1,2,4-triazolyl, 1,4-dihydropyridinyl, 3,4-dihydropyrido[3,4-d]pyrimidinyl, 1H-benzo[d][1,2,3]triazolyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{16}, -$N(R^{16})_2$, -$C(O)N(R^{16})_2$, -$C(O)OR^{16}$, -$OC(O)R^{16}$, -$N(R^{16})C(O)R^{16}$ -NO_2, =O, and -CN; and

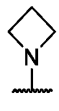
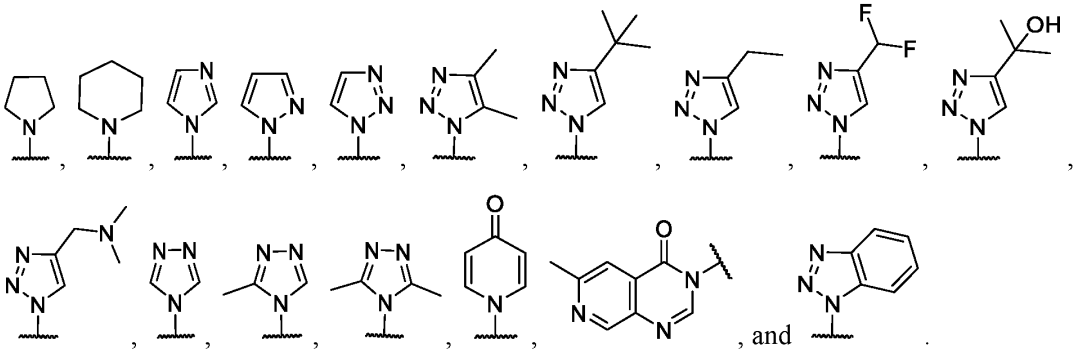
C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{16}, -$N(R^{16})_2$, -NO_2, and -CN.

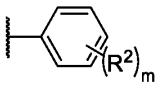
[0084] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from azetidinyl, cyclopentyl, cyclohexyl, imidazolyl, pyrazolyl, 1H-1,2,3-triazolyl, 4H-1,2,4-triazolyl,

1,4-dihydropyridinyl, 3,4-dihydropyrido[3,4-d]pyrimidinyl, 1H-benzo[d][1,2,3]triazolyl, each of which is optionally substituted with one or more substituents independently selected from:

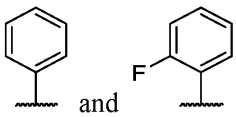
halogen, $-OR^{16}$, $-N(R^{16})_2$, and =O; and

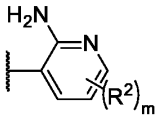
C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, and $-N(R^{16})_2$.

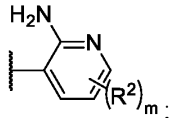
[0085] In some embodiments, for the compound or salt of Formula (I), R^5 is selected from , , and .

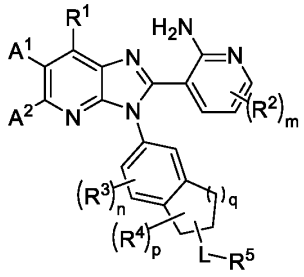
[0086] In some embodiments, for the compound or salt of Formula (I), Ring B is .

[0087] In some embodiments, for the compound or salt of Formula (I), R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl. In some embodiments, R^2 is halogen. In some embodiments, R^2 is fluoro.

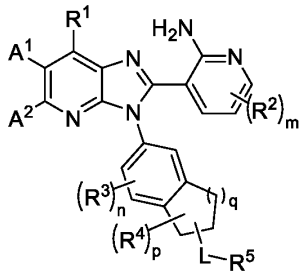
[0088] In some embodiments, for the compound or salt of Formula (I), Ring B is selected from .

[0089] In some embodiments, for the compound or salt of Formula (I), Ring B is .

[0090] In some embodiments, for the compound or salt of Formula (I), Ring B is ; and the compound or salt of Formula (I) is represented by the structure of Formula (II):



[0091] In some aspect, the present disclosure provides compounds represented by the structure of Formula (II):

 (II),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$,$-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, -

$N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$,

$-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN;

L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN;

R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN;

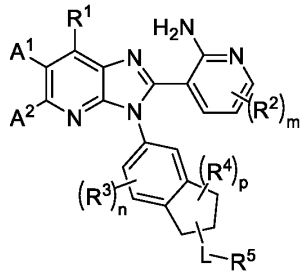
C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

[0092] In some embodiments, for the compound or salt of Formula (I) or Formula (II), q is selected from 1, 2, and 3. In some embodiments, q is selected from 1 and 2. In some embodiments, q is selected from 1 and 3. In some embodiments, q is selected from 2 and 3. In some embodiments, q is selected from 1 and 2. In some embodiments, q is 1.

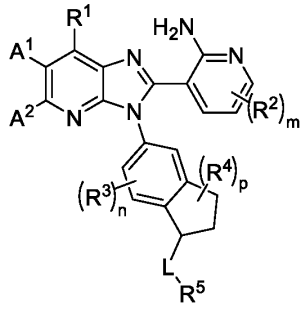
[0093] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (II-A):



(II-A),

or a pharmaceutically acceptable salt thereof, wherein A^1, A^2, R^1, R^2, R^3, R^4, R^5, m, n, p, and L are each defined as in Formula (II).

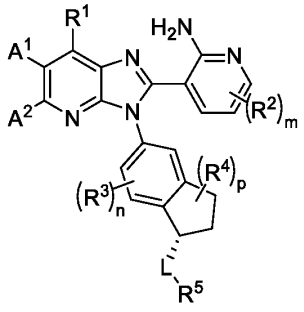
[0094] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (III):



(III);

or a pharmaceutically acceptable salt thereof, wherein A^1, A^2, R^1, R^2, R^3, R^4, R^5, m, n, p, and L are each defined as in Formula (II).

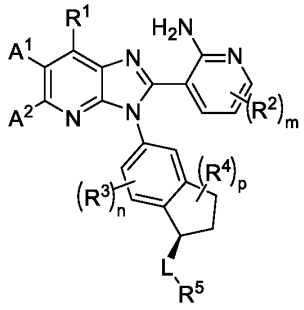
[0095] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (III-A):



(III-A);

or a pharmaceutically acceptable salt thereof, wherein A^1, A^2, R^1, R^2, R^3, R^4, R^5, m, n, p, and L are each defined as in Formula (II).

[0096] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (III-B):



(III-B);

or a pharmaceutically acceptable salt thereof, wherein A^1, A^2, R^1, R^2, R^3, R^4, R^5, m, n, p, and L are each defined as in Formula (II).

[0097] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), m is selected from 0, 1, 2, and 3. In some embodiments, m is selected from 0, 1, and 2. In some embodiments, m is selected from 0 and 1. In some embodiments, m is 0.

[0098] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), n is selected from 0, 1, 2, and 3. In some embodiments, n is selected from 0, 1, and 2. In some embodiments, n is selected from 0 and 1. In some embodiments, n is 0.

[0099] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), p is selected from 0, 1, 2, 3, 4, and 5. In some embodiments, p is selected from 0, 1, 2, 3, and 4. In some embodiments, p is selected from 0, 1, 2, and 3. In some embodiments, p is selected from 0, 1, and 2. In some embodiments, p is selected from 0 and 1. In some embodiments, p is 0.

[00100] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

[00101] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle

and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$C(O)OR^{11}$, -$OC(O)R^{11}$, -NO_2, =O, =S, =$N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, -OR^{11}, -SR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, -$C(O)OR^{11}$, -$OC(O)R^{11}$, -NO_2, =O, =S, =$N(R^{11})$, and -CN; and

R^{11} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl.

[00102] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, -OR^{11}, -$N(R^{11})_2$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, -NO_2, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$,

$-N(R^{11})S(O)_2R^{11}$, =O, and -CN.

[00103] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-N(R^{11})_2$, and -CN;

(ii) C_{1-6} alkyl and C_{2-6} alkynyl, any of which is optionally substituted with one or more halogen; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more C_{1-6} alkyl.

[00104] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from (i) and (iii):

(i) hydrogen, halogen, $-OR^{11}$, C_{1-6} alkyl and C_{2-6} alkynyl; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:
halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, and 4- to 10-membered heterocycle; wherein the 4- to 10-membered heterocycle is optionally substituted with one or more C_{1-6} alkyl.

[00105] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from: hydrogen, 5- to 10-membered heterocycle, and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl.

[00106] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from: hydrogen, and 5- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl.

[00107] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 and A^2 are each independently selected from: hydrogen, and 5- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen.

[00108] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$,

$-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

[00109] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and
C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

R^{11} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl.

[00110] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with

one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, -NO_2, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, -$N(R^{11})S(O)_2R^{11}$, =O, and -CN.

[00111] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, -OR^{11}, -$N(R^{11})_2$, and -CN;

(ii) C_{1-6} alkyl and C_{2-6} alkynyl, any of which is optionally substituted with one or more halogen; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, -OR^{11}, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more C_{1-6} alkyl.

[00112] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from (i) and (iii):

(i) hydrogen, halogen, -OR^{11}, C_{1-6} alkyl and C_{2-6} alkynyl; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, and 4- to 10-membered heterocycle; wherein the

4- to 10-membered heterocycle is optionally substituted with one or more C_{1-6} alkyl.

[00113] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from: hydrogen, 5- to 10-membered heterocycle, and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl. In some embodiments, A^1 is selected from: hydrogen, and 5- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl. In some embodiments, A^1 is selected from: hydrogen and 5- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen. In some embodiments, A^1 is hydrogen.

[00114] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), A^1 is selected from hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{11}$, $-N(R^{11})_2$ and -CN. In some embodiments, A^1 is selected from hydrogen, halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl. In some embodiments, A^1 is selected from hydrogen, fluoro, and methyl. In some embodiments, A^1 is hydrogen.

[00115] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN. In some embodiments, R^2 is independently selected at each instance from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN; and R^{12} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl. In some embodiments, R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00116] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN.

[00117] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected

from: halogen, -OR^{13}, -SR^{13}, -$N(R^{13})_2$, -$C(O)R^{13}$, -$C(O)N(R^{13})_2$, -$N(R^{13})C(O)R^{13}$, -$C(O)OR^{13}$, -$OC(O)R^{13}$, -NO_2, =O, =S, =$N(R^{13})$, and -CN.

[00118] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^3 is independently selected at each instance from:

halogen, -OR^{13}, -$N(R^{13})_2$, -$C(O)R^{13}$, -$C(O)N(R^{13})_2$, -$N(R^{13})C(O)R^{13}$, -$C(O)OR^{13}$, -$OC(O)R^{13}$, -NO_2, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{13}, -SR^{13}, -$N(R^{13})_2$, -$C(O)R^{13}$, -$C(O)N(R^{13})_2$, -$N(R^{13})C(O)R^{13}$, -$C(O)OR^{13}$, -$OC(O)R^{13}$, -NO_2, =O, =S, =$N(R^{13})$, and -CN; and

R^{13} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl.

[00119] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^3 is independently selected at each instance from:

halogen, -OR^{13}, -SR^{13}, -$N(R^{13})_2$, -$C(O)R^{13}$, -$C(O)N(R^{13})_2$, -$N(R^{13})C(O)R^{13}$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{13}, -$N(R^{13})_2$, -$C(O)R^{13}$, -$C(O)N(R^{13})_2$, -$N(R^{13})C(O)R^{13}$, =O, and -CN.

[00120] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^3 is independently selected at each instance from halogen, -OR^{13}, -$N(R^{13})_2$, -CN, C_{1-6} alkyl, and C_{1-6} haloalkyl. In some embodiments, R^3 is independently selected at each instance from halogen, -OR^{13}, -$N(R^{13})_2$, -CN, C_{1-6} alkyl, and C_{1-6} haloalkyl; and R^{13} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl. In some embodiments, R^3 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and -CN.

[00121] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, -OR^{14}, -SR^{14}, -$N(R^{14})_2$, -$C(O)R^{14}$, -$C(O)N(R^{14})_2$, -$N(R^{14})C(O)R^{14}$, -$C(O)OR^{14}$, -$OC(O)R^{14}$, -NO_2, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents selected from halogen, -OR^{14}, -SR^{14}, -$N(R^{14})_2$, -$C(O)R^{14}$, -$C(O)N(R^{14})_2$, -$N(R^{14})C(O)R^{14}$, -$C(O)OR^{14}$, -$OC(O)R^{14}$, -NO_2, =O, =S, =$N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and =$N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the

carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN.

[00122] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN; and

R^{14} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl.

[00123] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, =O, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-N(R^{14})_2$, and -CN.

[00124] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-N(R^{14})_2$, =O, and -CN; or

two R^4 attached to the same atom are taken together to form =O; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle; and

R^{14} is selected from hydrogen and C_{1-4} alkyl.

[00125] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, C_{1-6} alkyl, and C_{2-6} alkynyl; or

two R^4 attached to the same atom are taken together to form =O; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle; and

R^{14} is selected from hydrogen and C_{1-4} alkyl.

[00126] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, -OH, C_{1-6} alkyl, and C_{2-6} alkynyl; or

two R^4 attached to the same atom are taken together to form =O; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a C_{3-8} carbocycle.

[00127] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN.

[00128] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from:

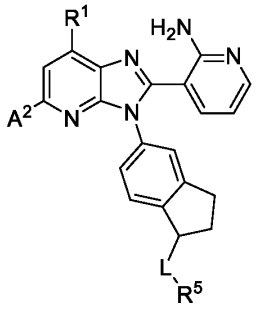
halogen, $-OR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, =O, and -CN.

[00129] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted with one or more substituents selected from halogen, $-OR^{14}$, $-N(R^{14})_2$, =O, and -CN. In some embodiments, R^4 is independently selected at each instance from halogen, $-OR^{14}$, C_{1-6} alkyl, and C_{2-6} alkynyl. In some embodiments, R^4 is independently selected at each instance from halogen, -OH, C_{1-6} alkyl, and C_{2-6} alkynyl.

[00130] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), or (III-B), R^4 is independently selected at each instance from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN. In some embodiments, R^4 is independently selected at each instance from halogen, $-OR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, and -CN. In some embodiments, R^4 is independently selected at each instance from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, and -CN. In some embodiments, R^4 is independently selected at each instance from halogen and $-OR^{14}$. In some embodiments, R^4 is halogen. In some embodiments, R^4 is independently selected at each instance from fluoro, chloro, and bromo.

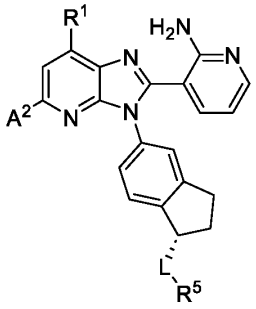
[00131] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (IV):



(IV);

or a pharmaceutically acceptable salt thereof, wherein A^2, R^1, R^5, and L are each defined as in Formula (II).

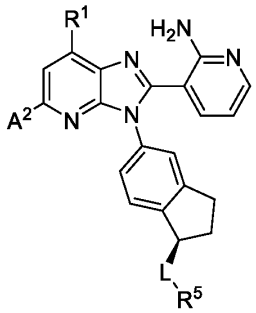
[00132] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (IV-A):



(IV-A);

or a pharmaceutically acceptable salt thereof, wherein A^2, R^1, R^5, and L are each defined as in Formula (II).

[00133] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (IV-B):



(IV-B);

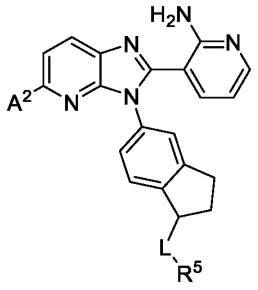
or a pharmaceutically acceptable salt thereof, wherein A^2, R^1, R^5, and L are each defined as in Formula (II).

[00134] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), or (IV-B), R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-N(R^{10})_2$, $-NO_2$, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, and $-N(R^{10})_2$. In some embodiments, R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-N(R^{10})_2$, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, and $-N(R^{10})_2$. In some embodiments, R^1 is selected from hydrogen, $-OR^{10}$, and -CN; and C_{1-6} alkyl optionally substituted with one or more $-OR^{10}$. In some embodiments, R^1 is selected from hydrogen, methoxy, -CN, methyl, ethyl, and (methoxy)methyl. In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is selected from methoxy, -CN, methyl, ethyl, and (methoxy)methyl.

[00135] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), or (IV-B), R^1 is selected from hydrogen, halogen, $-OR^{10}$, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from

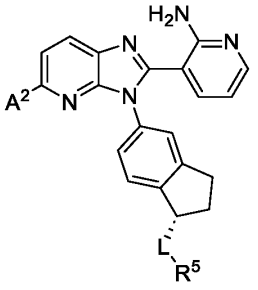
halogen, -OR^{10}. In some embodiments, R^1 is selected from hydrogen, fluoro, methoxy, -CN, methyl, ethyl, (methoxy)methyl, and .

[00136] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (V):

 (V);

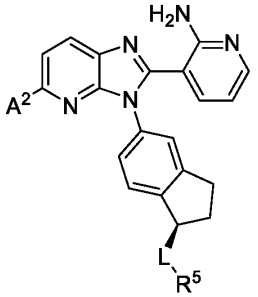
or a pharmaceutically acceptable salt thereof, wherein A^2, R^5, and L are each defined as in Formula (II).

[00137] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (V-A):

 (V-A);

or a pharmaceutically acceptable salt thereof, wherein A^2, R^5, and L are each defined as in Formula (II).

[00138] In some embodiments, for the compound or salt of Formula (II) is represented as the structure of Formula (V-B):

 (V-B);

or a pharmaceutically acceptable salt thereof, wherein A^2, R^5, and L are each defined as in Formula (II).

[00139] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and
C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from:
halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

[00140] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from selected from (i), (ii), and (iii):

(i) hydrogen, halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

[00141] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from:

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN; and

5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

[00142] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from:

C_{1-6} alkyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN; and

5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

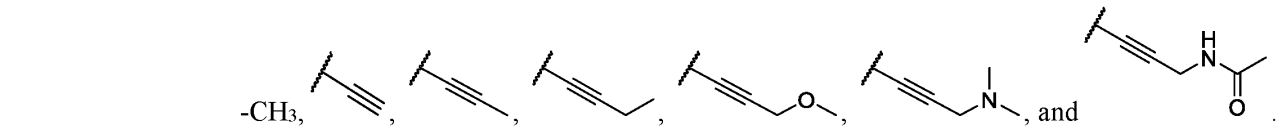
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

C_{3-8} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O, -CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

[00143] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from C_{1-6} alkyl and C_{2-}

6 alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN. In some embodiments, A^2 is selected from C_{1-6} alkyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN. In some embodiments, A^2 is selected from C_{1-4} alkyl and C_{2-4} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN. In some embodiments, A^2 is selected from C_{1-4} alkyl and C_{2-4} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, and $-N(R^{11})_2$. In some embodiments, A^2 is selected from C_{1-4} alkyl and C_{2-4} alkynyl, each of which is optionally substituted with one or more substituents independently selected from $-OR^{11}$ and $-N(R^{11})_2$. In some embodiments, A^2 is selected from methyl, ethyl, propyl, isopropyl, ethylnyl, propylnyl, and isopropylnyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN. In some embodiments, A^2 is selected from methyl, ethyl, propyl, isopropyl, ethylnyl, propylnyl, and isopropylnyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, and $-N(R^{11})_2$.

[00144] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from:



[00145] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heteroaryl, 5- to 10-membered heterocycloalkyl, C_{4-8} aryl, and C_{3-10} cycloalkyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$,

and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN.

[00146] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heteroaryl, 5- to 10-membered heterocycloalkyl, C_{4-8} aryl, and C_{3-10} cycloalkyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

[00147] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from pyrazolyl, triazolyl, oxazolyl, thiazolyl, morpholinyl, phenyl, and cyclopropyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, -

$C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

[00148] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heteroaryl, 5- to 10-membered heterocycloalkyl, C_{4-8} aryl, and C_{3-10} cycloalkyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, -CN, C_{1-6} alky, and C_{1-6} haloalkyl.

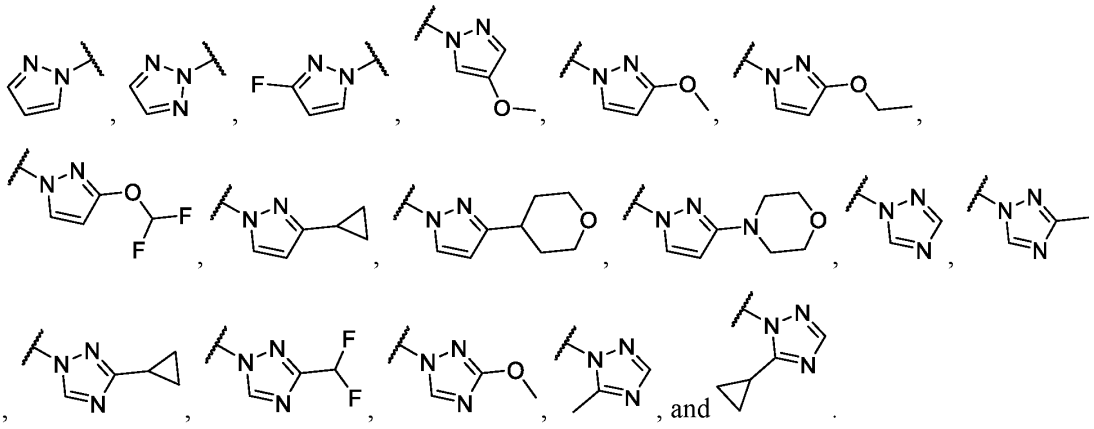
[00149] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from pyrazolyl, triazolyl, oxazolyl, thiazolyl, morpholinyl, phenyl, and cyclopropyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN;

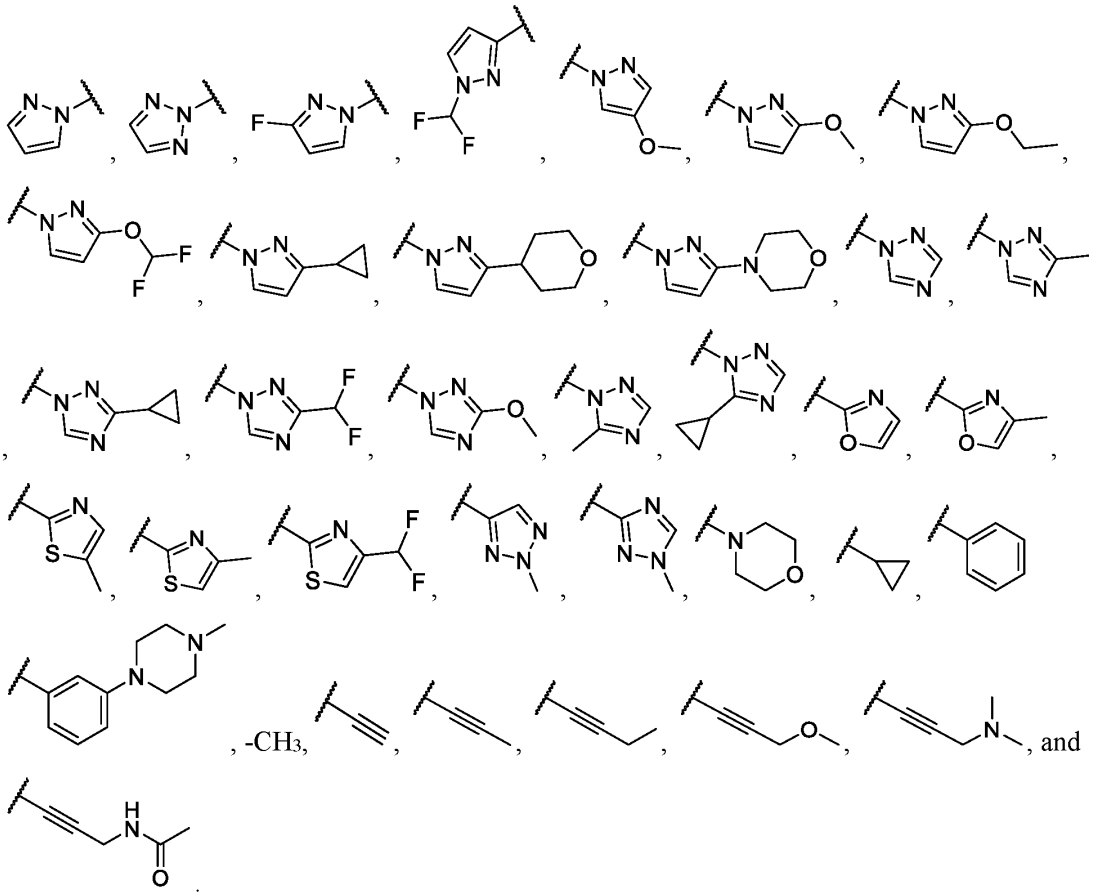
C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, -CN, C_{1-6} alky, and C_{1-6} haloalkyl.

[00150] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from:



[00151] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from:



[00152] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from (i), (ii), and (iii):

(i) halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, -

$N(R^{11})S(O)_2R^{11}$, =O, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

(iii) C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN.

[00153] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from (i), (ii), and (iii):

(i) halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$

, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

R^{11} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl.

[00154] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from (i), (ii), and (iii):

(i) halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

(iii) C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN.

[00155] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from (i), (ii), and (iii):

(i) halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN;

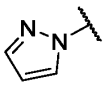
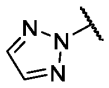
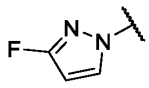
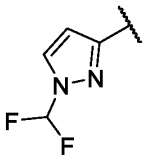
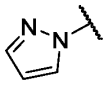
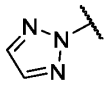
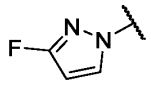
(ii) C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, and =O; and

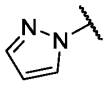
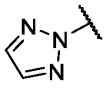
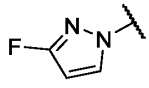
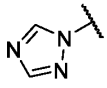
(iii) C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted

with one or more substituents independently selected from: halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, and =O.

[00156] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{11}, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more C_{1-6} alkyl.

[00157] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, and =O. In some embodiments, A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, and 4- to 10-membered heterocycle; wherein the 4- to 10-membered heterocycle is optionally substituted with one or more C_{1-6} alkyl. In some embodiments, A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from halogen, -OR^{11}, -$N(R^{11})_2$, -$C(O)R^{11}$, -$C(O)N(R^{11})_2$, -$N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, -OR^{11}, and -$N(R^{11})_2$. In some embodiments, A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl. In some embodiments, A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from halogen; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen. In some embodiments, A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen, C_{1-6} alkyl, and C_{1-6} haloalkyl. In some embodiments, A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen. In some embodiments, A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from fluoro. In some embodiments, A^2 is optionally substituted 5- to 10-membered heteroaryl. In some embodiments, A^2 is optionally substituted 5-membered heteroaryl. In some embodiments, A^2 is selected from optionally substituted pyrazolyl and optionally substituted triazolyl. In some embodiments, A^2 is

selected from , , , and . In some embodiments, A^2 is selected from , , and .

[00158] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), A^2 is selected from , , , and .

[00159] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent; and

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

[00160] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN; and

R^{15} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, C_{3-8}

carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

wherein L^2, L^3, and L^4 are each optionally absent; and

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

[00161] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2$ $-N(R^{15})N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-6} carbocyclene, and 4- to 6-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, =O, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent; and

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

[00162] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, and $-N(R^{15})C(O)-$; and

(b) C_{1-6} alkylene, C_{2-6} alkynylene, and C_{3-6} carbocyclene;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent; and

R^{15} is selected from hydrogen and C_{1-4} alkyl.

[00163] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, and $-N(R^{15})C(O)-$; and

(b) C_{1-6} alkylene and C_{3-6} carbocyclene;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent; and

R^{15} is selected from hydrogen and C_{1-4} alkyl.

[00164] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -NH-, and -N(H)C(O)-; and

(b) methylene;

wherein L^2, L^3, and L^4 are each optionally absent; and

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

[00165] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is selected from:

(a) -O-, -N(R^{15})-, -S-, -S(O)-, -S$(O)_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S$(O)_2$-, -N(R^{15})S$(O)_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene.

[00166] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is selected from:

(a) -O-, -N(R^{15})-, -S-, -S(O)-, -S$(O)_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S$(O)_2$-, -N(R^{15})S$(O)_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene; and

R^{15} is selected from hydrogen and C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00167] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-; and R^{15} is selected from hydrogen and C_{1-4} alkyl. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-; and R^{15} is selected from hydrogen and methyl. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^2, L^3, and L^4 are absent; and L^1 is -N(H)C(O)-.

[00168] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; and

L^1 is selected from -O-, -N(R^{15})-, -S-, -S(O)-, -S(O)$_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$-, -N(R^{15})S(O)$_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-; and

L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, -SR^{15}, =O, =S, and -CN.

[00169] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; and

L^1 is selected from -O-, -N(R^{15})-, -S-, -S(O)-, -S(O)$_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$-, -N(R^{15})S(O)$_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-; and

L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, -SR^{15}, =O, =S, and -CN; and

R^{15} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00170] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-; and L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{3-8} carbocyclene. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-; and L^2 is selected from C_{1-6} alkylene and C_{3-6} carbocyclene. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; L^1 is selected from -N(R^{15})- and -N(R^{15})C(O)-; L^2 is selected from C_{1-6} alkylene and C_{3-6} carbocyclene; and R^{15} is selected from hydrogen and C_{1-4} alkyl. In some embodiments, L is represented by -L^1- L^2-L^3-L^4-, wherein L^3 and L^4 are absent; L^1 is -N(H)C(O)-; and L^2 is selected from methylene.

[00171] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4-, wherein L^4 is absent; and

L^1 is selected from -O-, -N(R^{15})-, -S-, -S(O)-, -S(O)$_2$-, -S(O)(NR^{15})-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$-, -N(R^{15})S(O)$_2$N(R^{15})-, -S(O)(NR^{15})N(R^{15})-, -N(R^{15})N(R^{15})-, -(R^{15})NC(O)N(R^{15})-, and -(R^{15})NC(O)N(R^{15})N(R^{15})-;

L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN; and

L^3 is selected from -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$.

[00172] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^4 is absent; and

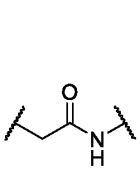
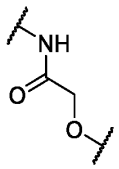
L^1 is selected from -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$;

L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

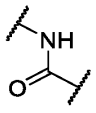
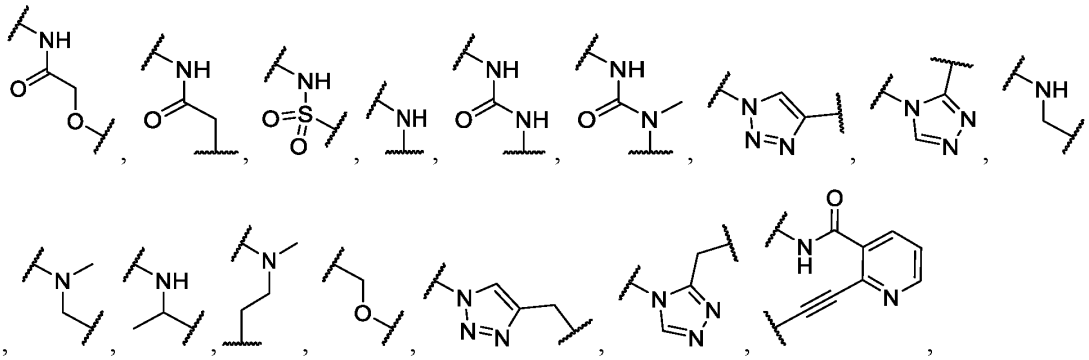
L^3 is selected from -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

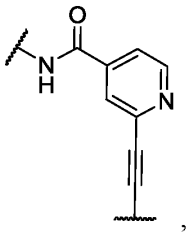
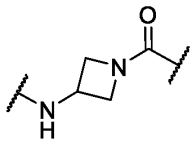
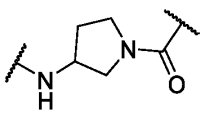
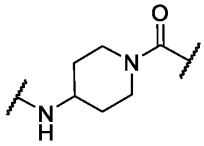
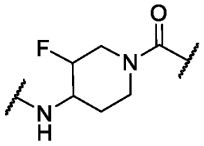
R^{15} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00173] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^4 is absent; L^1 is selected from $-N(R^{15})-$ and $-N(R^{15})C(O)-$; L^2 is selected from C_{1-6} alkylene, C_{2-6} alkenylene, C_{3-8} carbocyclene; and L^3 is -O-. In some embodiments, L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^4 is absent; L^1 is selected from $-N(R^{15})-$ and $-N(R^{15})C(O)-$; L^2 is selected from C_{1-6} alkylene and C_{3-6} carbocyclene; and L^3 is -O-. In some embodiments, L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^4 is absent; L^1 is selected from $-N(R^{15})-$ and $-N(R^{15})C(O)-$; L^2 is selected from C_{1-6} alkylene and C_{3-6} carbocyclene; L^3 is -O-; and R^{15} is selected from hydrogen and C_{1-4} alkyl. In some embodiments, L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^4 is absent; L^1 is -N(H)C(O)-; L^2 is methylene; and L^3 is -O-.

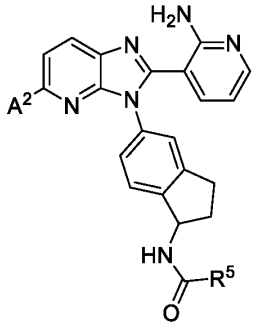
[00174] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is selected from -N(H)C(O)-,  , and  .

[00175] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is represented by -L^1- L^2-L^3-L^4. In some embodiments, L^4 is absent. In some embodiments, L^3 is absent, -O-, ethynyl, or methylene substituted with =O. In some embodiments, L^3 is absent or -O-. In some embodiments, L^2 is absent or methylene. In some embodiments, L^2 is absent, methylene, (methyl)methylene, ethylene, or -O-. In some embodiments, The compound or salt of any one of claims 64-70, wherein L^1 is -N(R^{15})C(O)-. In some embodiments L^1 is selected from -N(R^{15})C(O)-, -N(R^{15})-, -N(R^{15})S(O)-, -(R^{15})NC(O)N(R^{15})-, and 4- to 6-membered heterocyclene optionally substituted with one or more halogen atoms. In some embodiment, R^{15} is hydrogen. In some embodiments, R^{15} is selected from hydrogen and -CH_3.

[00176] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), or (V-B), L is selected from  ,  .

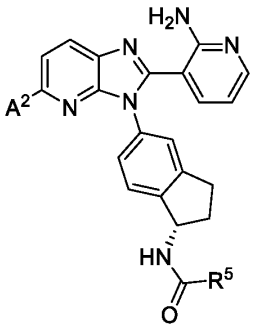

, 
, 
, 
, and 
.

[00177] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (VI):


(VI);

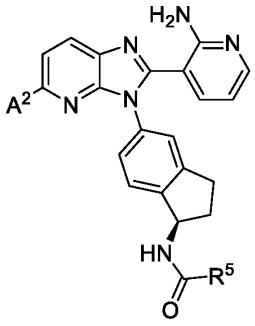
or a pharmaceutically acceptable salt thereof, wherein A^2 and R^5 are each defined as in Formula (II).

[00178] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (VI-A):


(VI-A);

or a pharmaceutically acceptable salt thereof, wherein A^2 and R^5 are each defined as in Formula (II).

[00179] In some embodiments, the compound or salt of Formula (II) is represented by the structure of Formula (VI-B):



(VI-B);

or a pharmaceutically acceptable salt thereof, wherein A^2 and R^5 are each defined as in Formula (II).

[00180] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[00181] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted by one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl,

C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[00182] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[00183] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[00184] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, and $-N(R^{16})_2$; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally

substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

[00185] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{2-6} alkynyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, =O, and -CN;

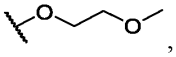
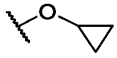
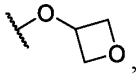
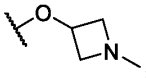
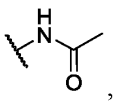
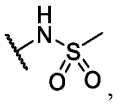
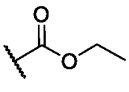
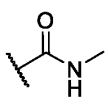
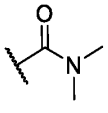
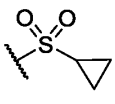
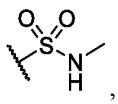
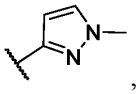
C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: $-N(R^{16})_2$; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen.

[00186] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: fluoro, chloro, methyl, ethyl, ethynyl, difluoromethyl, hydroxy, methoxy, trifluoromethoxy, dimethylamino, =O, -CN, cyclopropyl, and pyrazolyl.

[00187] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, =O, -CN, and C_{3-8} carbocycle. In some embodiments, R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: fluoro, chloro, methyl, ethyl, ethynyl, difluoromethyl, hydroxy, methoxy, trifluoromethoxy, dimethylamino, =O, -CN, cyclopropyl, and pyrazolyl.

[00188] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, =O, -CN, C_{3-8} carbocycle, and 3- to 8- membered heterocycle, wherein the C_{3-8} carbocycle and 4- to 8- membered heterocycle are each optionally substituted with one or more substituents selected from halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl. In some embodiments, R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected

from: fluoro, chloro, methyl, ethyl, ethynyl, propynyl, fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, -CH_2OH, methoxy, -CH_2OCH_3, , , , , difluoromethoxy, trifluoromethoxy, -NH_2, dimethylamino, -$CH_2N(CH_3)_2$, , , , , , , , =O, -CN, cyclopropyl, phenyl, morpholinyl, pyrazolyl, , and pyridinyl.

[00189] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is optionally substituted 3- to 10-membered heteroaryl. In some embodiments, R^5 is optionally substituted 5- to 10-membered heteroaryl. In some embodiments, R^5 is optionally substituted 5- to 6-membered heteroaryl. In some embodiments, R^5 is selected from: optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl. In some embodiments, R^5 is selected from: optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl. In some embodiments, R^5 is selected from: optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl.

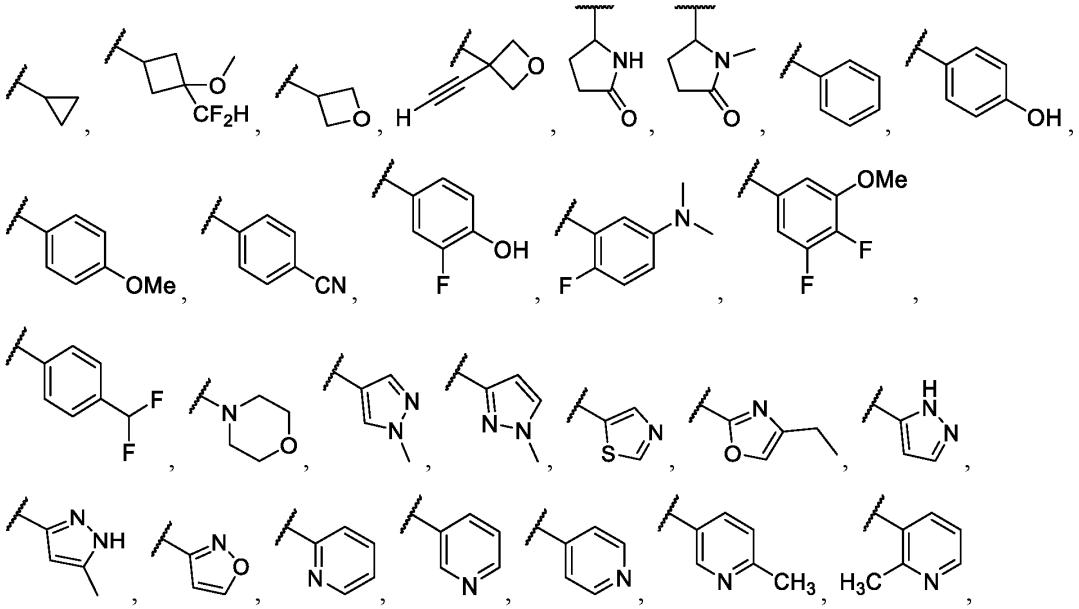
[00190] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is

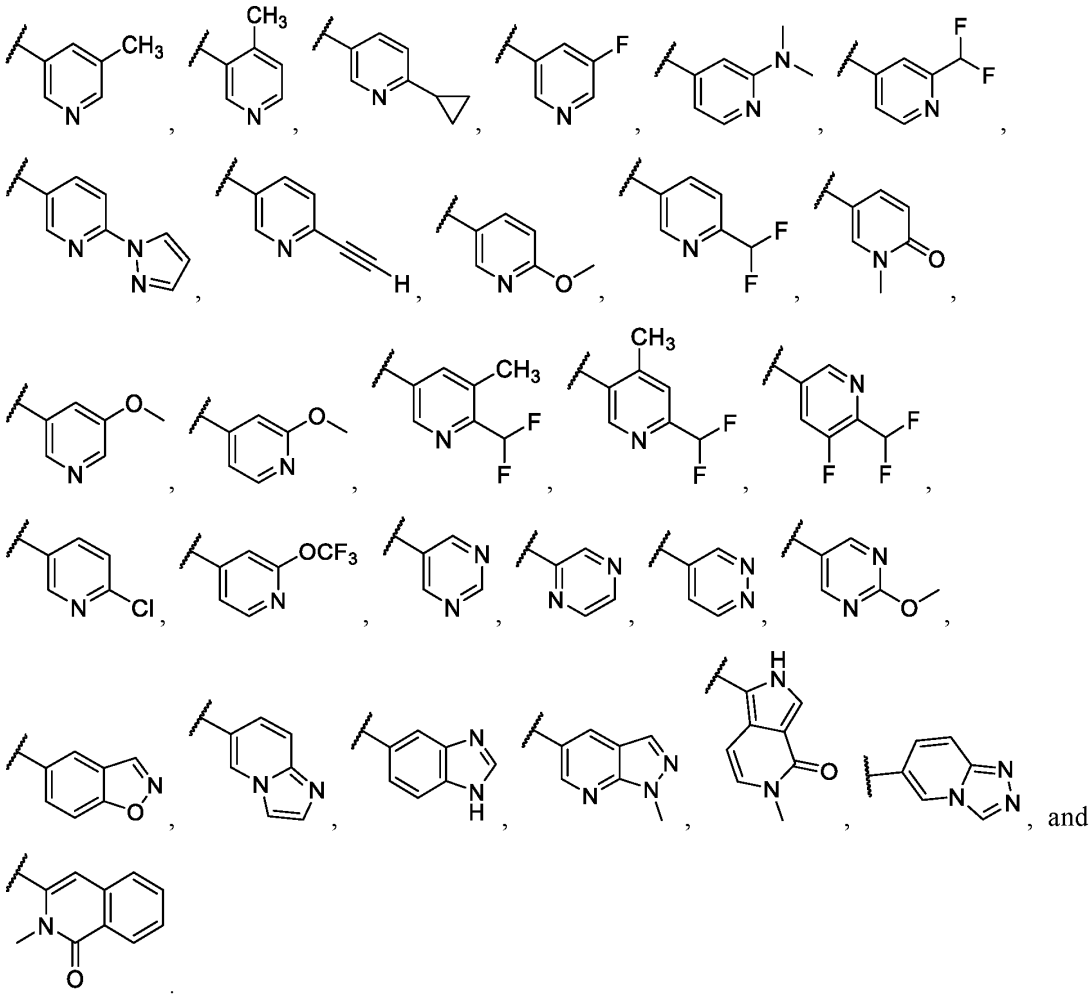
optionally substituted 4- to 10-membered heterocycle. In some embodiments, R^5 is optionally substituted 4- to 10- membered heteroaryl.

[00191] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is optionally substituted 3- to 8-membered heterocycloalkyl. In some embodiments, R^5 is optionally substituted 3- to 6-membered heterocycloalkyl. In some embodiments, R^5 is optionally substituted 4- to 6-membered heterocycloalkyl. In some embodiments, R^5 is selected from optionally substituted oxetanyl, optionally substituted pyrrolyl, and optionally substituted morpholinyl.

[00192] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from optionally substituted C_{3-6} cycloalkyl and optionally substituted phenyl. In some embodiments, R^5 is optionally substituted C_{3-5} cycloalkyl and optionally substituted phenyl. In some embodiments, R^5 is selected from optionally substituted cyclopropyl, optionally substituted cyclobutyl, and optionally substituted phenyl. In some embodiments, R^5 is optionally substituted C_{3-6} cycloalkyl. In some embodiments, R^5 is optionally substituted C_{3-5} cycloalkyl. In some embodiments, R^5 is selected from optionally substituted cyclopropyl and optionally substituted cyclobutyl. In some embodiments, R^5 is optionally substituted phenyl.

[00193] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from:





[00194] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl.

[00195] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl,

optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl, optionally substituted isoxazolyl, optionally substituted isothiazole, optionally substituted 1,2,3-thiadiazolyl, optionally substituted 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazolyl, optionally substituted 2,3-dihydropyrazolo[5,1-b]oxazolyl, optionally substituted 5,6-dihydro-3H-furo[2,3-d]imidazolyl, optionally substituted indolizinyl, optionally substituted pyrazolo[1,5-a]pyridinyl, optionally substituted pyrrolo[1,2-a]pyrimidinyl, optionally substituted pyrazolo[1,5-a]pyrimidinyl, optionally substituted imidazo[1,2-a]pyrimidinyl, optionally substituted imidazo[1,2-b]pyridazinyl, optionally substituted [1,2,4]triazolo[1,5-a]pyridinyl, optionally substituted 6,7-dihydro-5H-cyclopenta[b]pyridinyl, optionally substituted 6,7-dihydro-5H-cyclopenta[c]pyridinyl, optionally substituted 5,6,7,8-tetrahydroisoquinolinyl, optionally substituted 3,4-dihydro-2H-pyrano[2,3-b]pyridinyl, optionally substituted 2,3-dihydro-[1,4]dioxino[2,3-b]pyridinyl, optionally substituted 5,7-dihydrofuro[3,4-b]pyridinyl, optionally substituted 2,3-dihydrofuro[2,3-c]pyridinyl, optionally substituted 2,3-dihydrofuro[2,3-b]pyridinyl, optionally substituted [1,3]dioxolo[4,5-b]pyridinyl, optionally substituted furo[2,3-b]pyridinyl, optionally substituted thieno[2,3-b]pyridinyl, optionally substituted 1,2-dihydro-3H-indazol-3-onyl, optionally substituted 1H-benzo[d][1,2,3]triazolyl, optionally substituted 1,3-dihydro-2H-benzo[d]imidazol-2-onyl, optionally substituted benzo[d]oxazol-2(3H)-onyl, optionally substituted benzo[d]thiazol-2(3H)-onyl, optionally substituted 1H-indazolyl, optionally substituted indolin-2-onyl, and optionally substituted 1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-onyl.

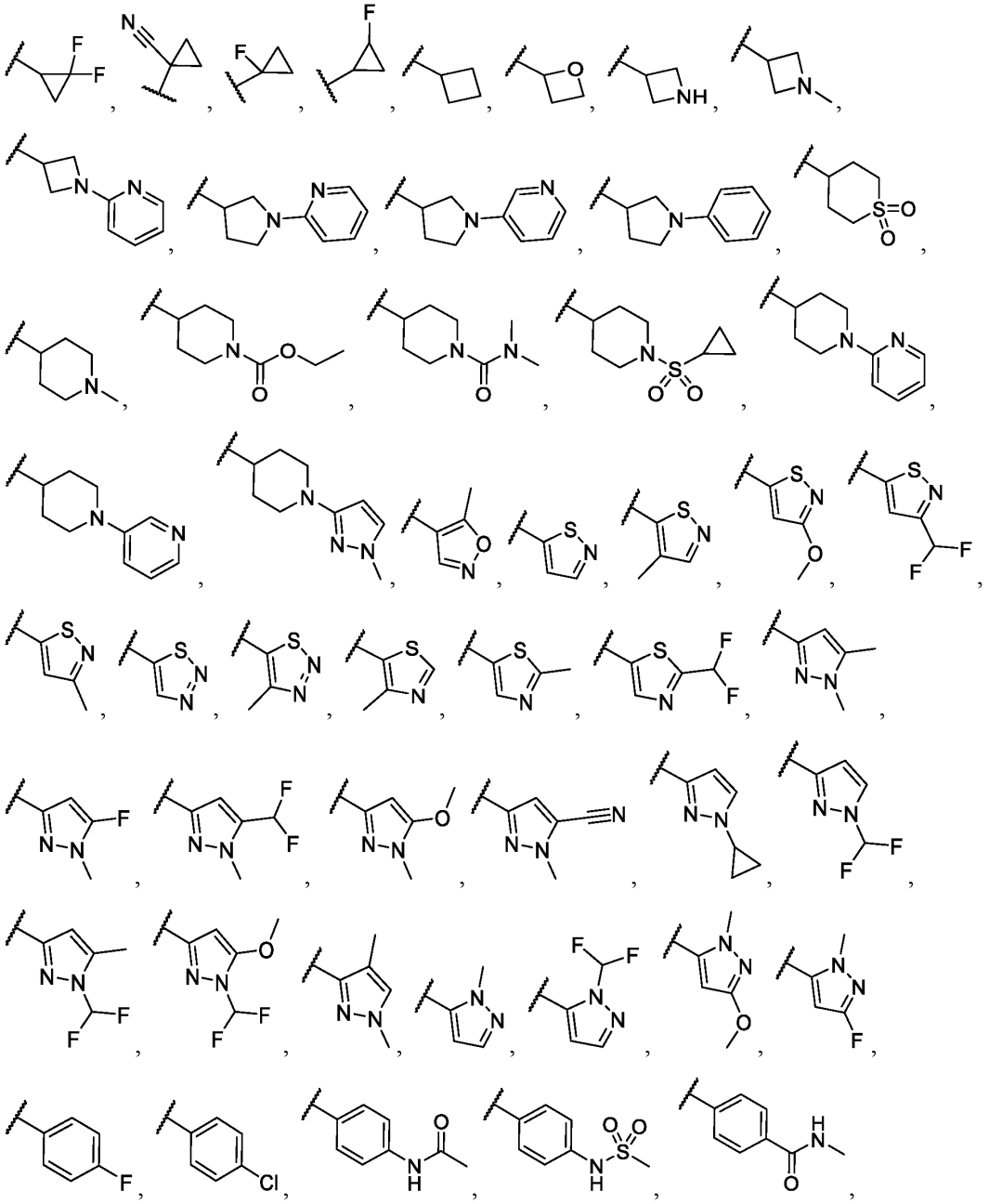
[00196] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is an optionally substituted 6- to 10-membered bicyclic heterocycle selected from optionally substituted 6- to 10-membered fused heterocycle, optionally substituted 6- to 10-membered bridged heterocycle, and optionally substituted 6- to 10-membered spirocyclic heterocycle.

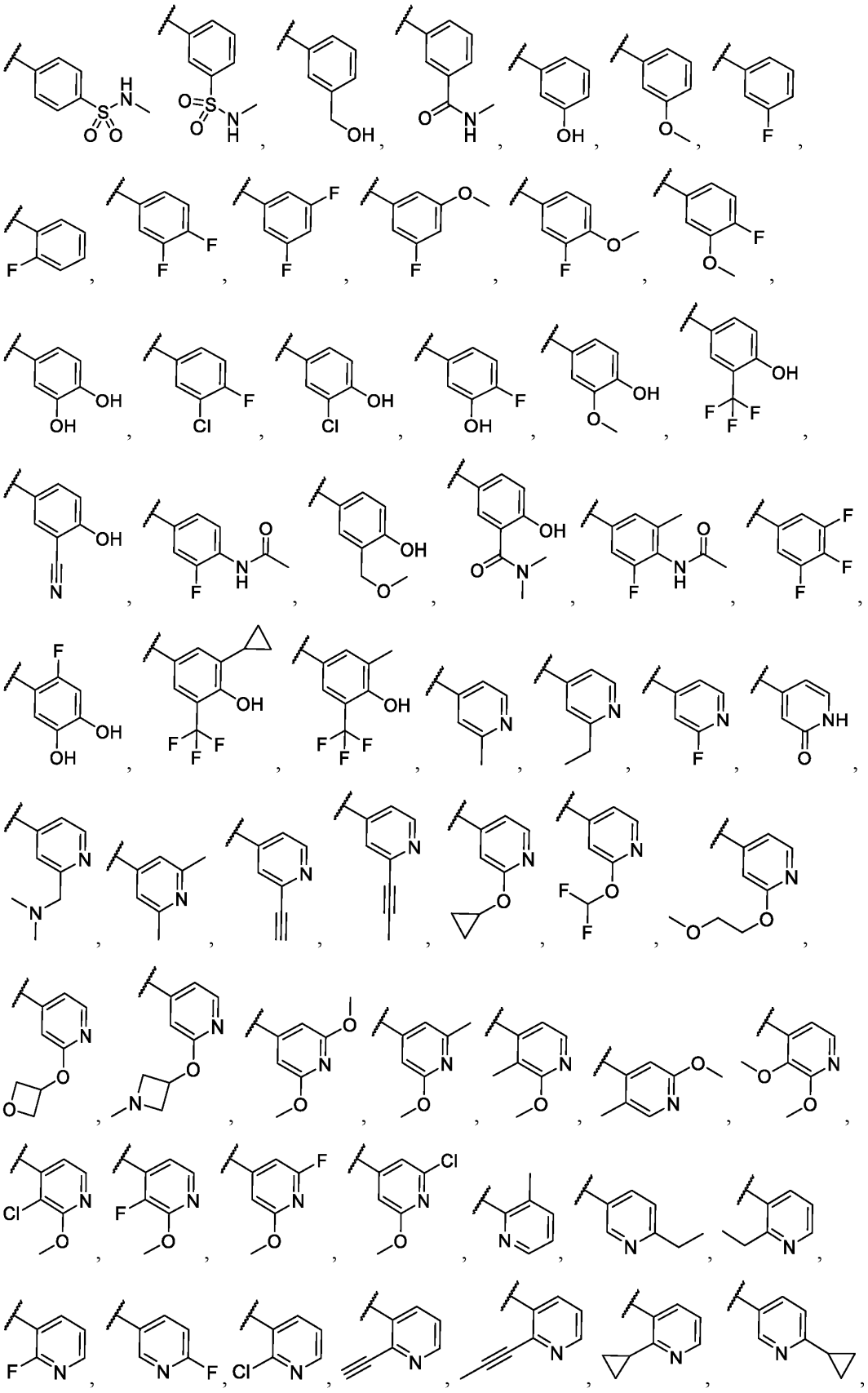
[00197] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is optionally substituted 6- to 10-membered spirocyclic heterocycle selected from optionally substituted 2-azaspiro[3.3]heptanyl, optionally substituted 6-azaspiro[3.4]octanyl, optionally substituted 5-azaspiro[3.4]octanyl, optionally substituted 2-azaspiro[3.5]nonanyl, optionally substituted 7-azaspiro[3.5]nonanyl, and optionally substituted 6-azaspiro[3.5]nonanyl.

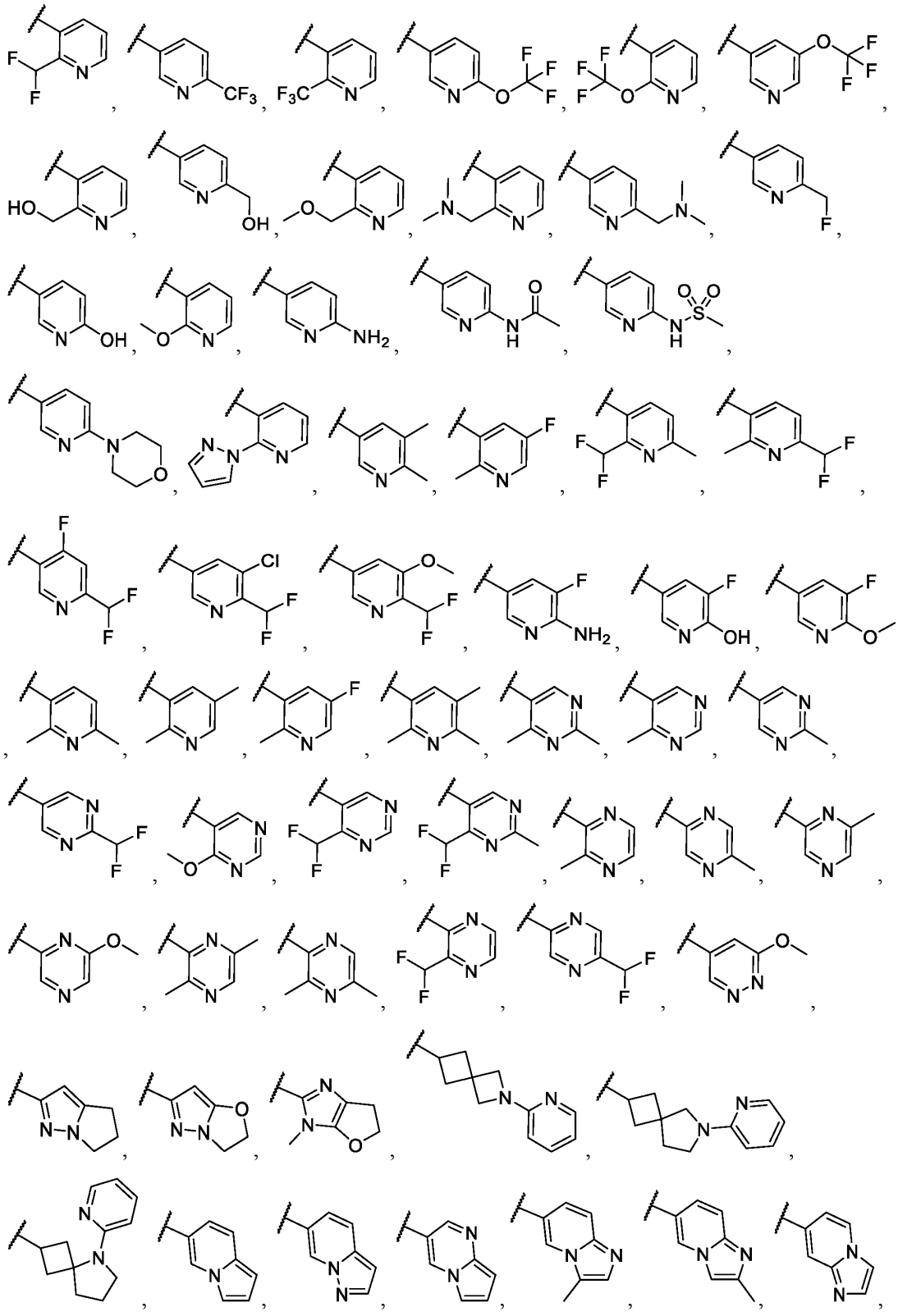
[00198] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from optionally substituted oxetanyl, optionally substituted pyrrolyl, optionally substituted

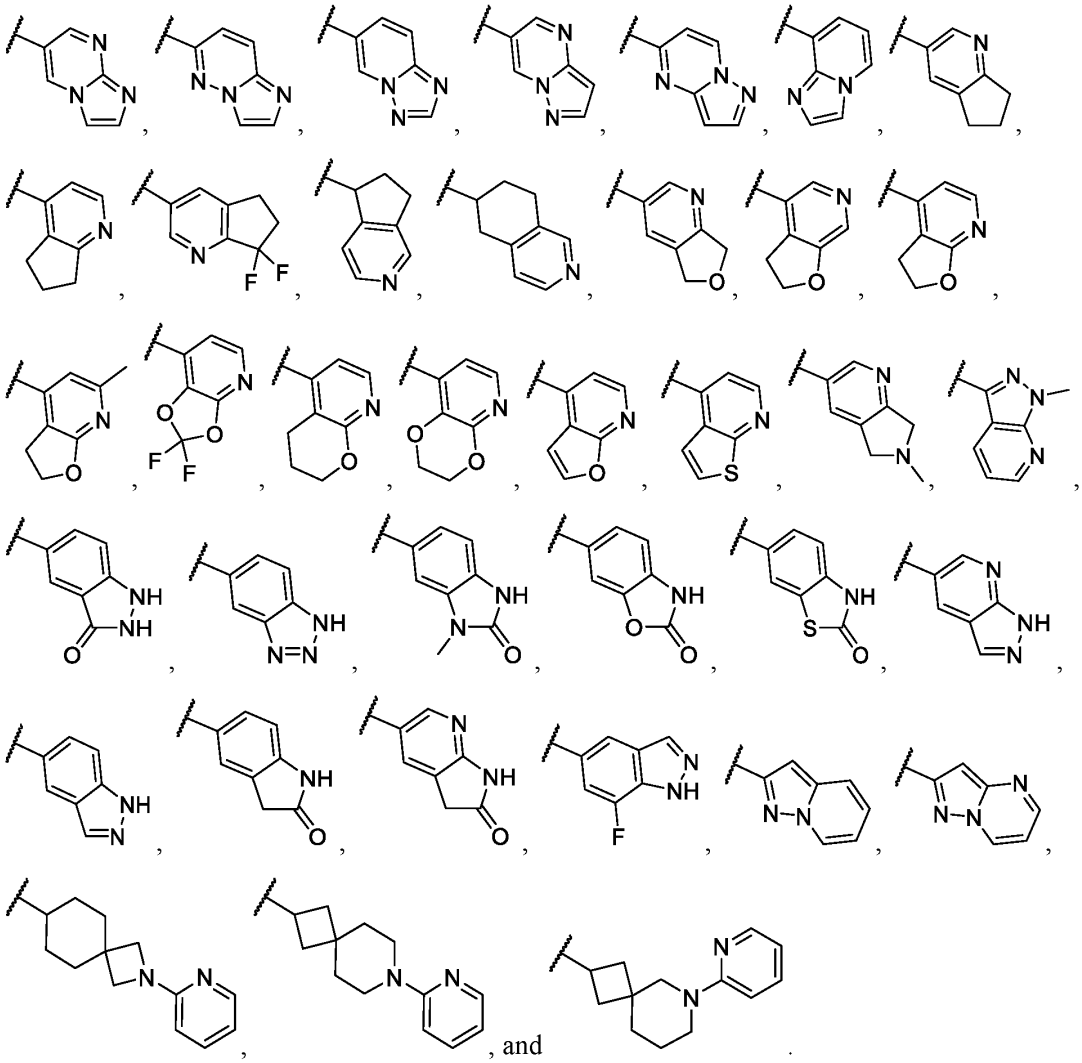
morpholinyl, optionally substituted azetidinyl, optionally substituted pyrrolidinyl, optionally substituted tetrahydro-2H-thiopyranyl, and optionally substituted piperidinyl.

[00199] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from:

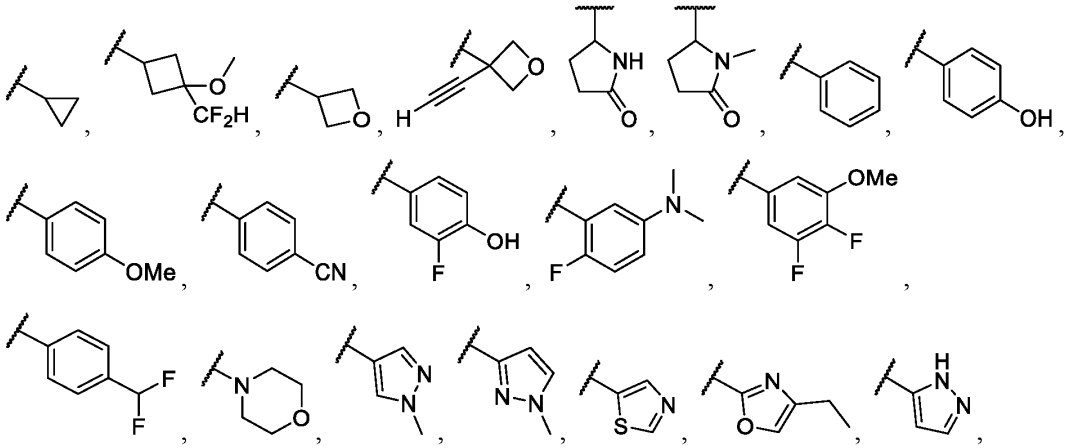


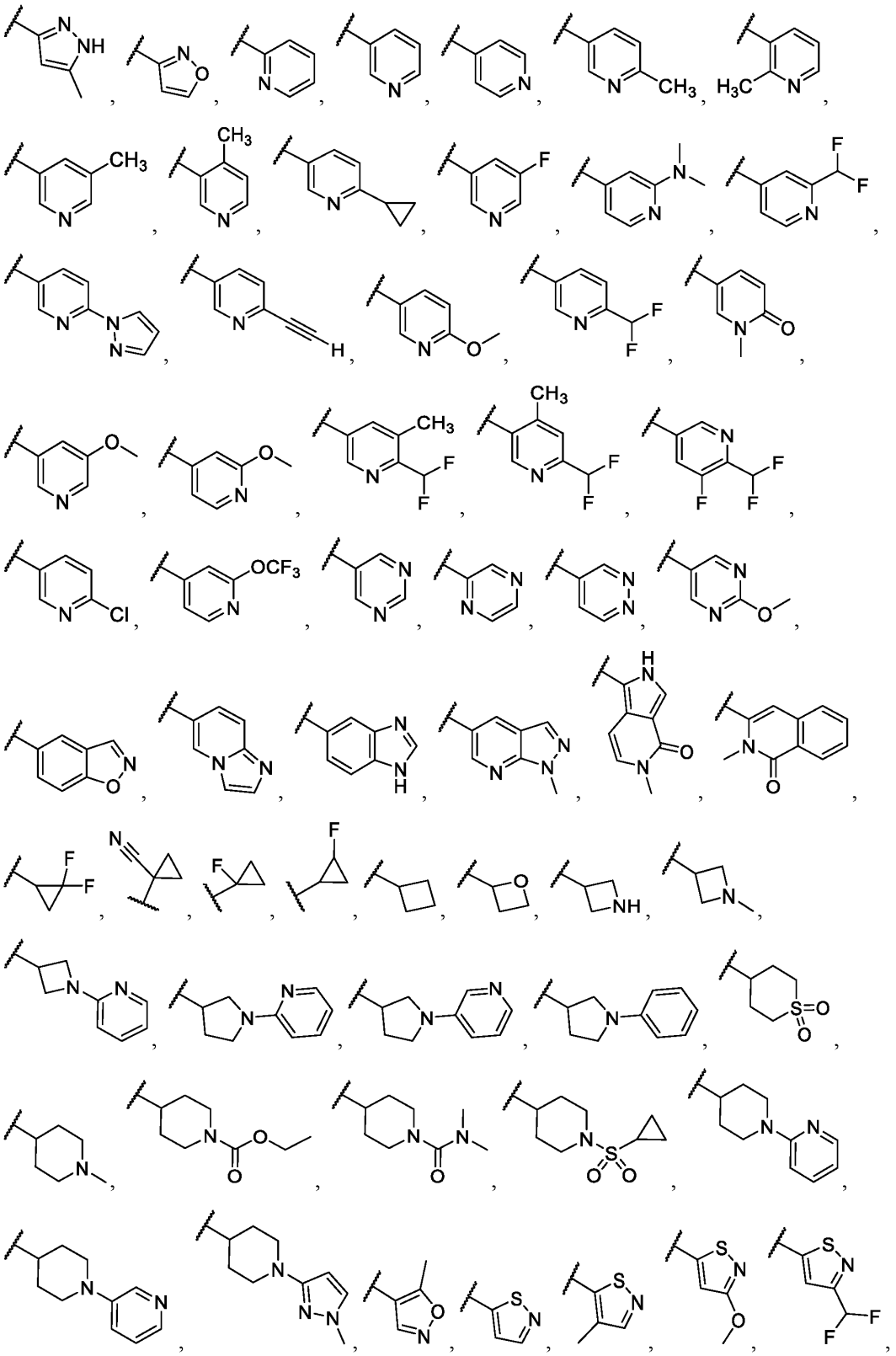


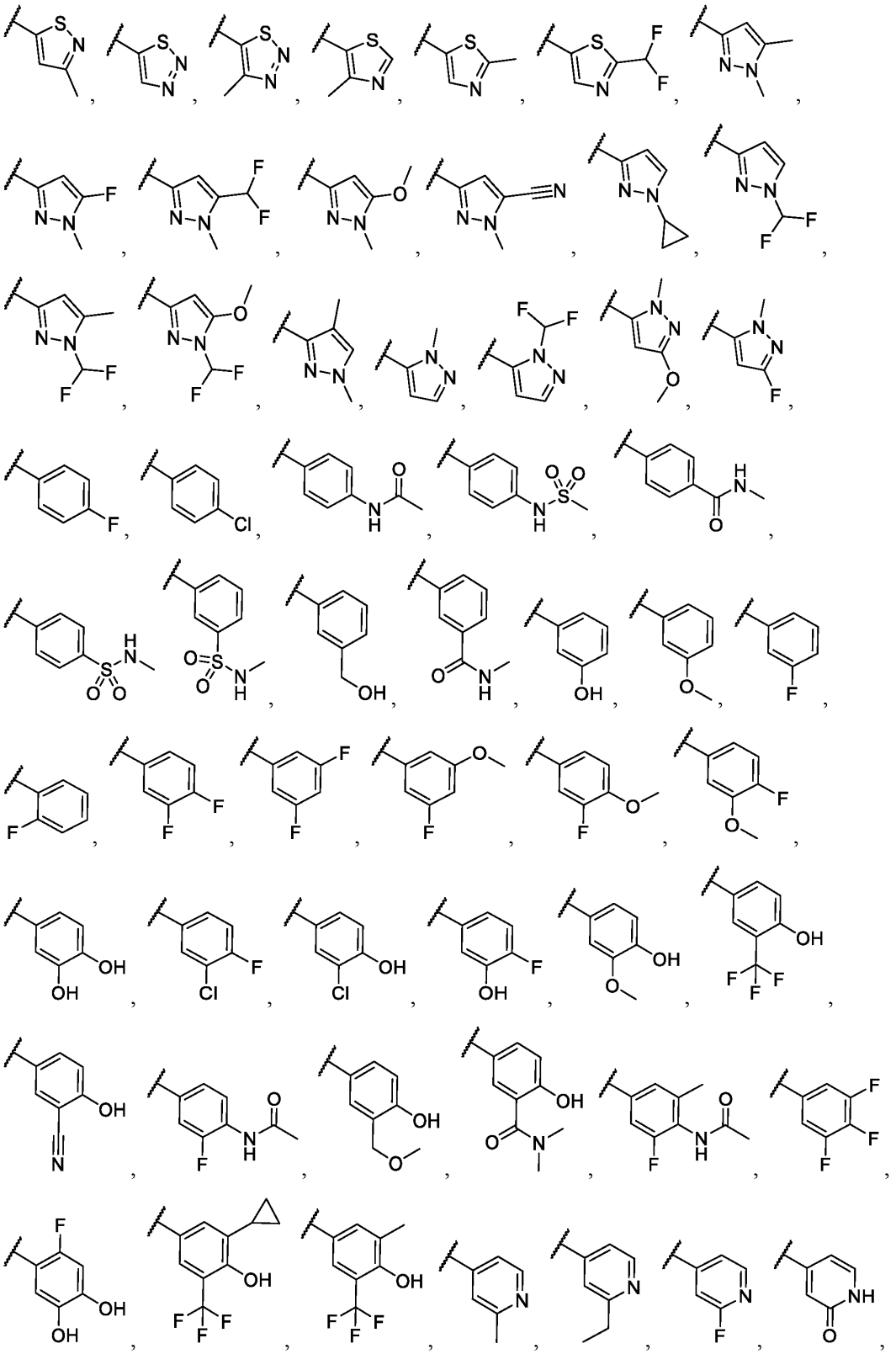


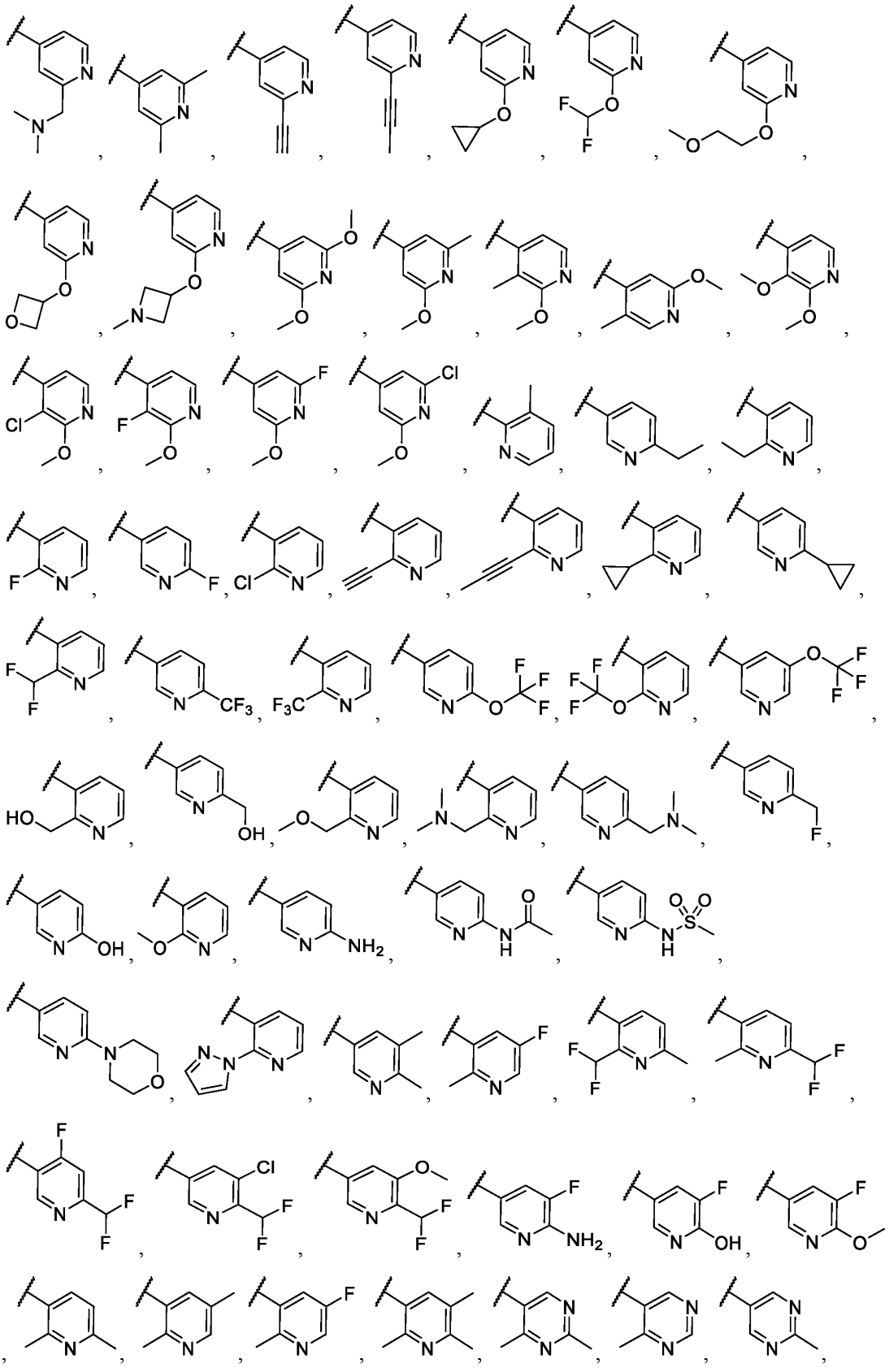


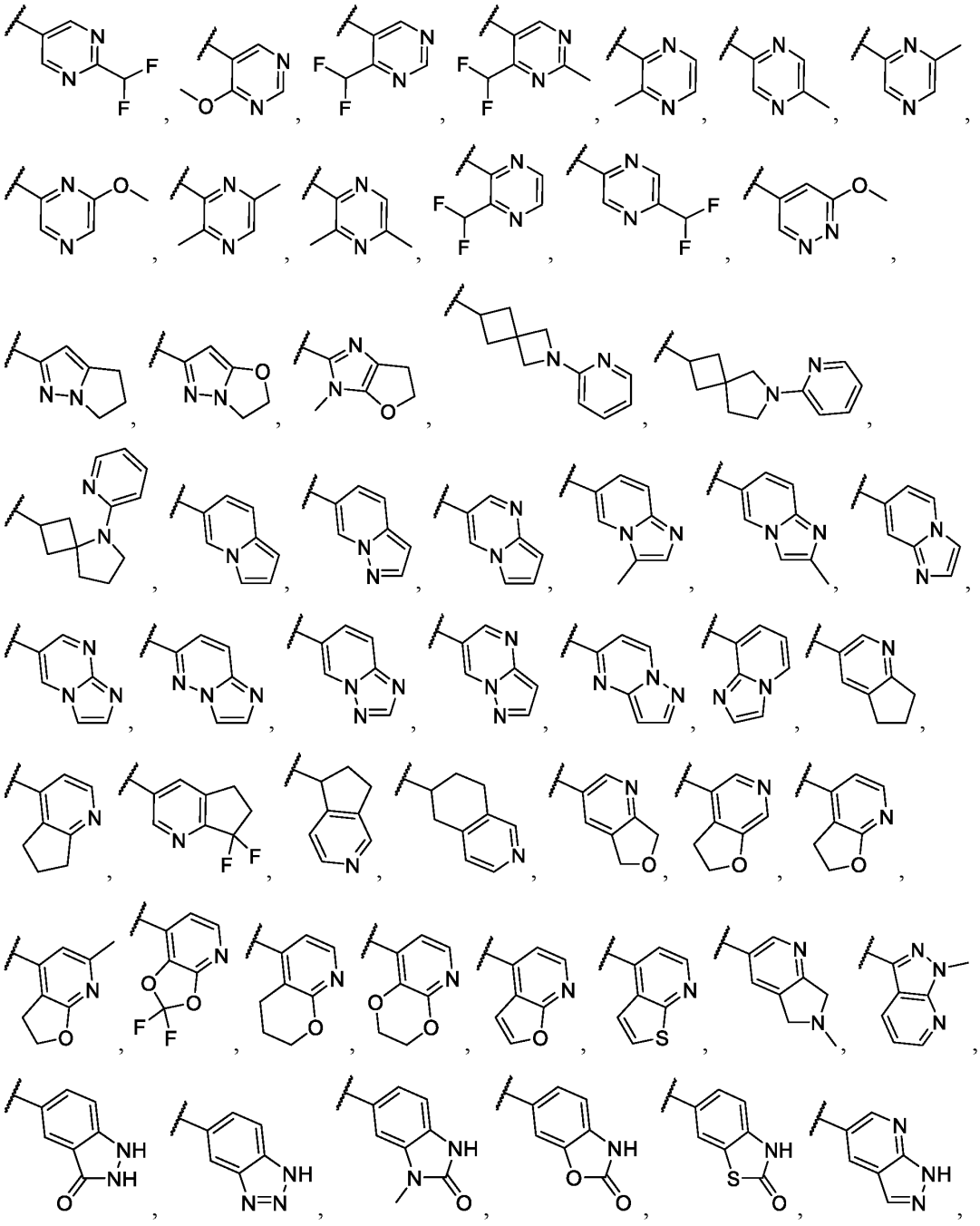
[00200] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^5 is selected from:

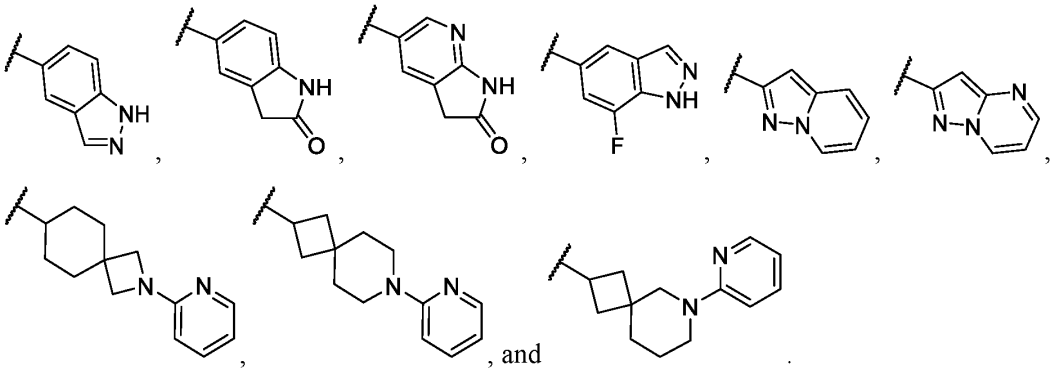












[00201] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-6} carbocycle, 4- to 6-membered heterocycle, and C_{1-4} haloalkyl. In some embodiments, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00202] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, -

$N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN.

[00203] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{16} is independently selected at each occurrence from hydrogen; and C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN.

[00204] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{16} is independently selected at each occurrence from (iv) and (v):

(iv) hydrogen; and

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN.

[00205] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{16} is independently selected at each occurrence from hydrogen; and C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN. In some embodiments, R^{16} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from halogen. In some embodiments, R^{16} is independently selected at each occurrence from hydrogen and C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from fluoro. In

some embodiments, R^{16} is independently selected at each occurrence from hydrogen and methyl, wherein the methyl is optionally substituted with one or more substituents independently selected from halogen. In some embodiments, R^{16} is independently selected at each occurrence from hydrogen and methyl, wherein the methyl is optionally substituted with one or more substituents independently selected from fluoro. In some embodiments, R^{16} is independently selected at each occurrence from hydrogen. In some embodiments, R^{16} is independently selected at each occurrence from C_{1-4} alkyl. In some embodiments, R^{16} is independently selected at each occurrence from methyl. In some embodiments, R^{16} is independently selected at each occurrence from C_{1-4} alkyl optionally substituted with one or more substituents independently selected at each occurrence from halogen. In some embodiments, R^{16} is independently selected at each occurrence from C_{1-4} alkyl optionally substituted with one or more substituents independently selected at each occurrence from fluoro. In some embodiments, R^{16} is independently selected at each occurrence from methyl optionally substituted with one or more substituents independently selected at each occurrence from fluoro. In some embodiments, R^{16} is independently selected at each occurrence from trifluoromethyl. In some embodiments, R^{16} is independently selected at each occurrence from hydrogen, methyl, and trifluoromethyl.

[00206] In some embodiments, for the compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-6} carbocycle, and 4- to 6-membered heterocycle. In some embodiments, R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl.

[00207] In some embodiments, the compound or salt of Formula (I) or Formula (II) is a compound of **Table 1**.

[00208] **Table 1.** Chemical structures of selected compounds. *Denotes a stereocenter with undetermined absolute stereochemistry of a single diastereomer.

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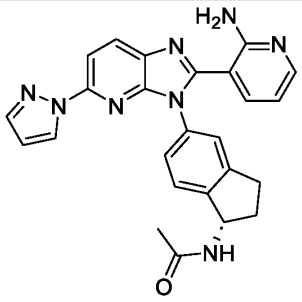
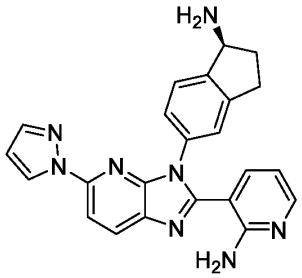
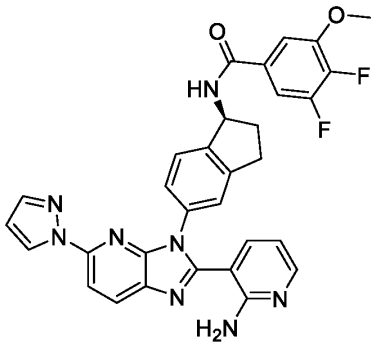
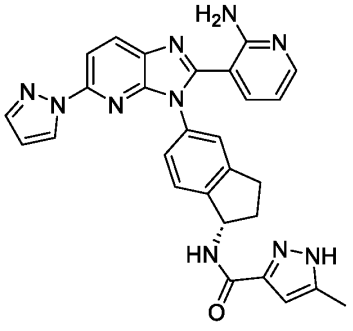
1	
2	
3	
4	

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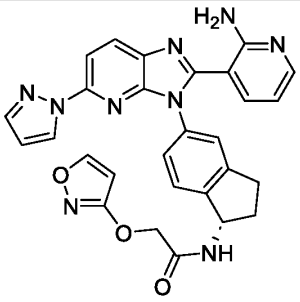
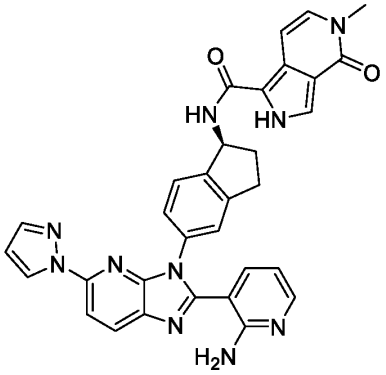
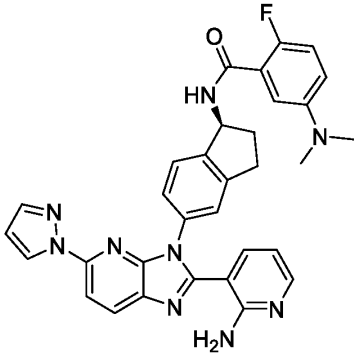
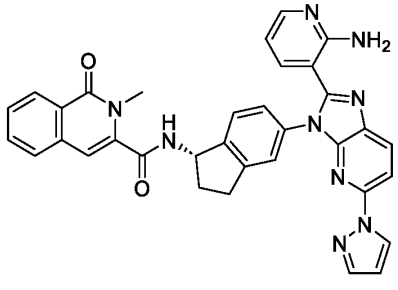
5	
6	
7	
8	

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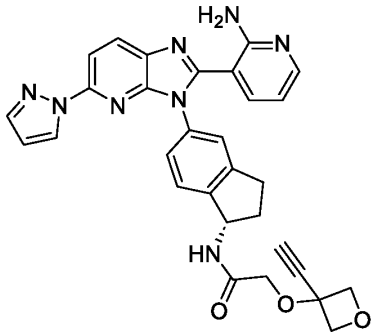
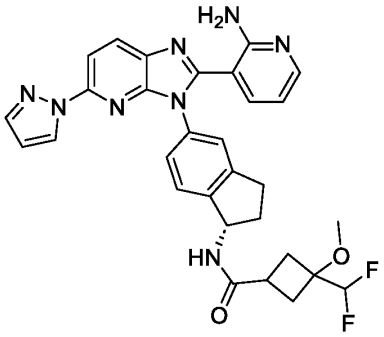
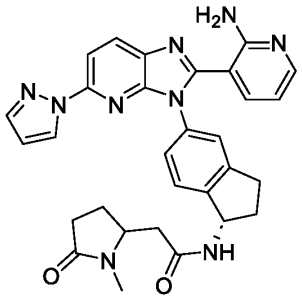
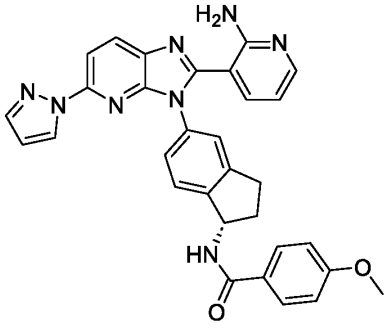
9	
10	
11	
12	

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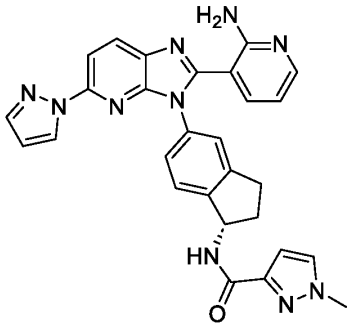
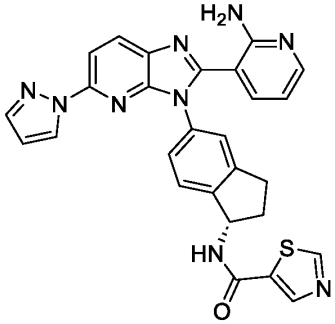
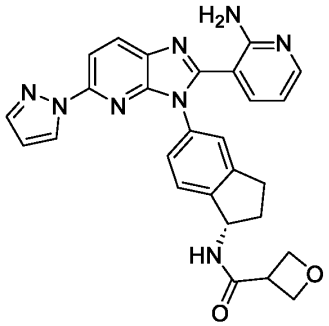
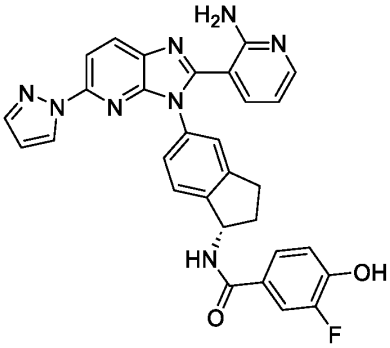
13	
14	
15	
16	

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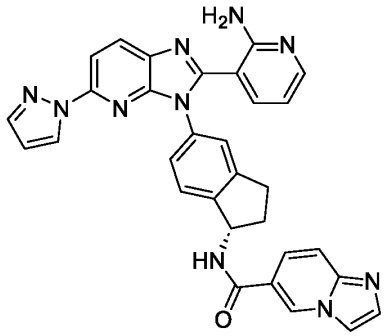
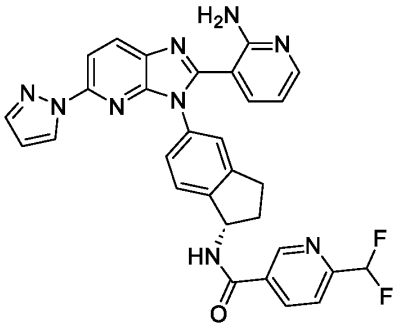
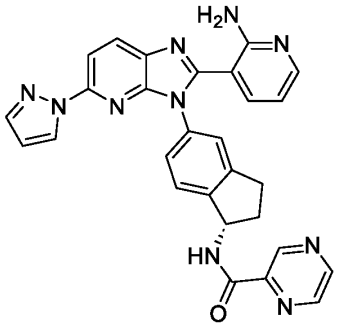
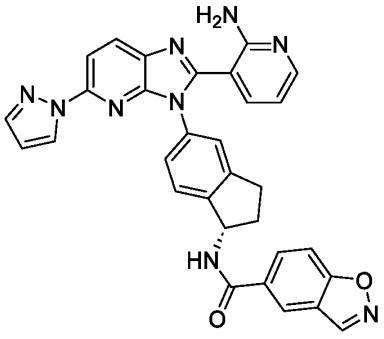
17	
18	
19	
20	

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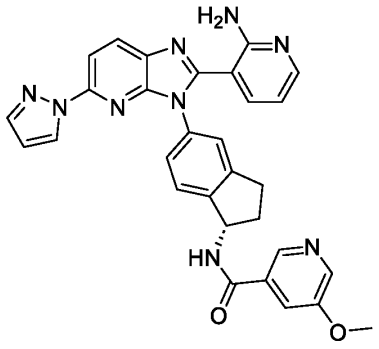
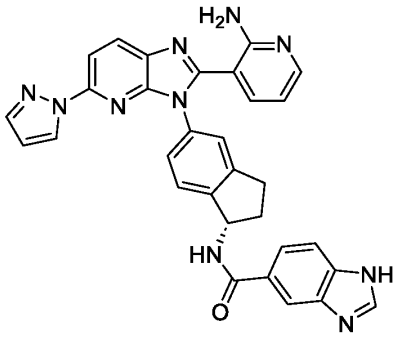
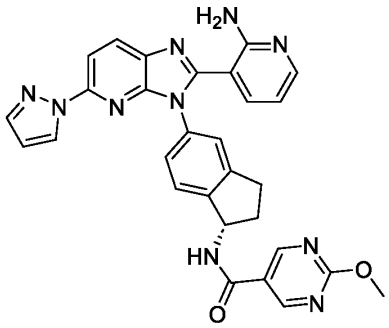
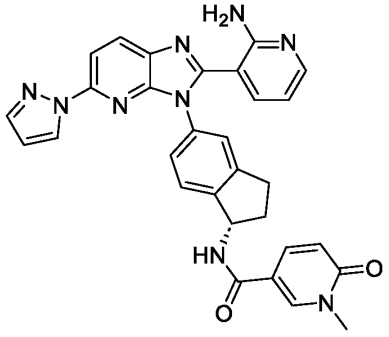
21	
22	
23	
24	

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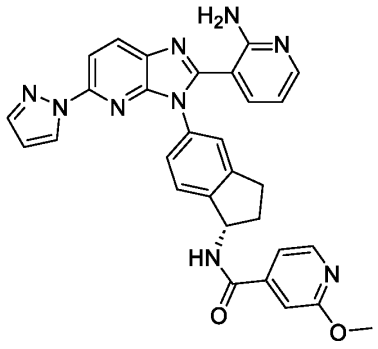
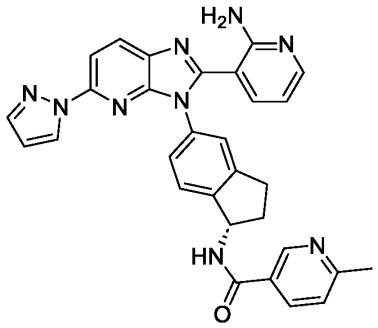
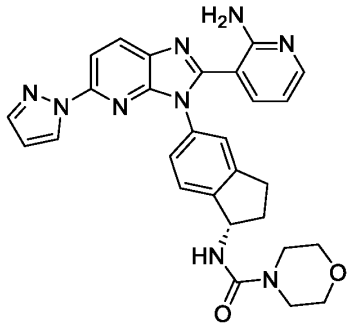
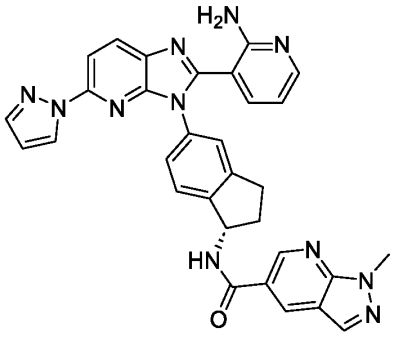
25	
26	
27	
28	

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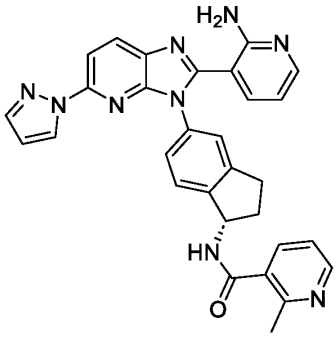
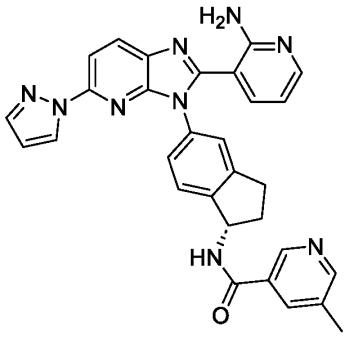
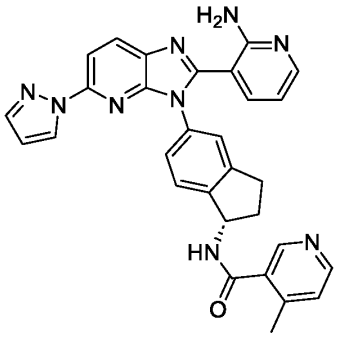
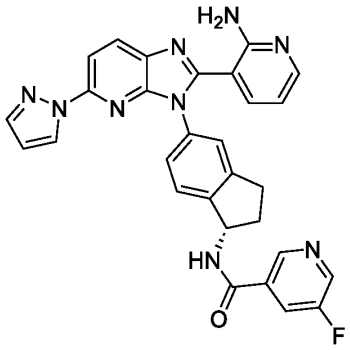
29	
30	
31	
32	

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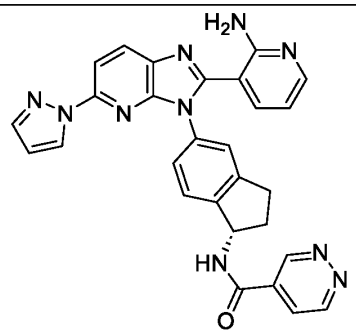
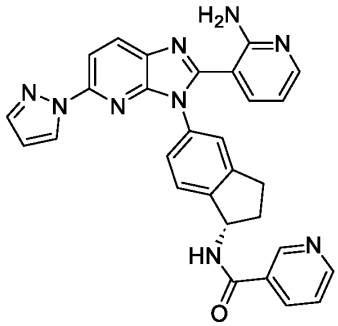
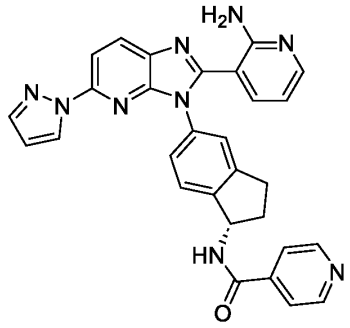
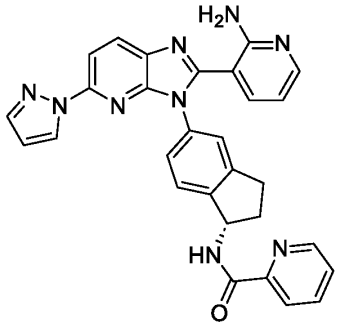
33	
34	
35	
36	

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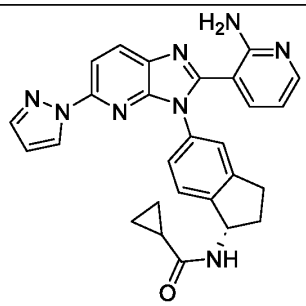
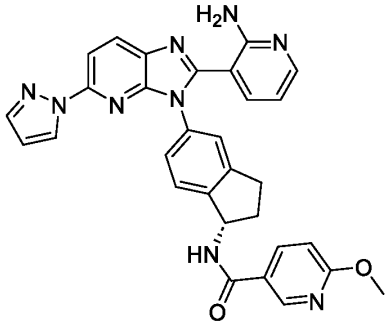
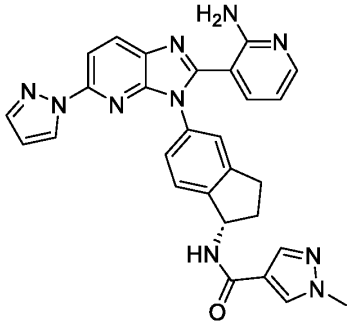
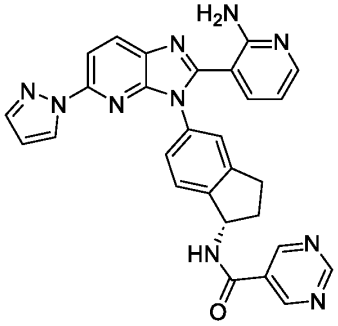
37	
38	
39	
40	

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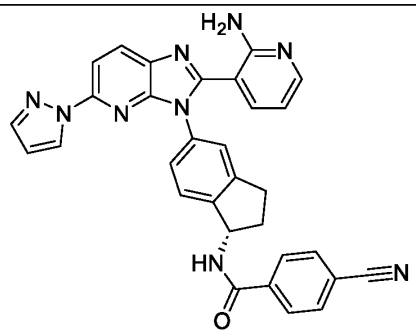
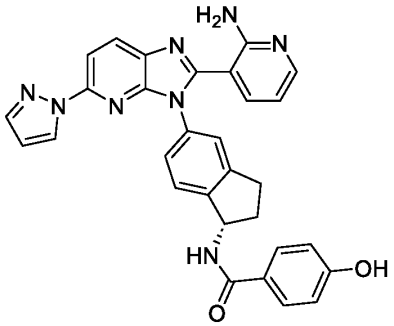
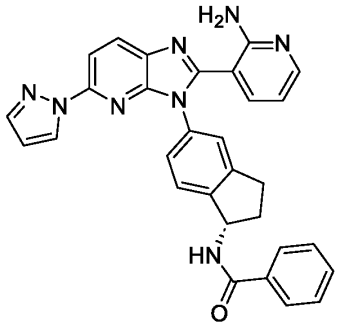
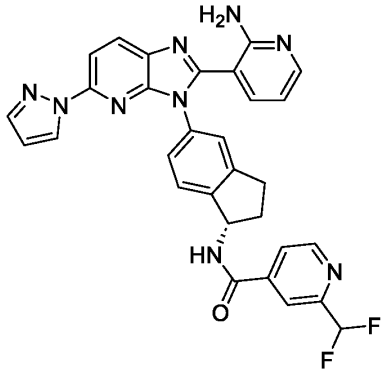
41	
42	
43	
44	

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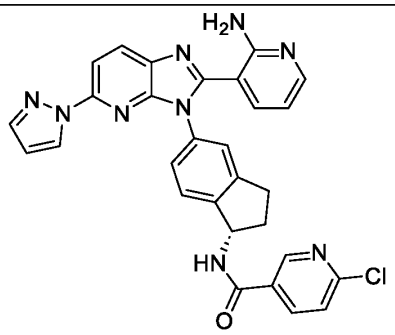
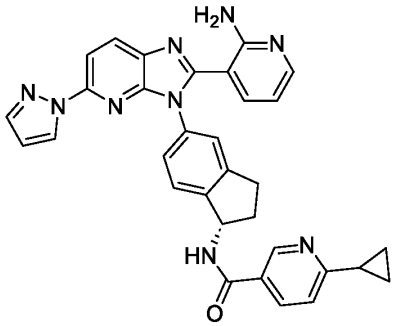
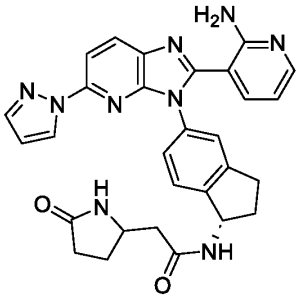
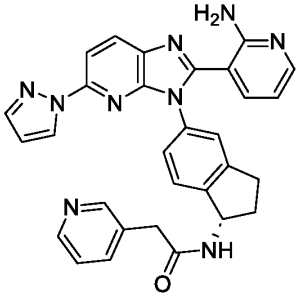
45	
46	
47	
48	

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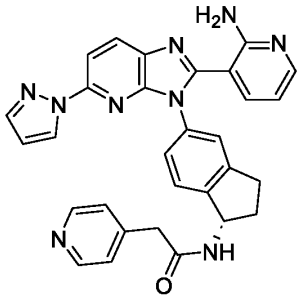
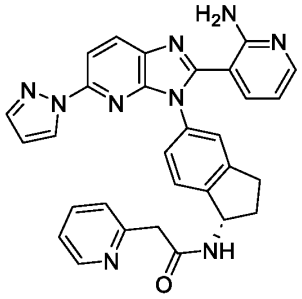
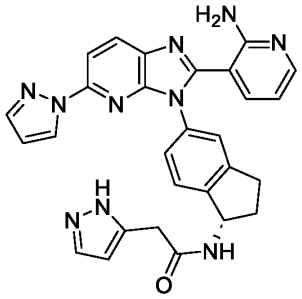
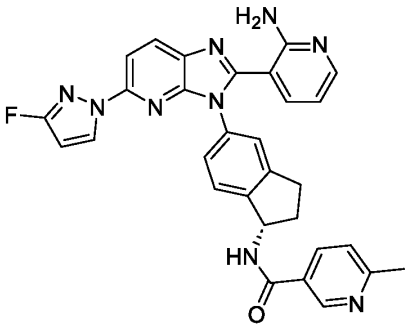
49	
50	
51	
52	

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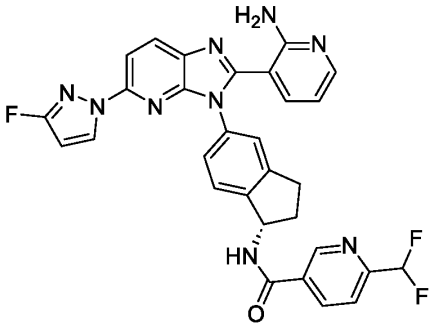
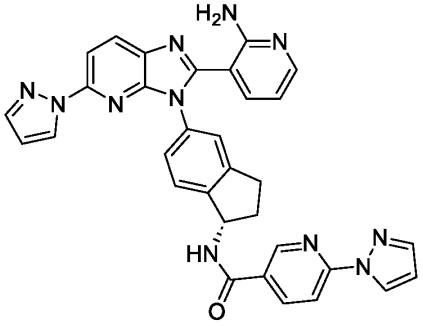
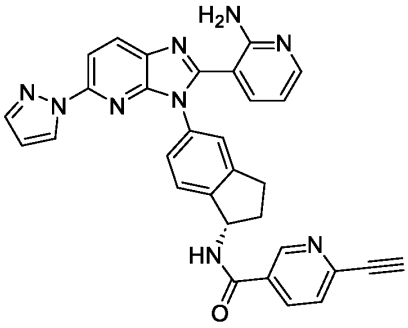
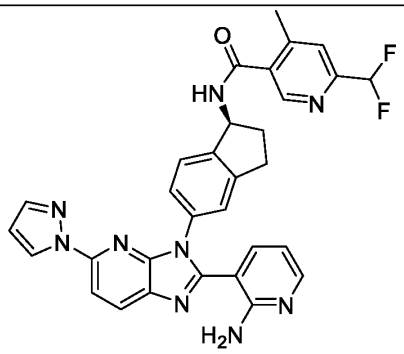
53	
54	
55	
56	

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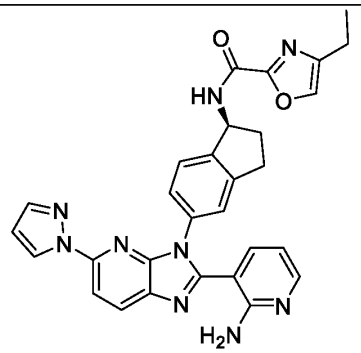
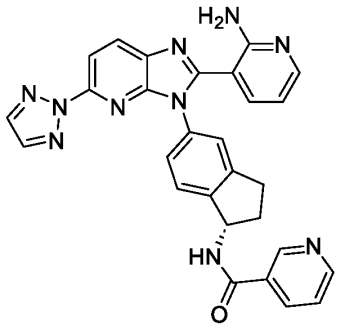
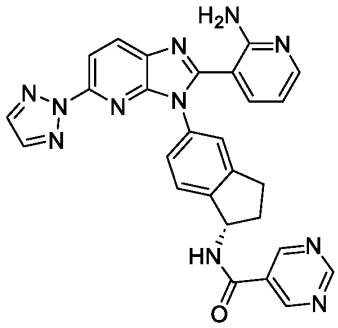
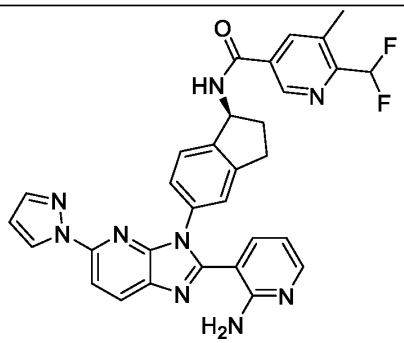
57	
58	
59	
60	

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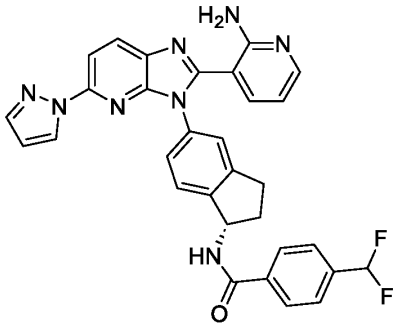
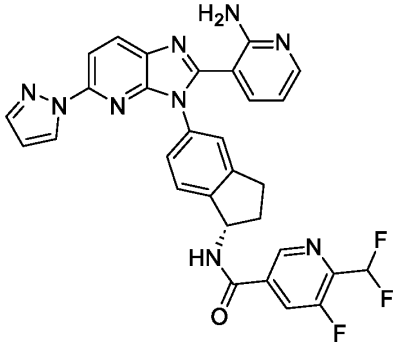
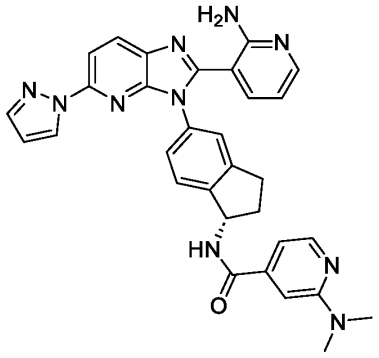
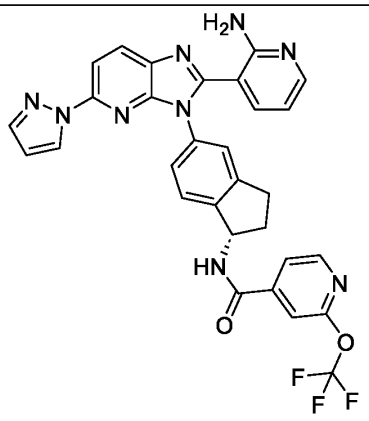
61	
62	
63	
64	

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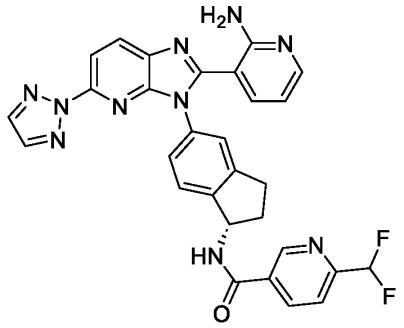
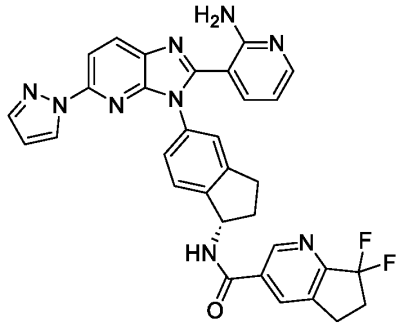
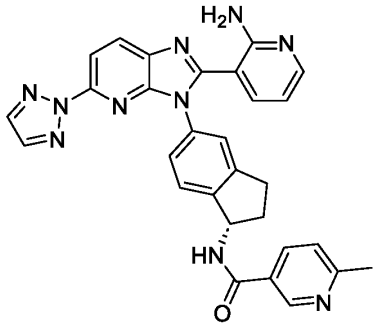
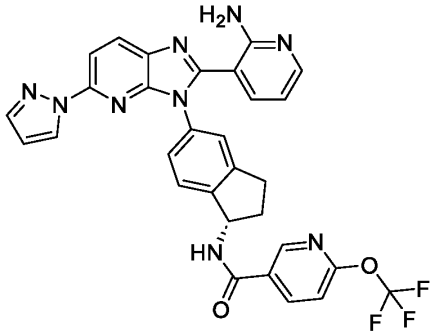
65	
66	
67	
68	

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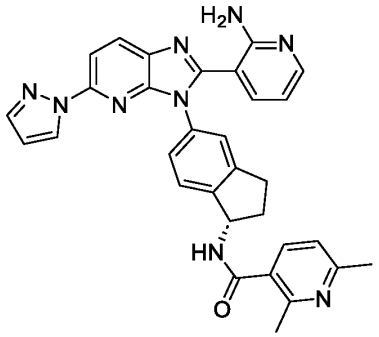
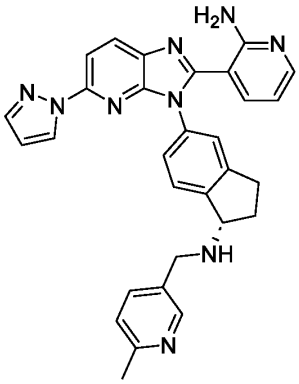
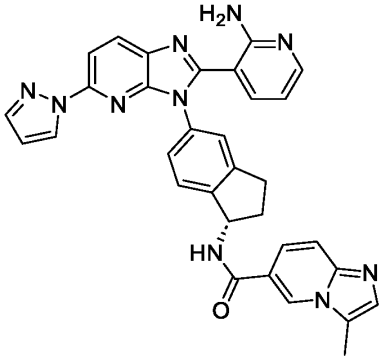
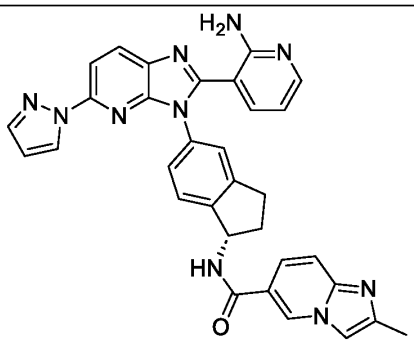
69	
70	
71	
72	

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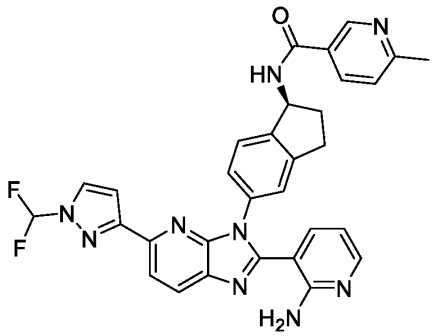
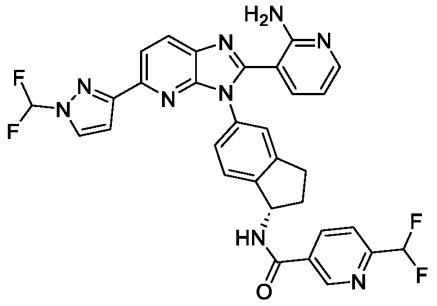
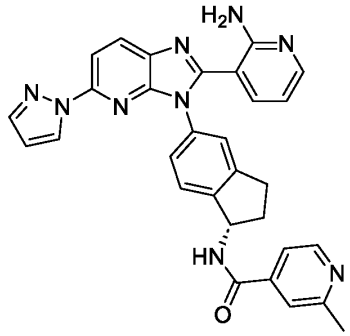
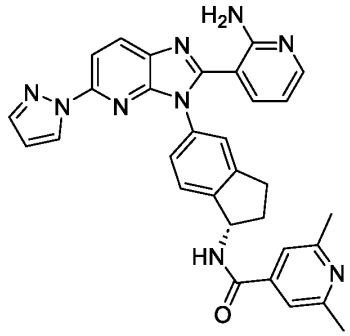
73	
74	
75	
76	

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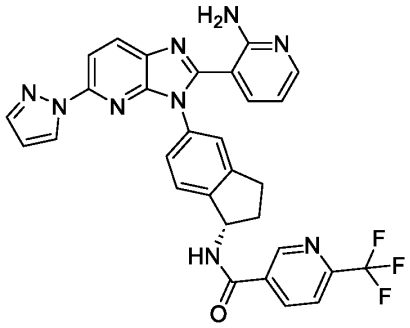
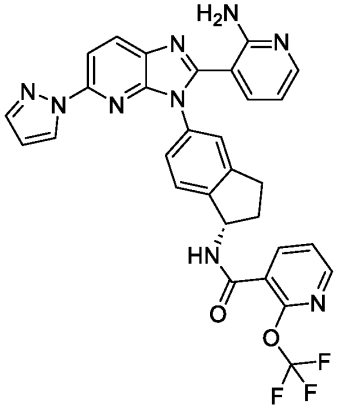
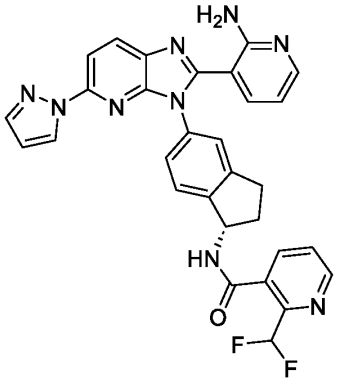
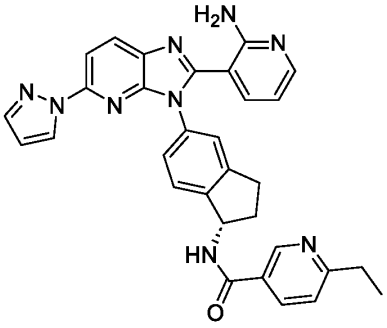
77	
78	
79	
80	

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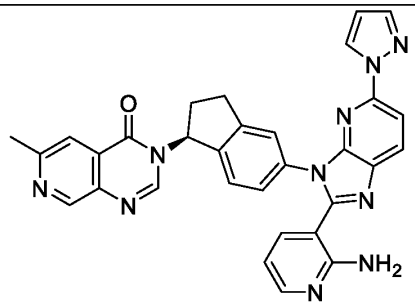
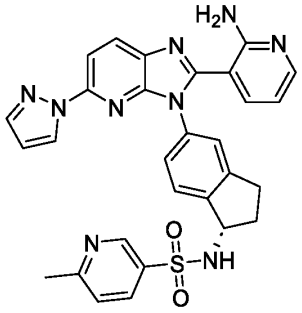
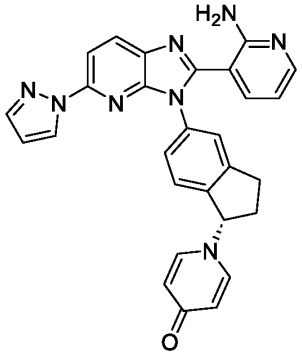
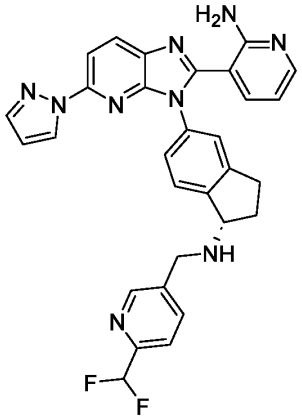
81	
82	
83	
84	

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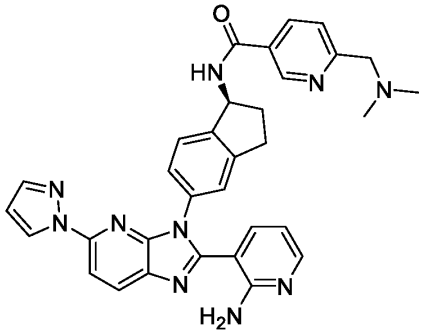
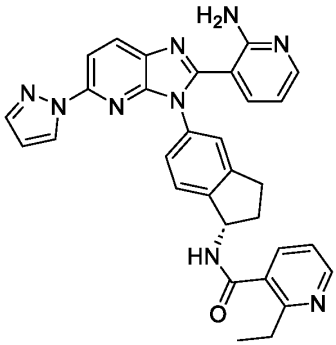
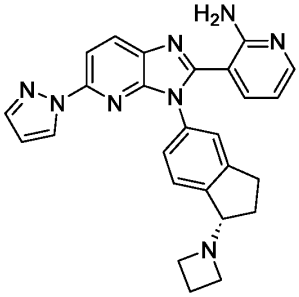
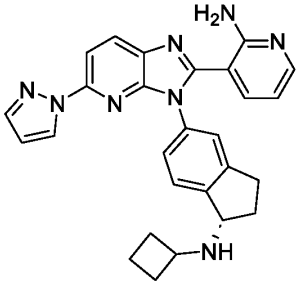
85	
86	
87	
88	

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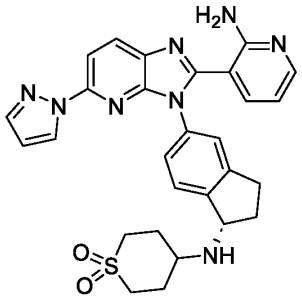
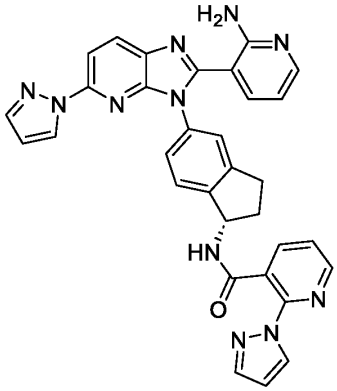
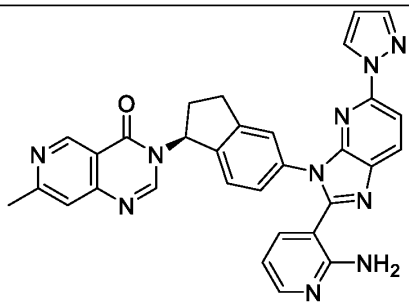
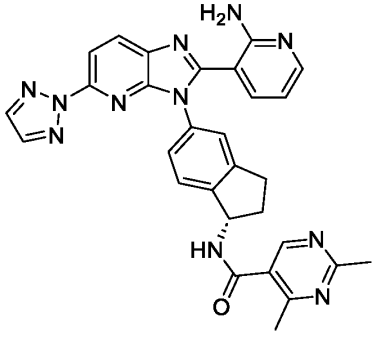
89	
90	
91	
92	

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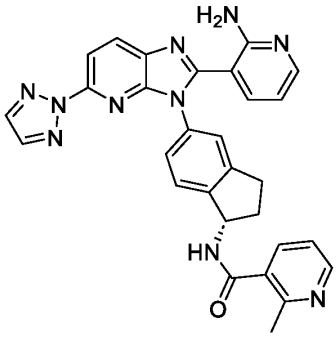
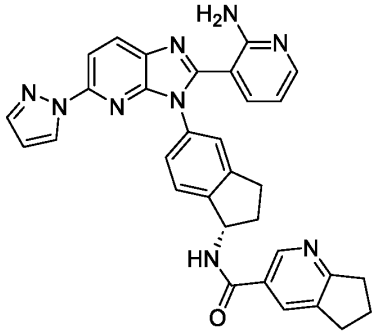
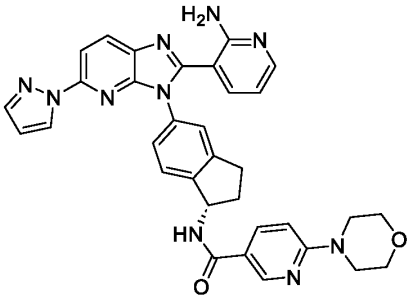
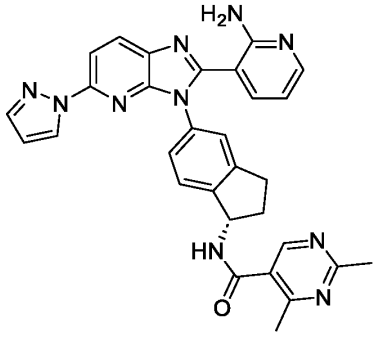
93	
94	
95	
96	

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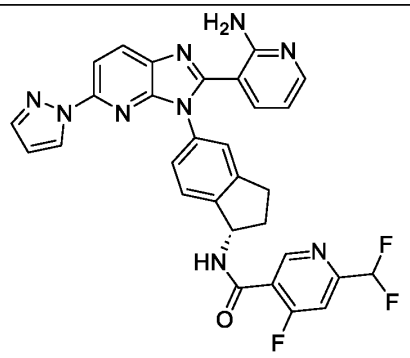
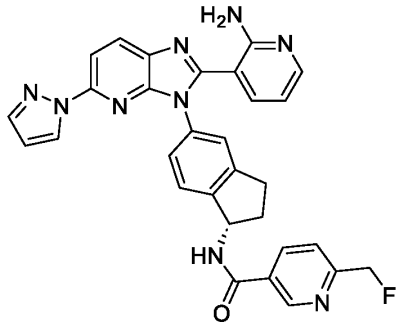
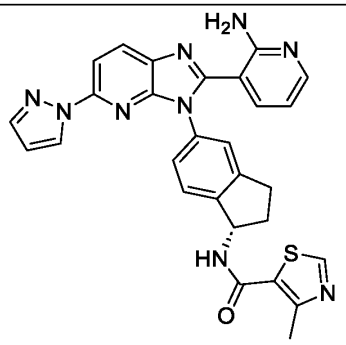
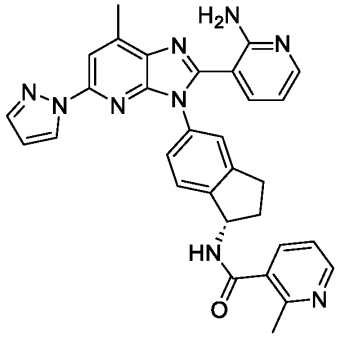
97	
98	
99	
100	

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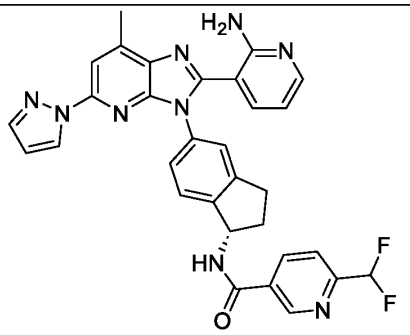
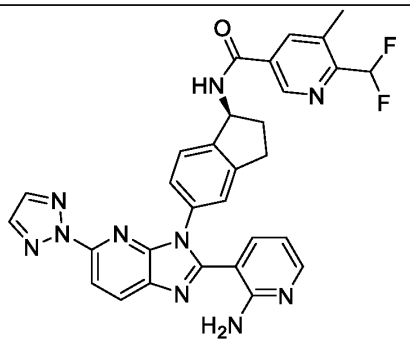
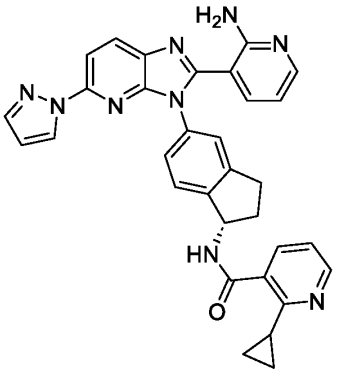
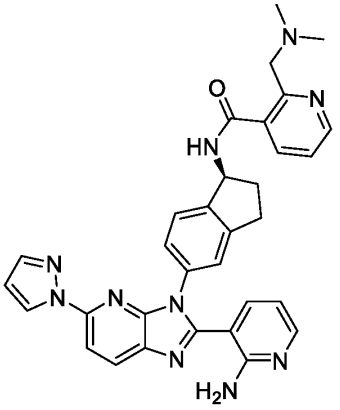
101	
102	
103	
104	

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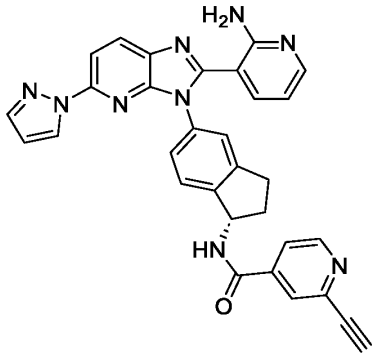
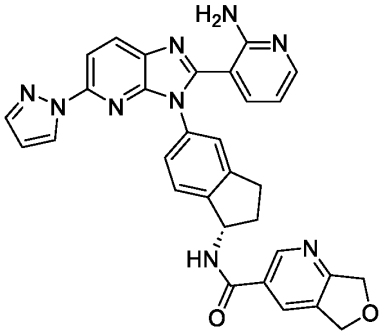
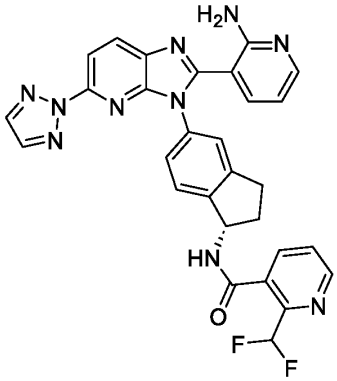
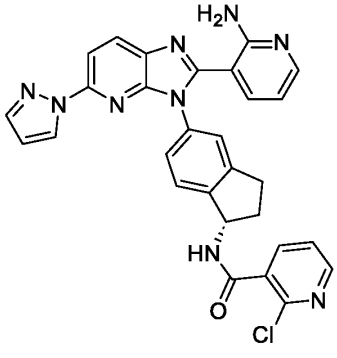
105	
106	
107	
108	

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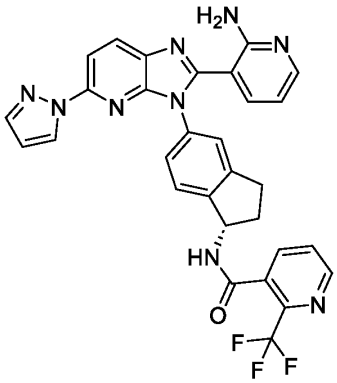
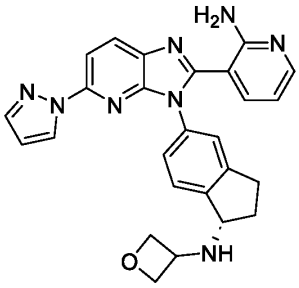
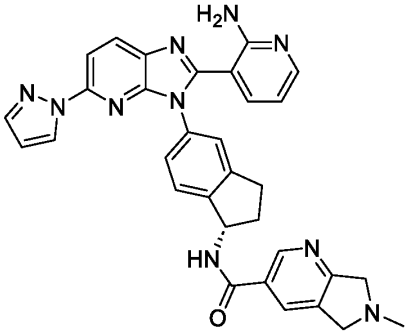
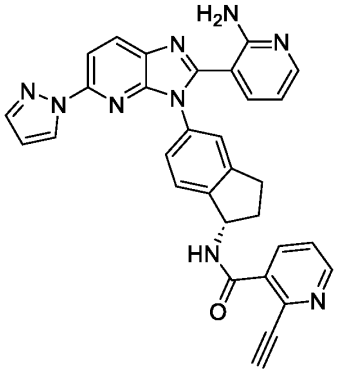
110	
111	
112	
113	

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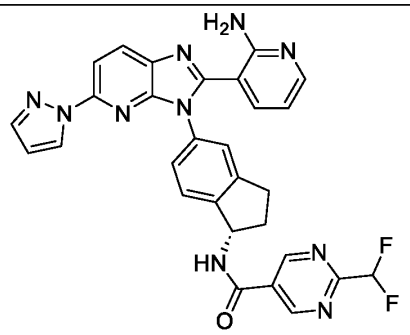
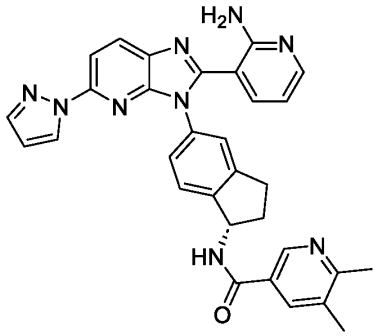
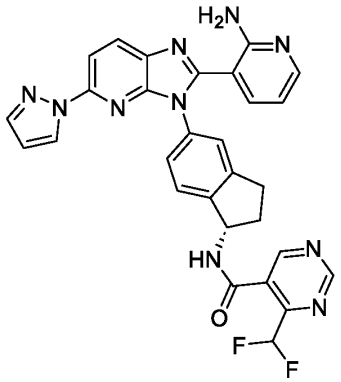
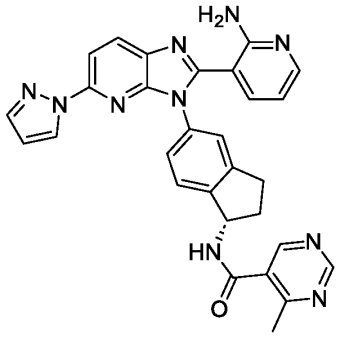
114	
115	
116	
117	

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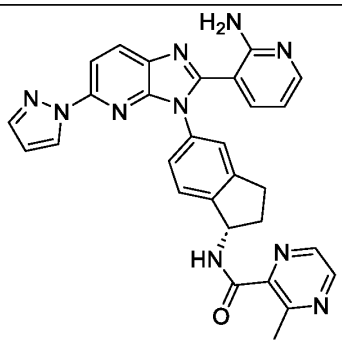
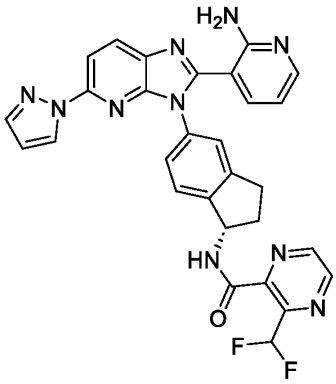
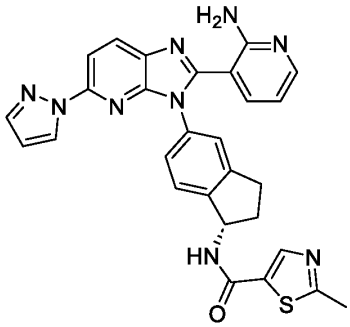
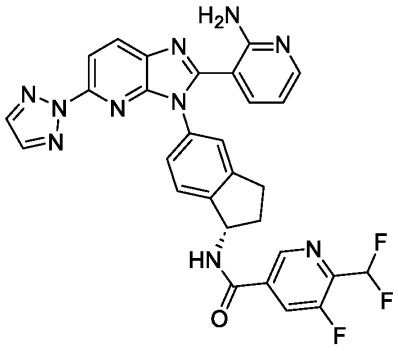
118	
119	
120	
121	

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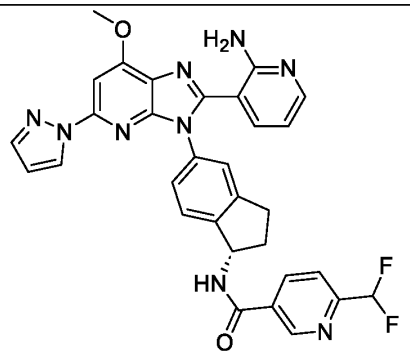
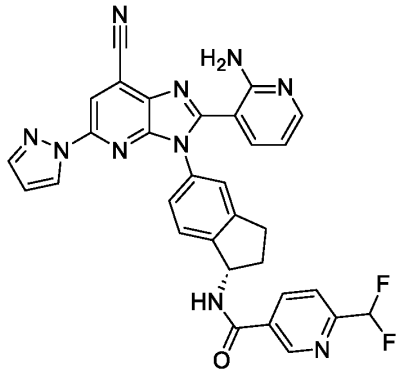
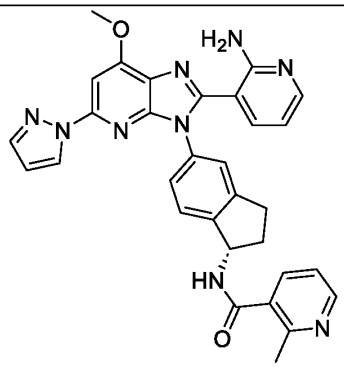
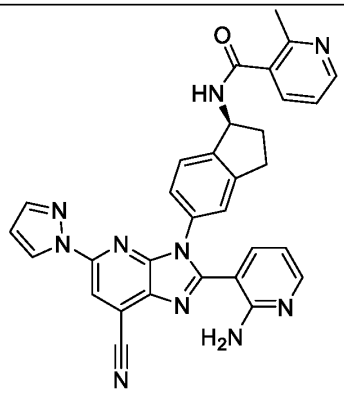
122	
123	
124	
125	

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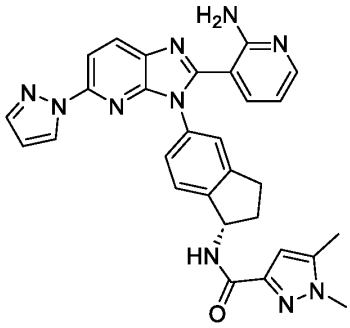
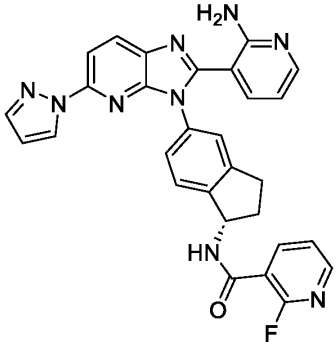
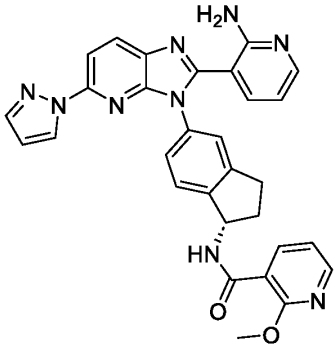
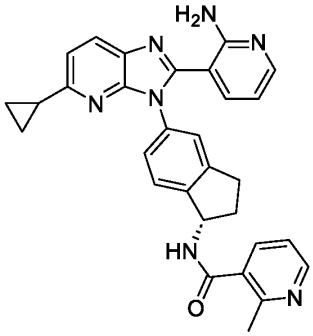
126	
127	
128	
129	

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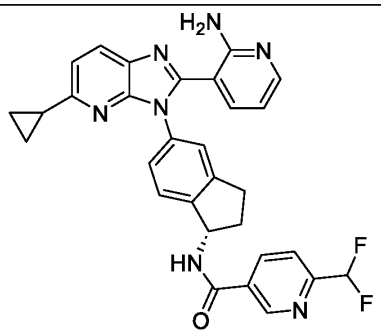
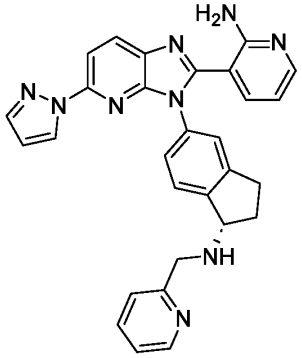
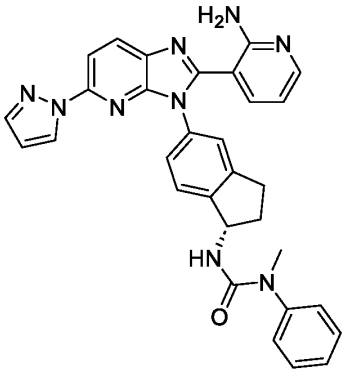
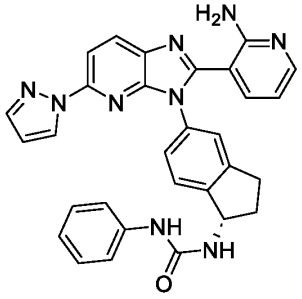
130	
131	
132	
133	

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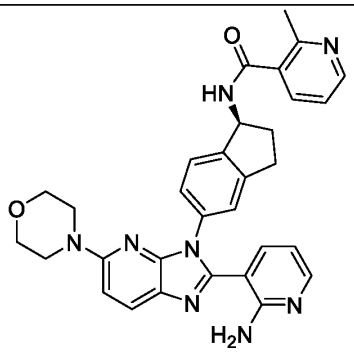
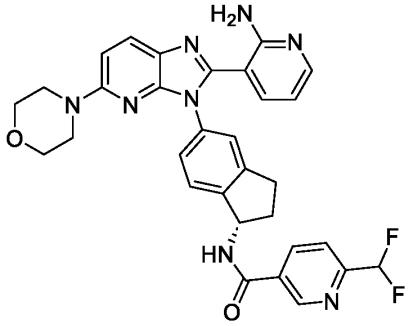
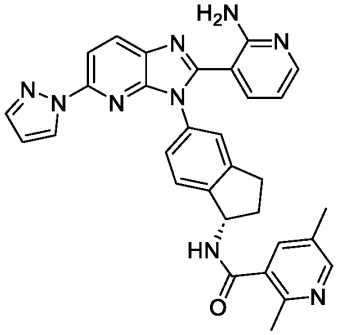
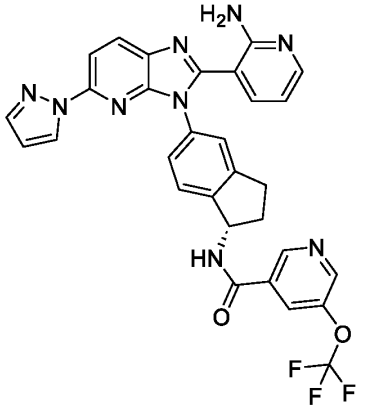
135	
136	
137	
138	

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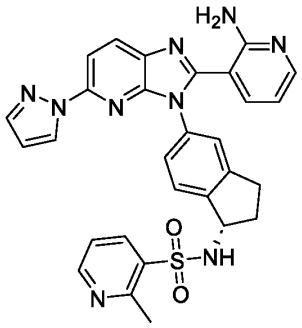
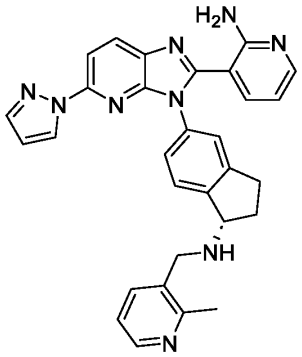
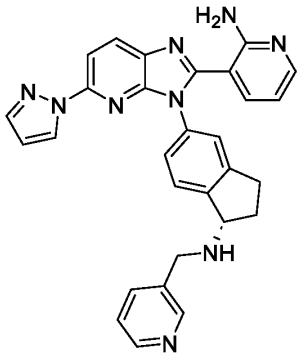
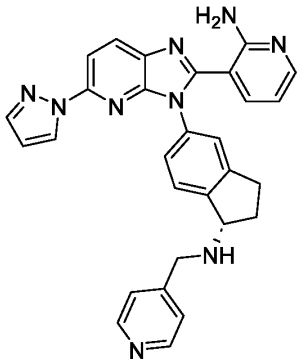
139	
140	
141	
142	

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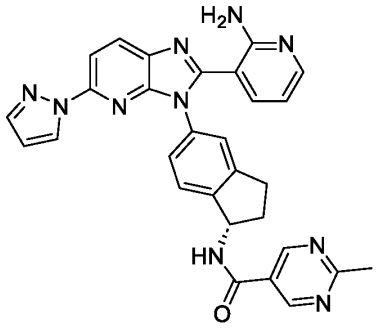
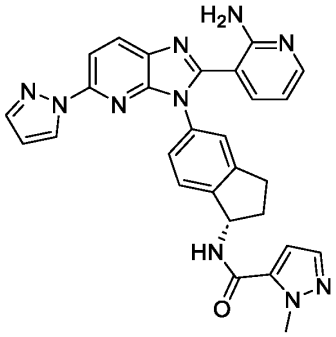
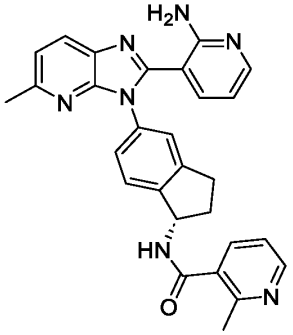
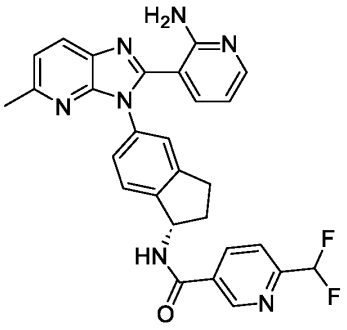
143	
144	
145	
146	

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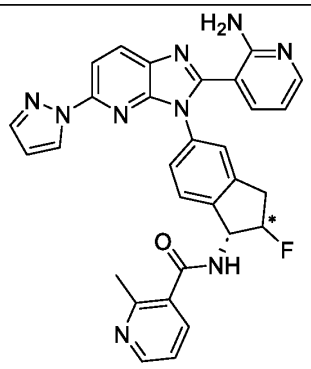
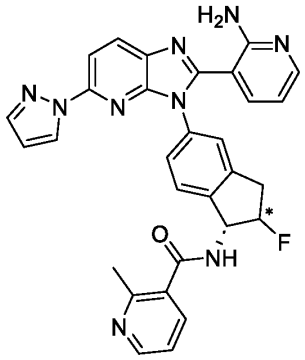
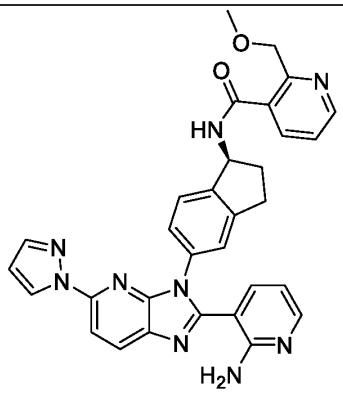
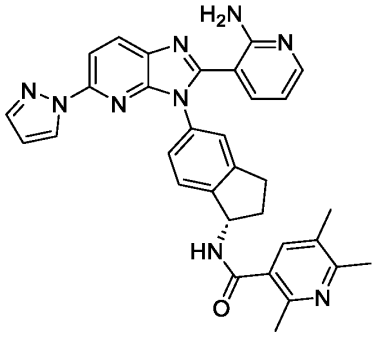
147	
148	
149	
150	

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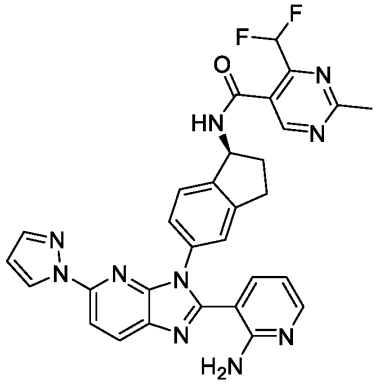
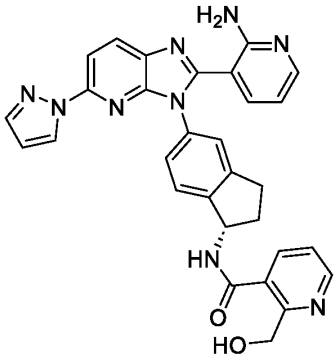
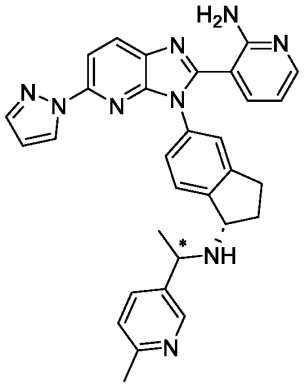
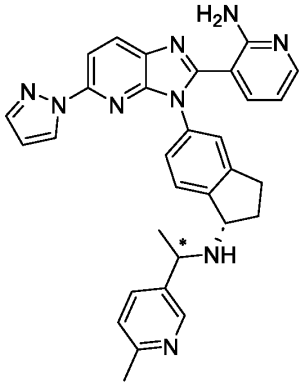
151	
152	
153	
154	

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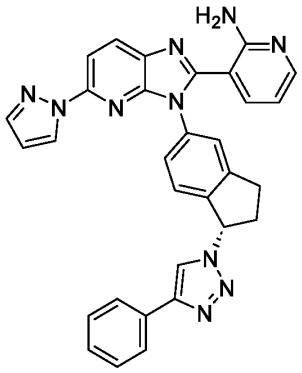
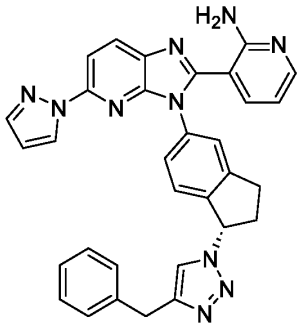
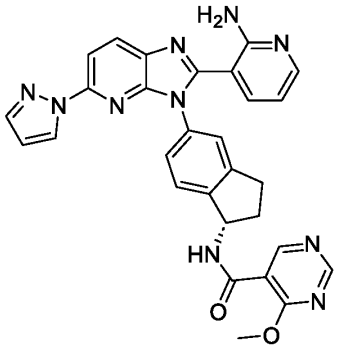
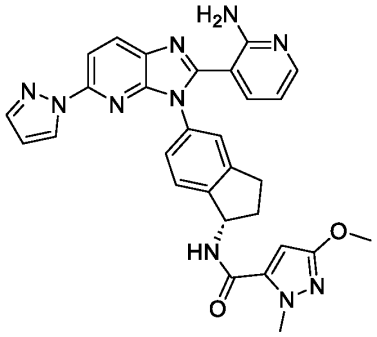
155	
156	
157	
158	

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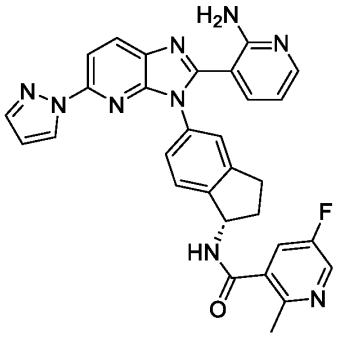
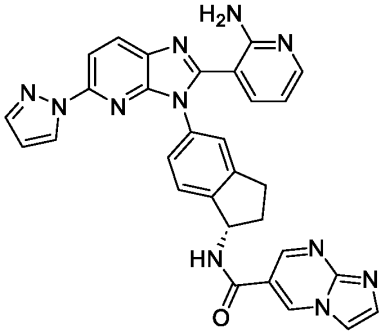
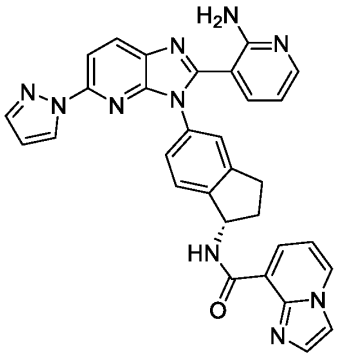
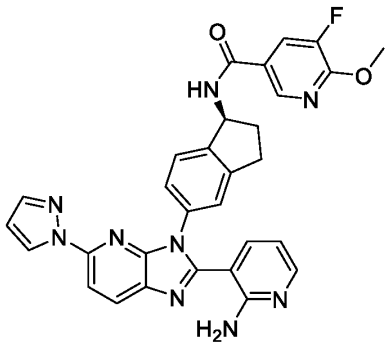
159	
160	
161	
162	

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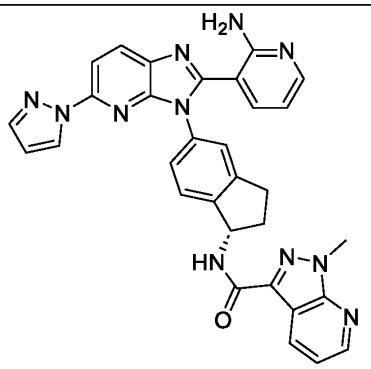
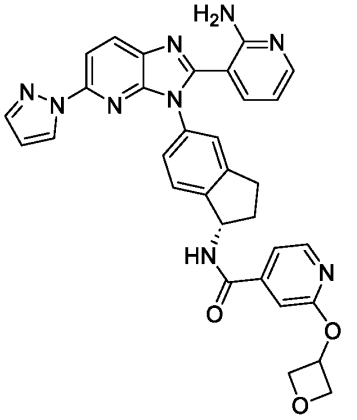
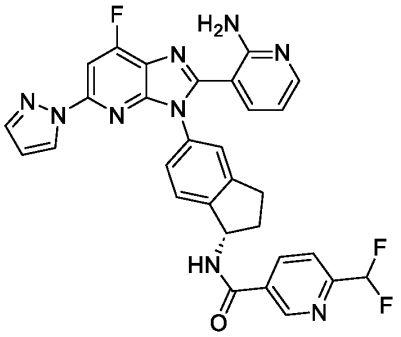
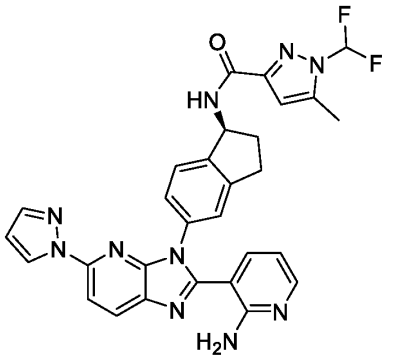
163	
164	
165	
166	

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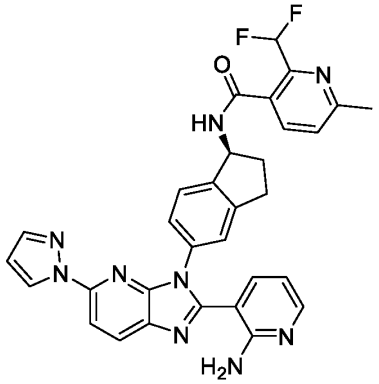
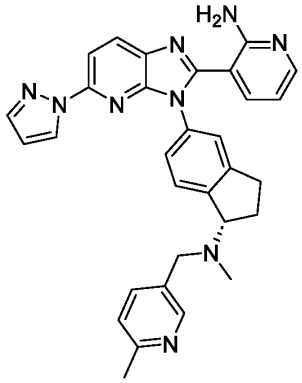
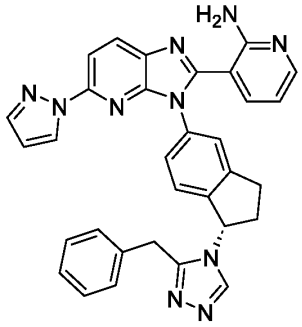
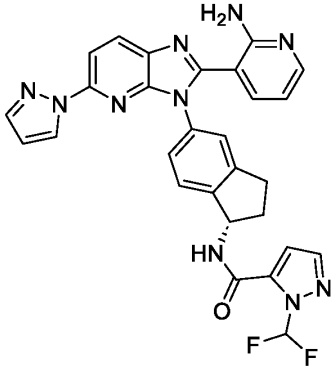
167	
168	
169	
170	

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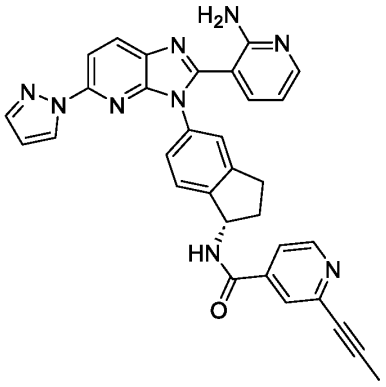
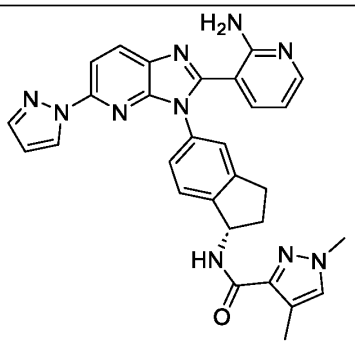
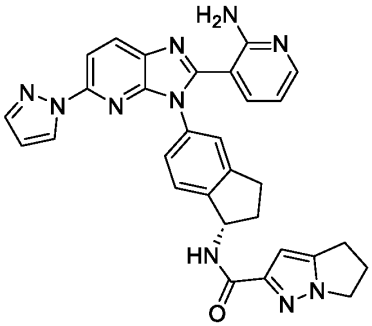
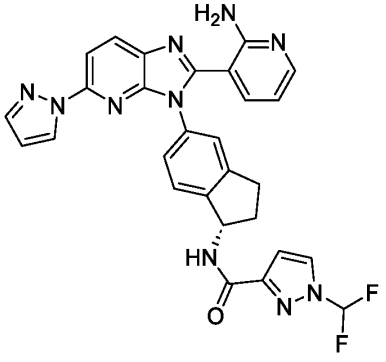
171	
172	
173	
174	

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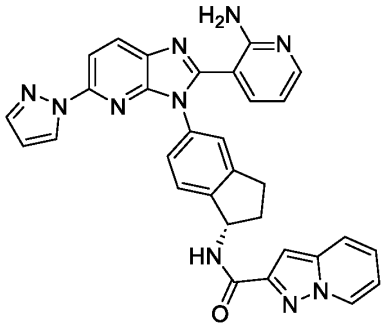
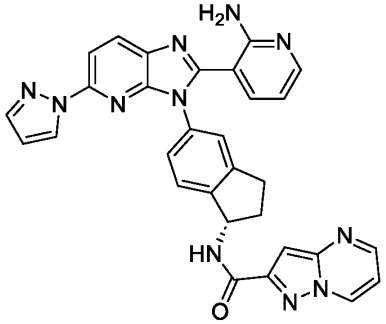
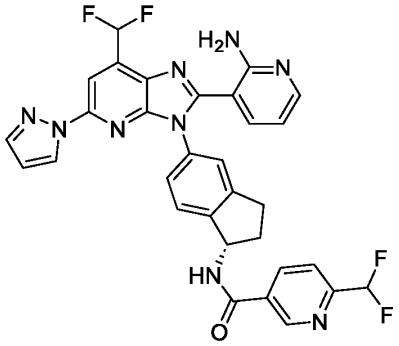
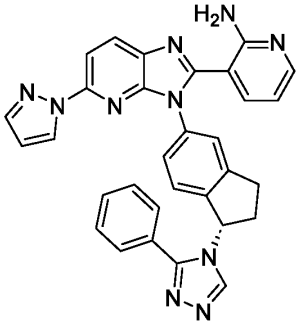
175	
176	
177	
178	

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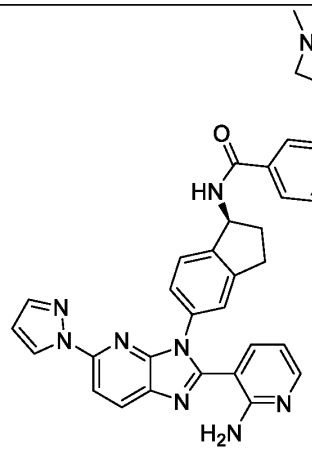
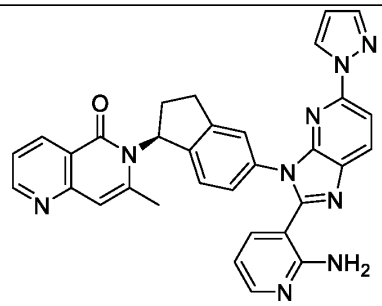
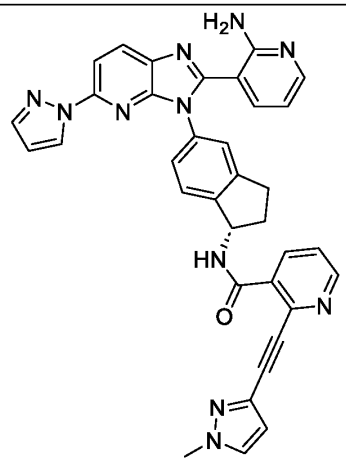
179	
180	
181	

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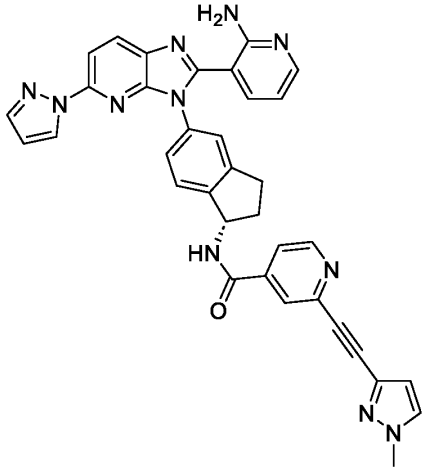
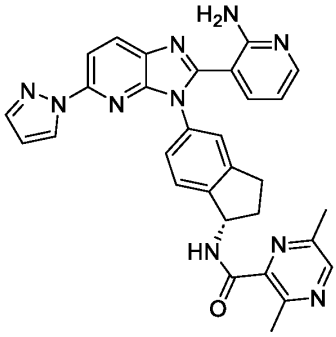
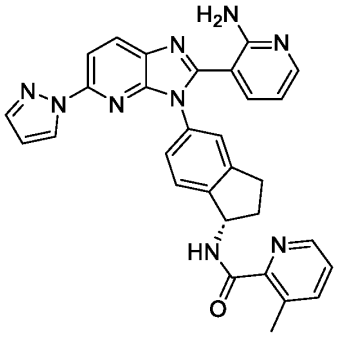
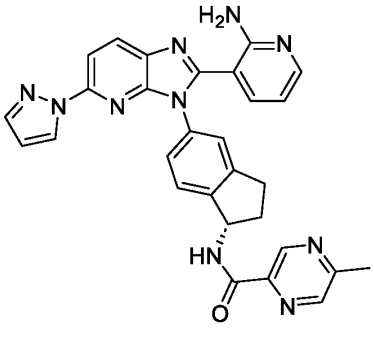
182	
183	
184	
185	

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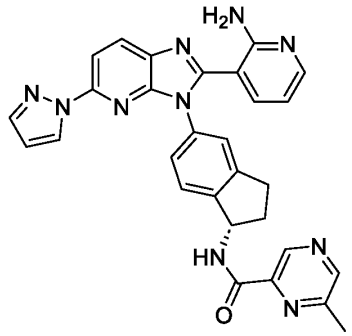
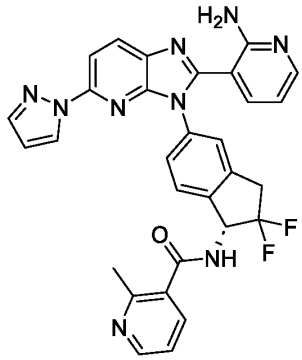
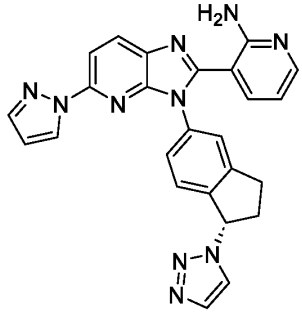
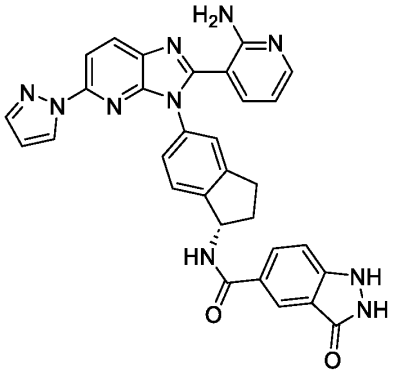
186	
187	
188	
189	

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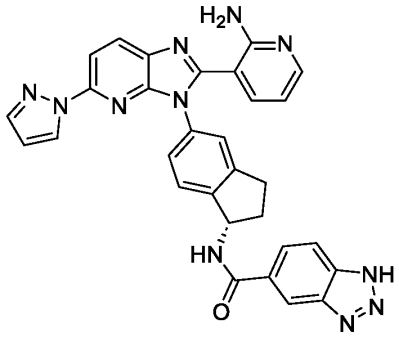
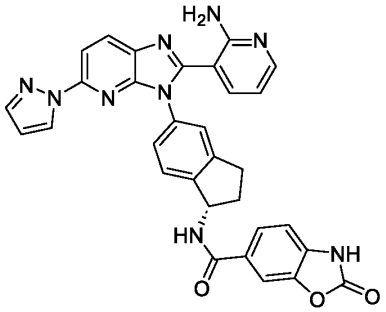
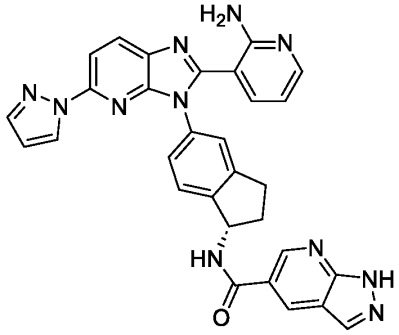
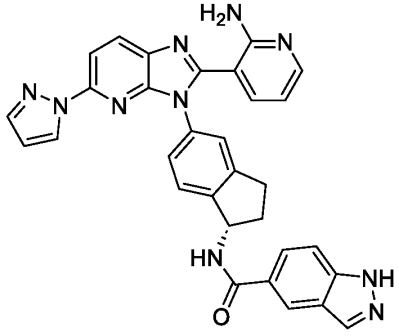
190	
191	
192	
193	

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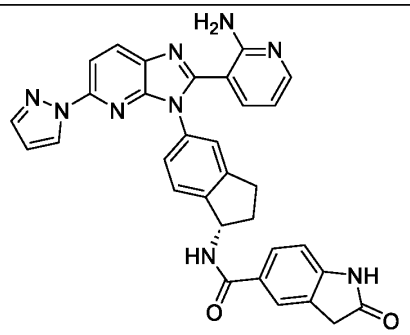
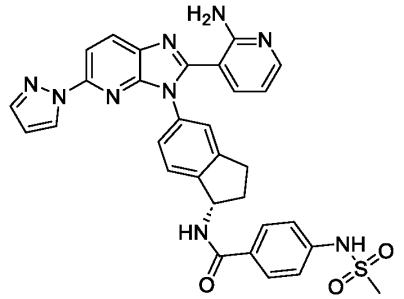
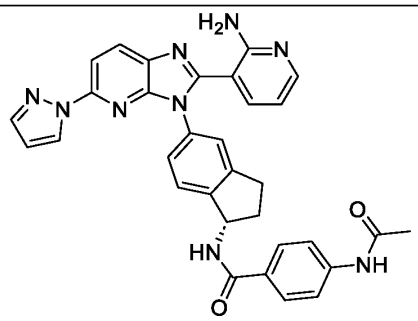
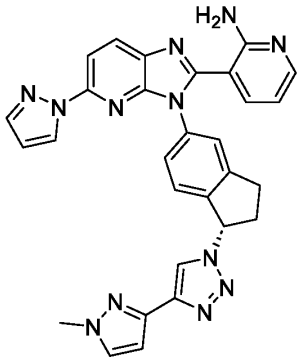
194	
195	
196	
197	

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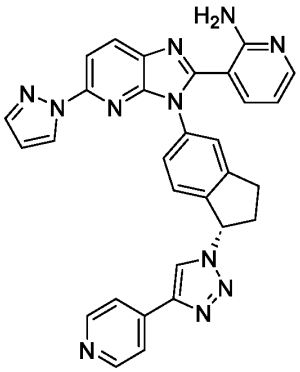
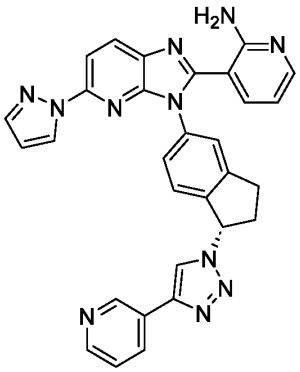
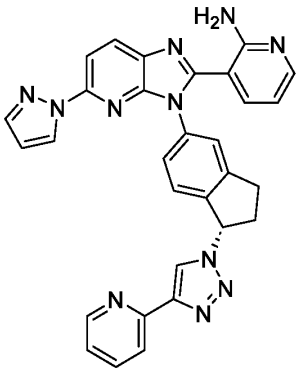
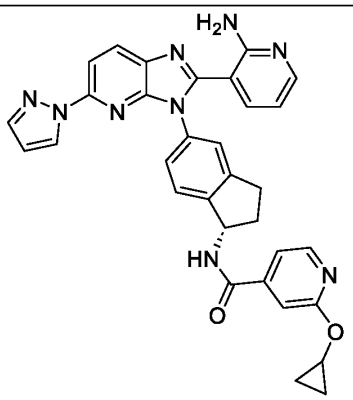
198	
199	
200	
201	

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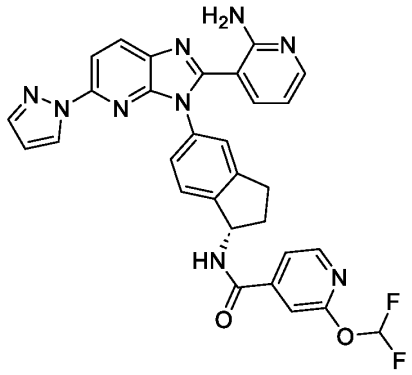
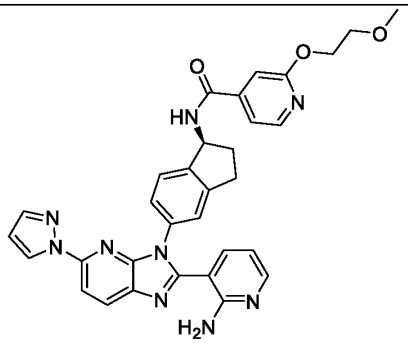
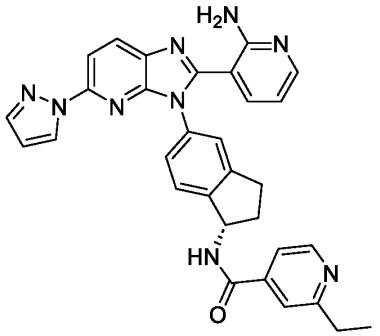
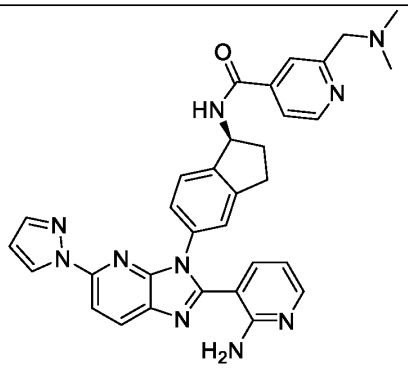
202	
203	
204	
205	

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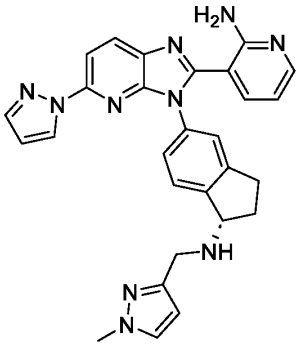
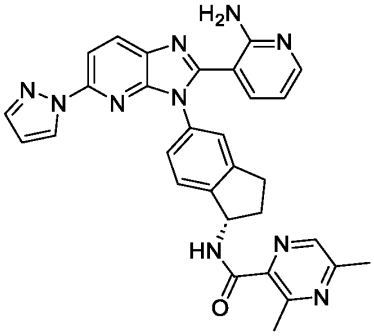
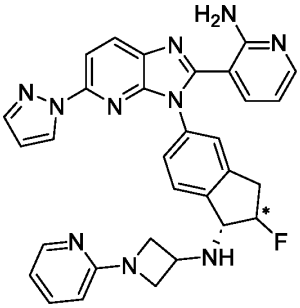
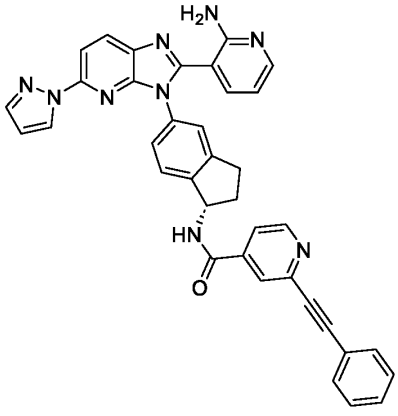
206	
207	
208	
209	

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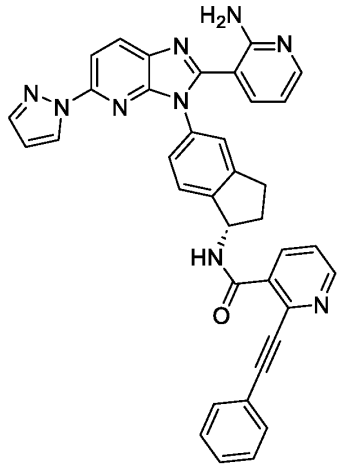
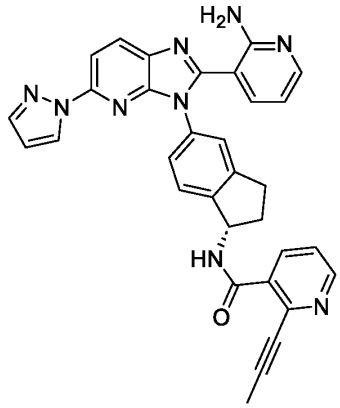
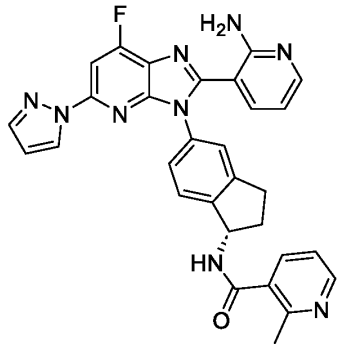
210	
211	
212	

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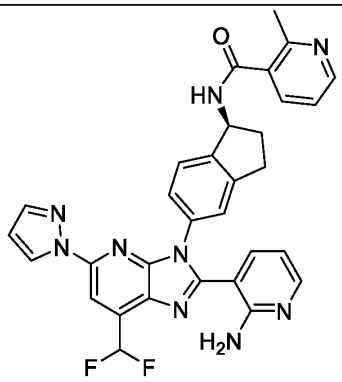
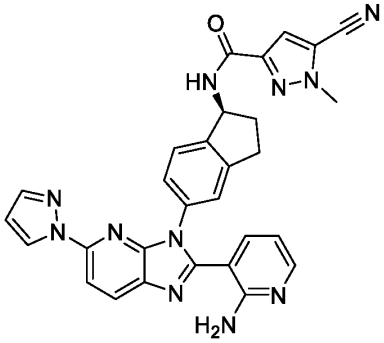
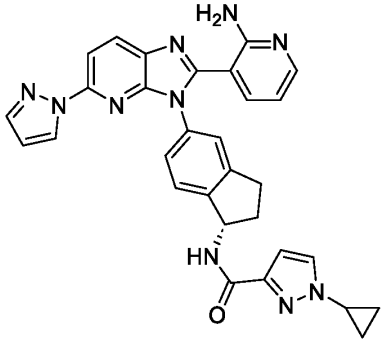
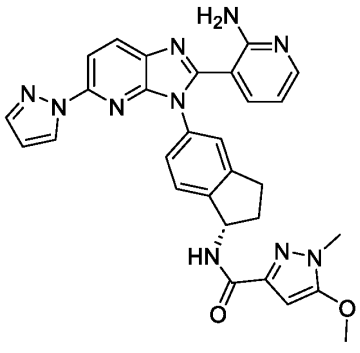
213	
214	
215	
216	

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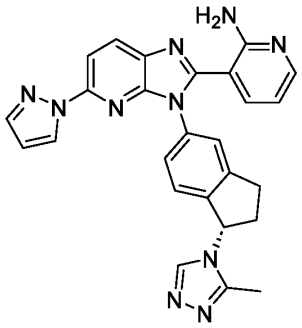
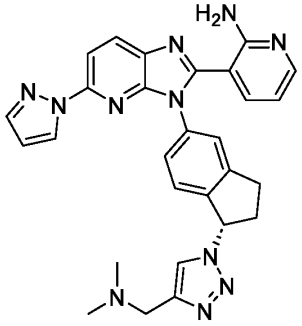
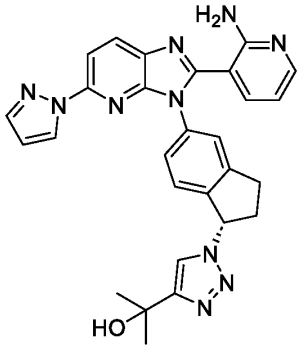
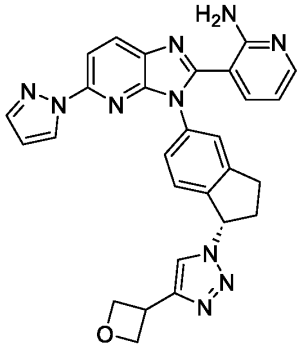
217	
218	
219	
220	

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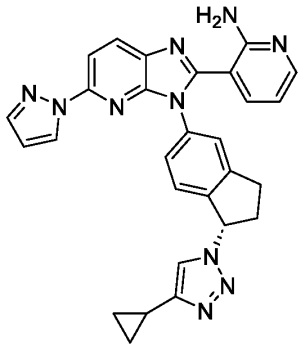
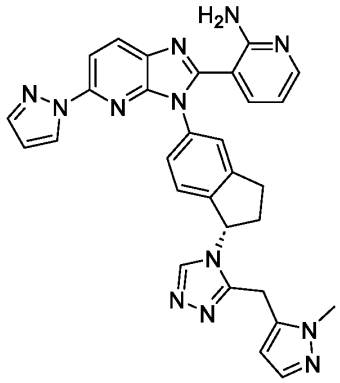
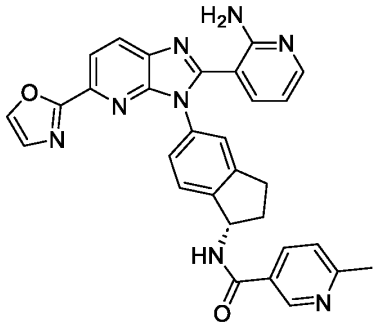
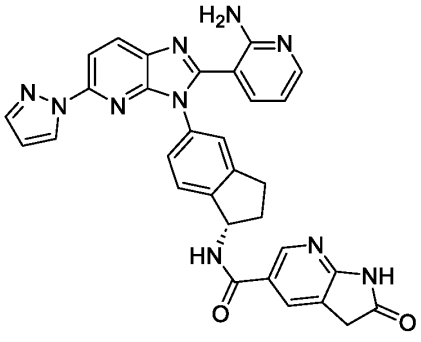
221	
222	
223	
224	

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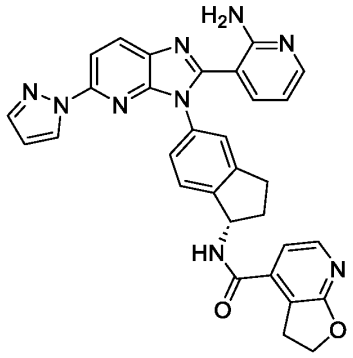
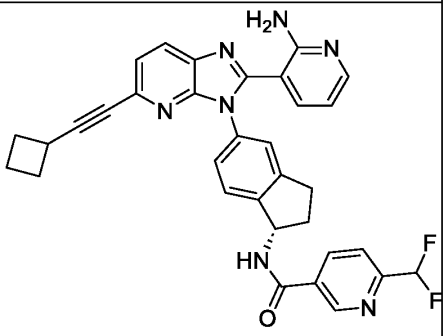
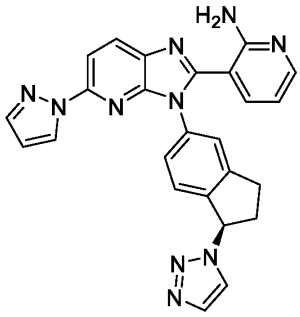
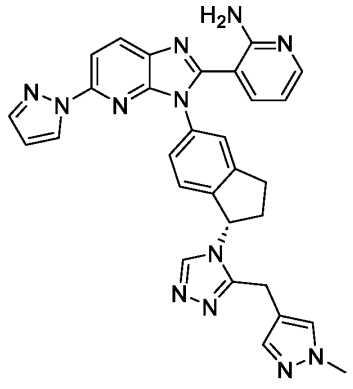
225	
226	
227	
228	

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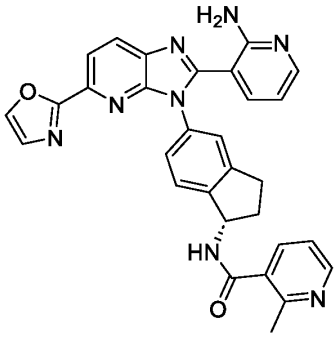
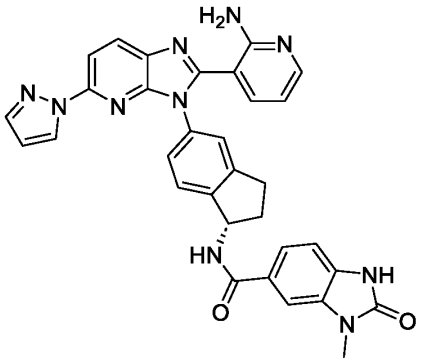
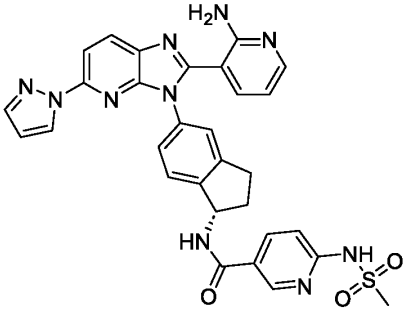
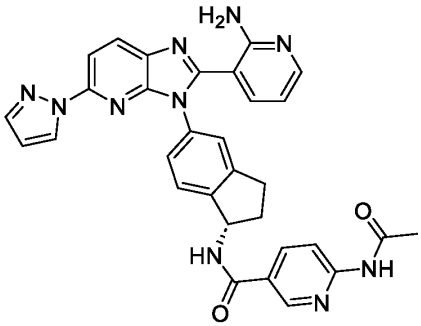
229	
230	
231	
232	

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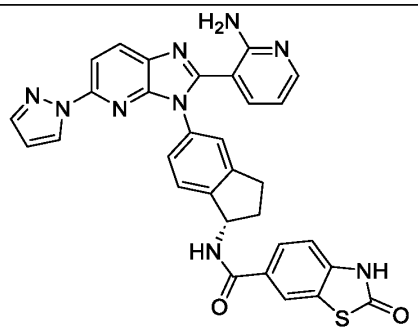
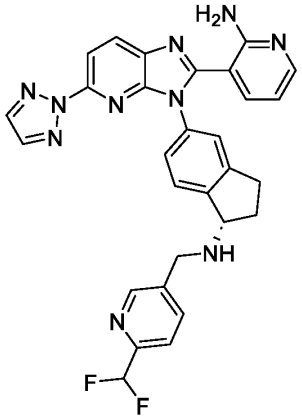
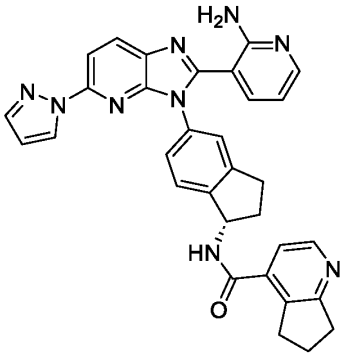
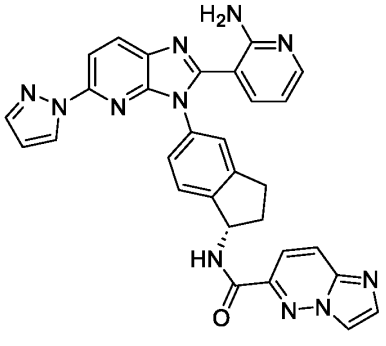
233	
234	
235	
236	

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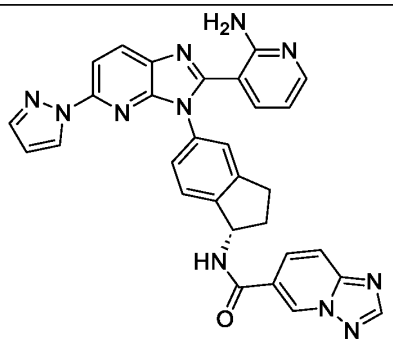
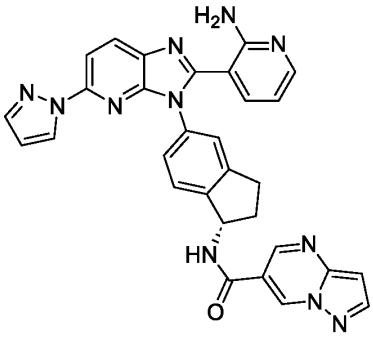
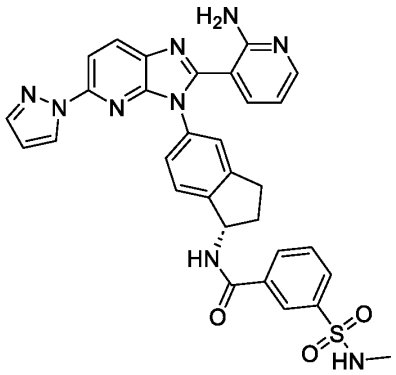
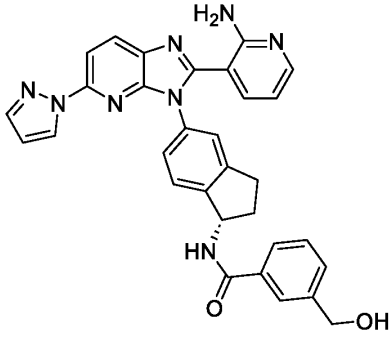
237	
238	
239	
240	

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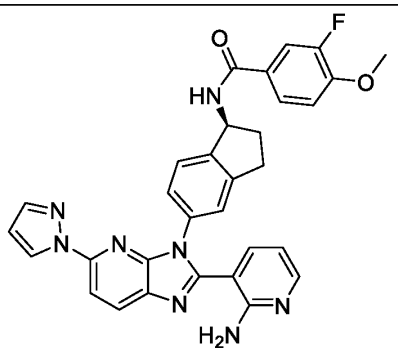
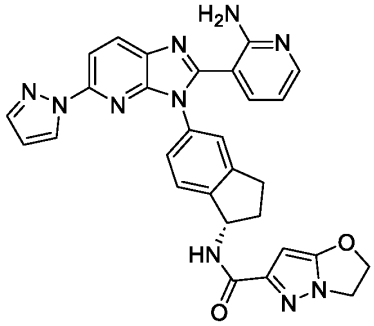
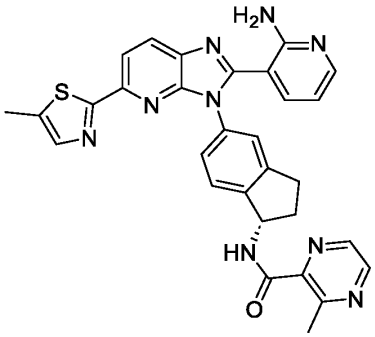
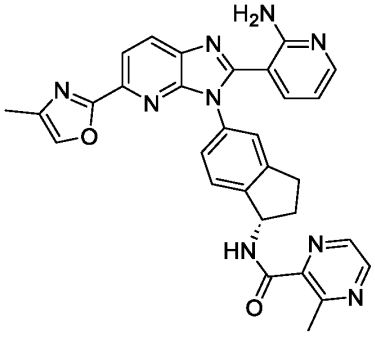
241	
242	
243	
244	

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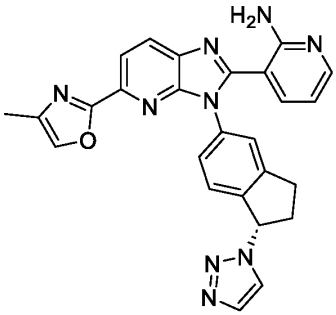
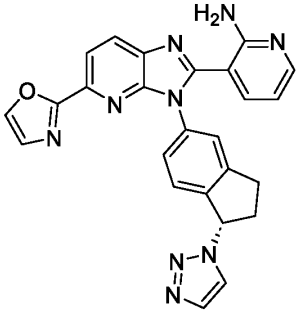
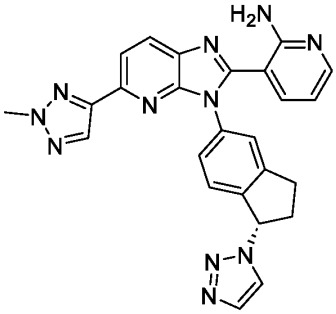
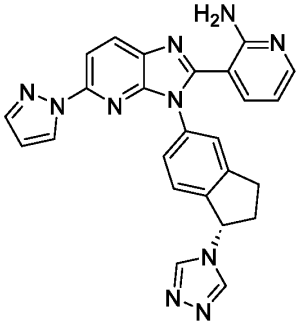
245	
246	
247	
248	

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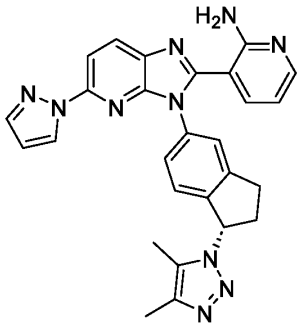
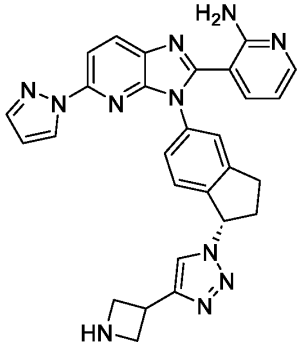
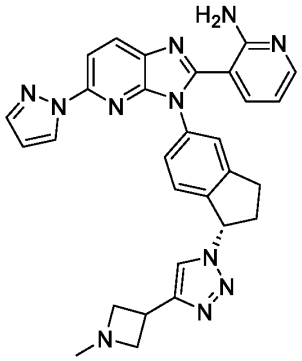
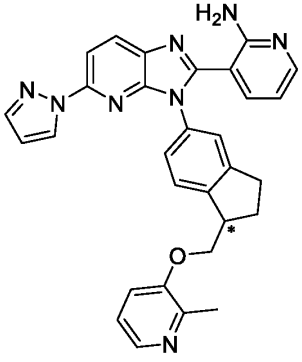
249	
250	
251	
252	

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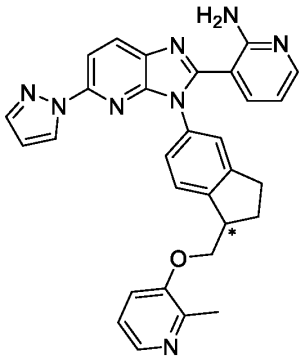
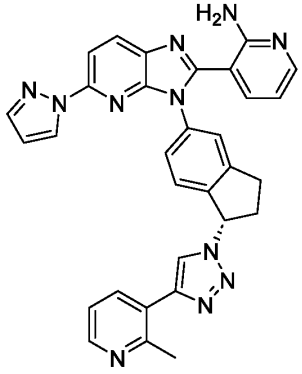
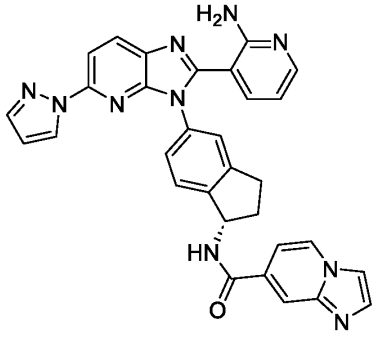
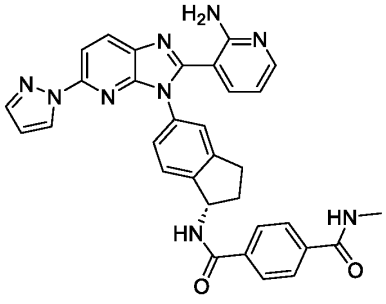
253	
254	
255	
256	

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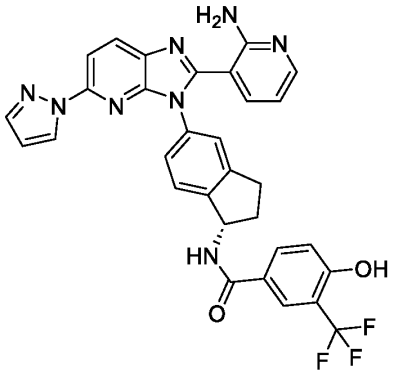
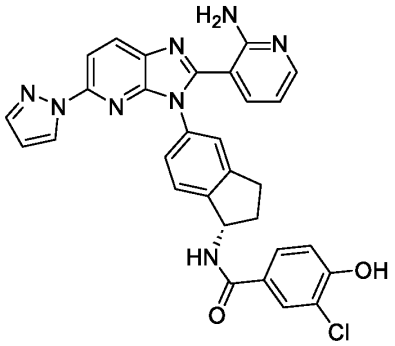
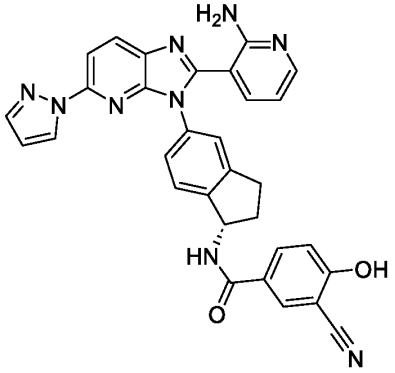
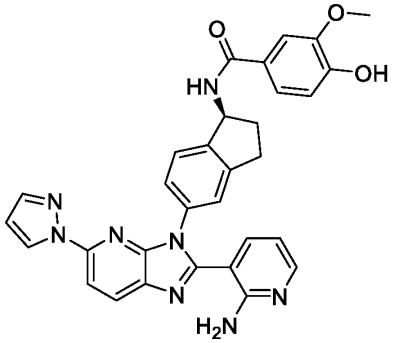
257	
258	
259	
260	

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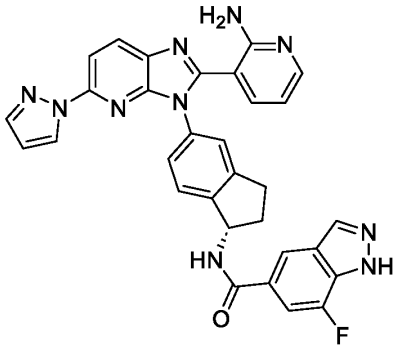
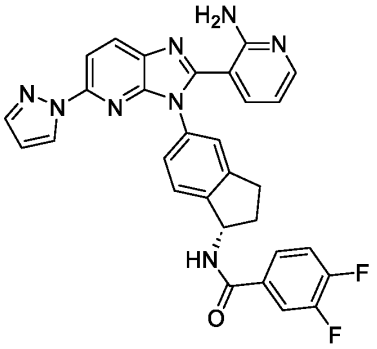
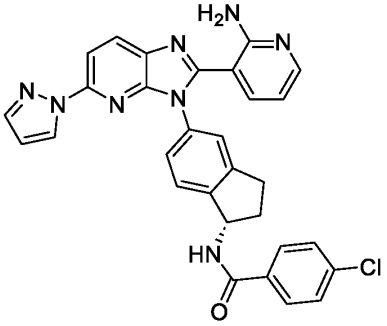
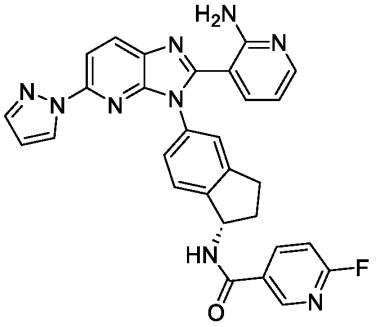
261	
262	
263	
264	

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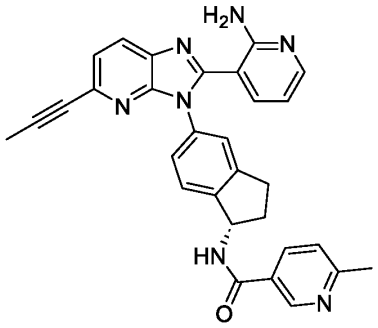
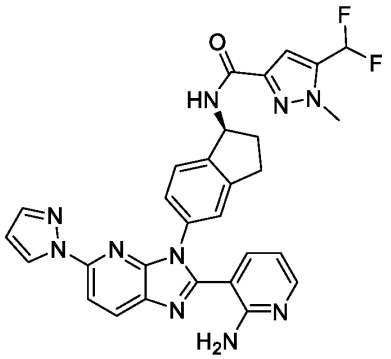
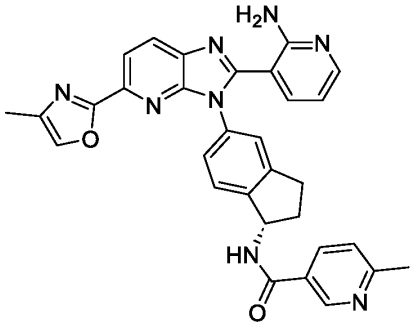
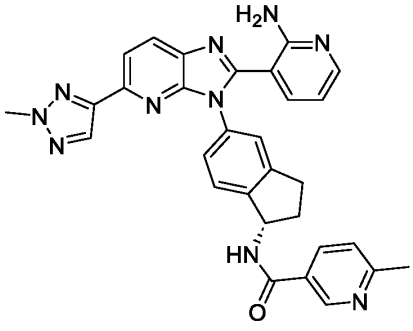
265	
266	
267	
268	

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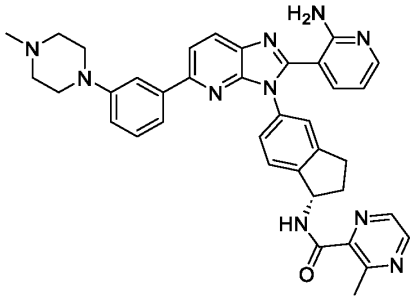
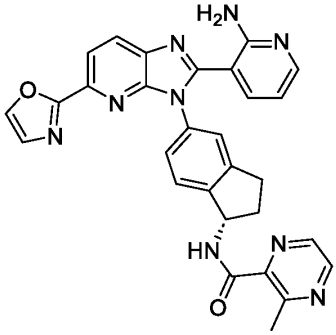
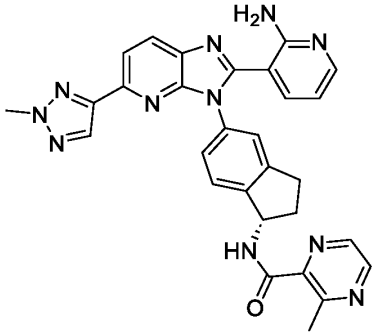
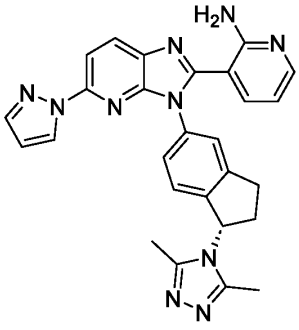
269	
270	
271	
272	

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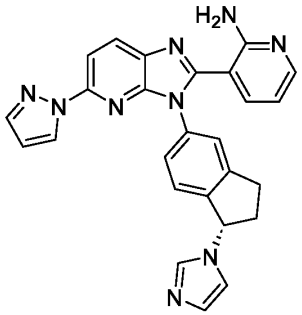
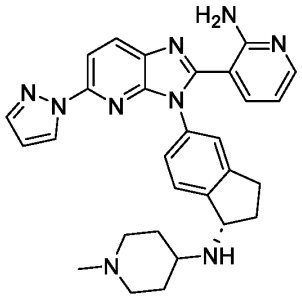
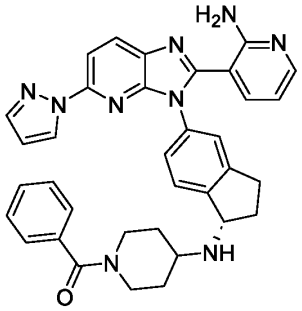
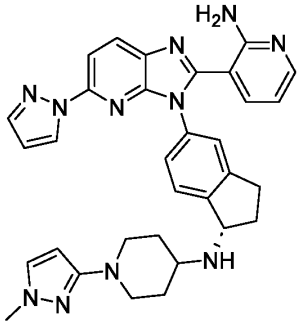
273	
274	
275	
276	

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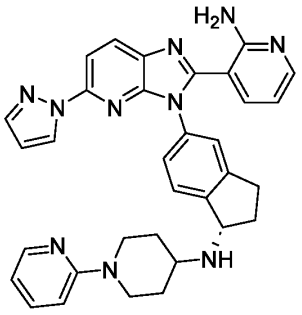
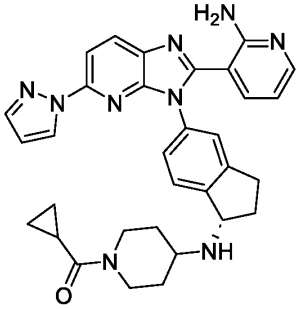
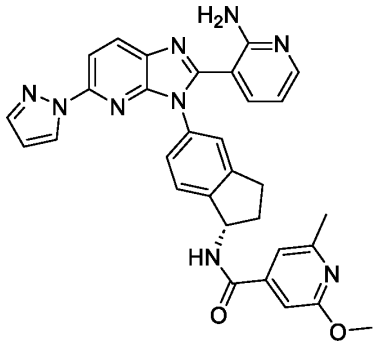
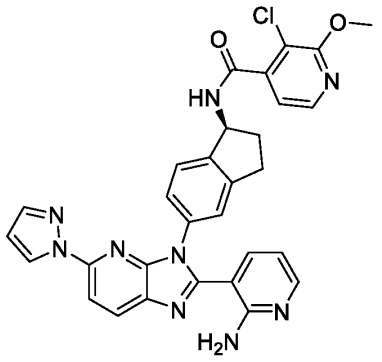
277	
279	
280	
281	

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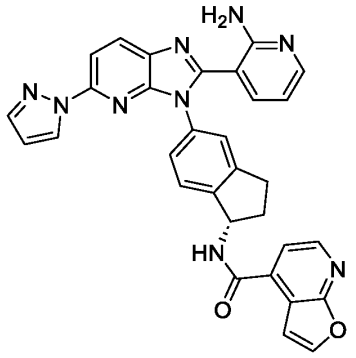
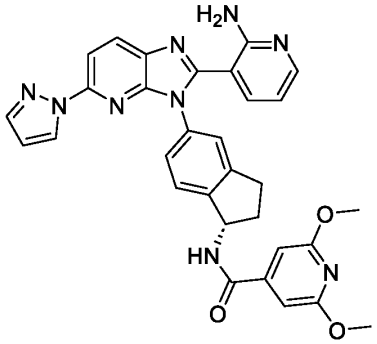
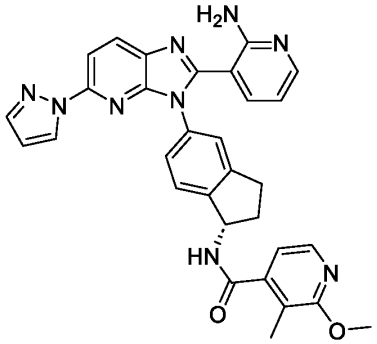
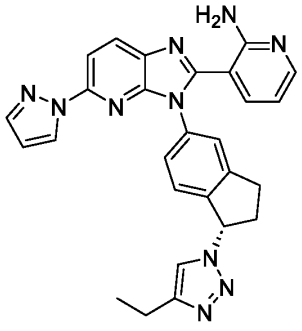
282	
283	
284	
285	

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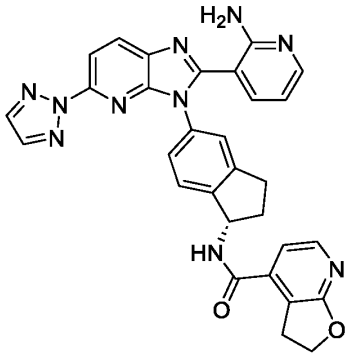
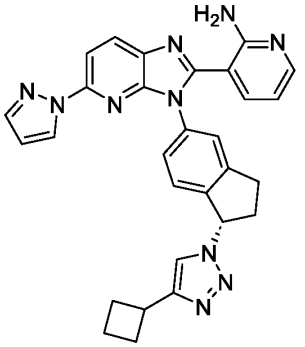
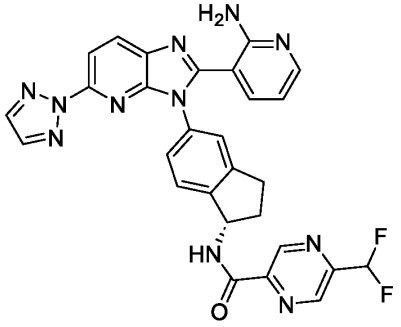
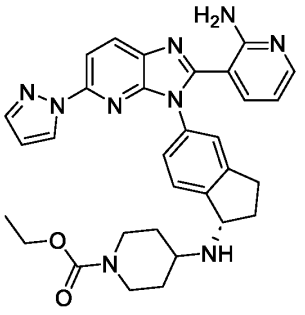
286	
287	
288	
289	

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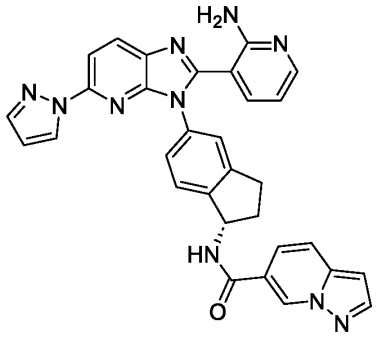
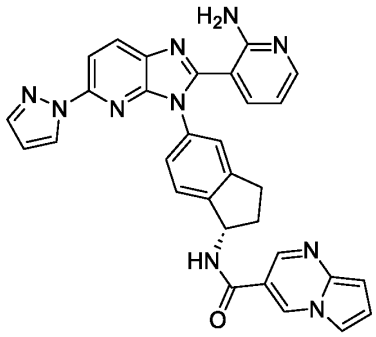
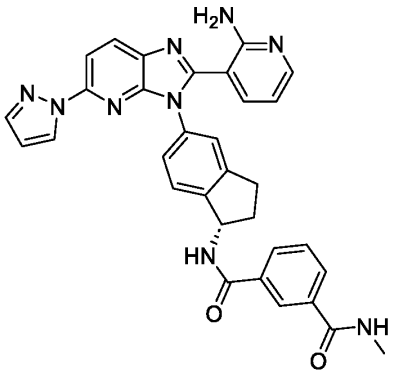
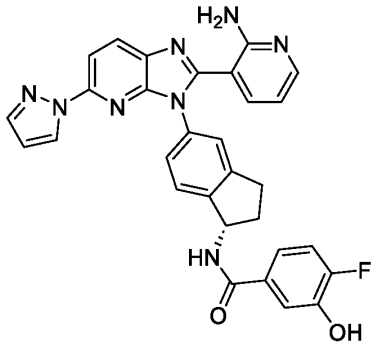
290	
291	
292	
293	

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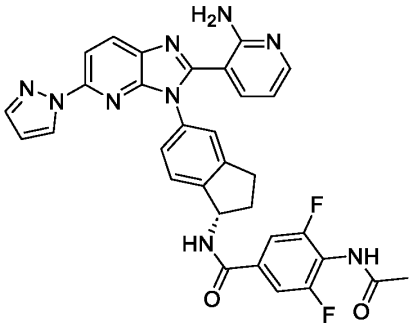
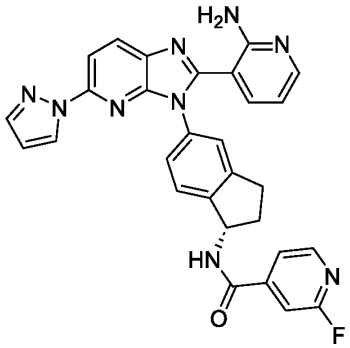
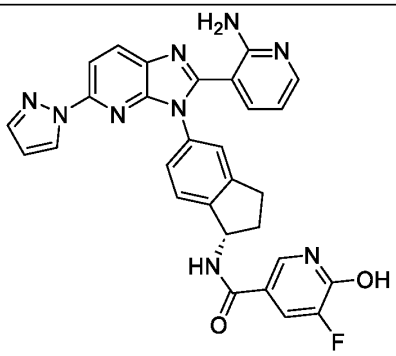
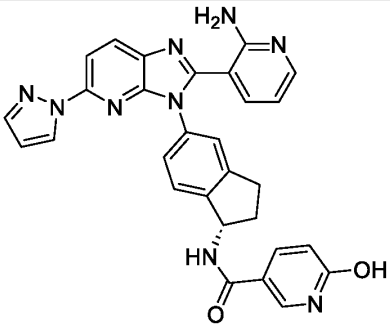
294	
295	
296	
297	

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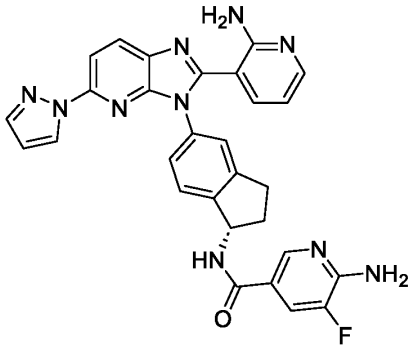
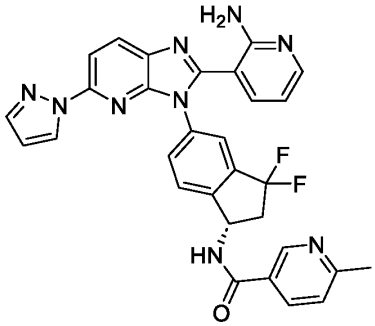
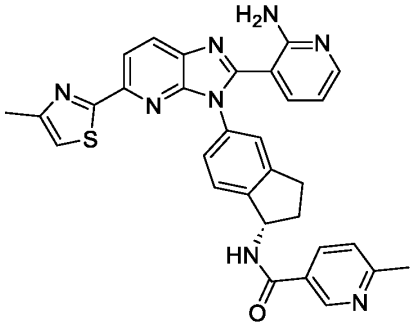
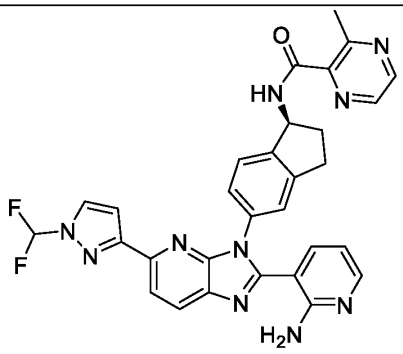
298	
299	
300	
301	

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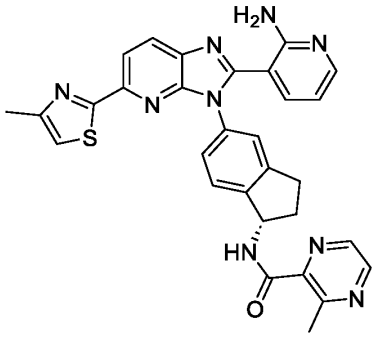
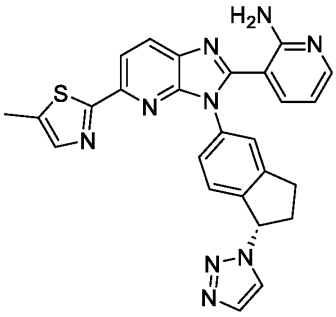
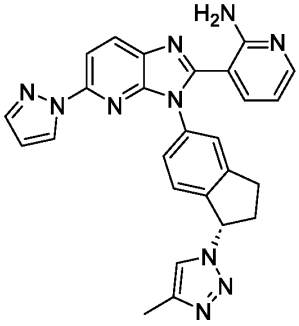
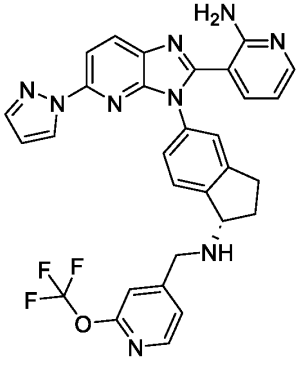
302	
303	
304	
305	

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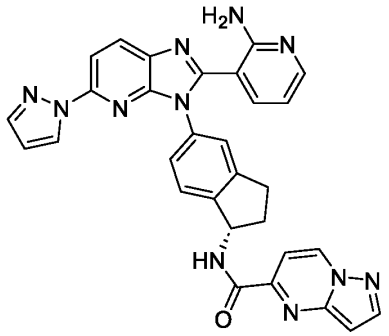
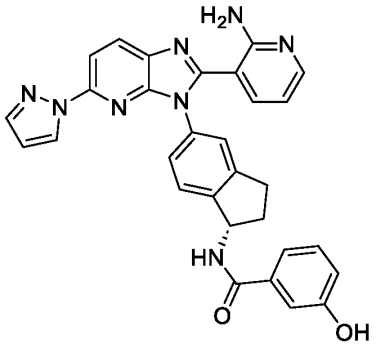
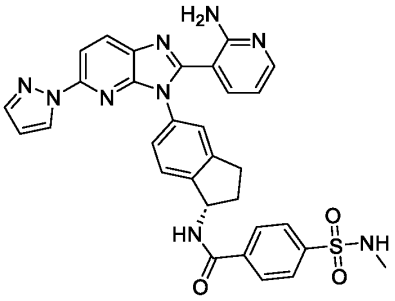
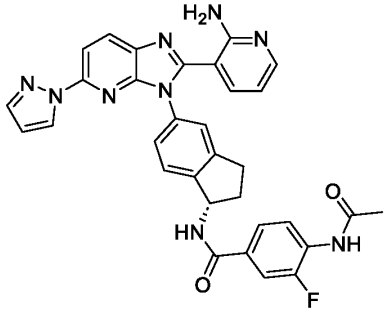
306	
307	
308	
309	

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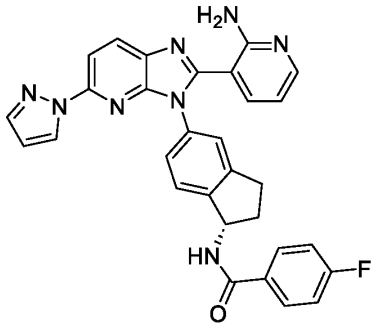
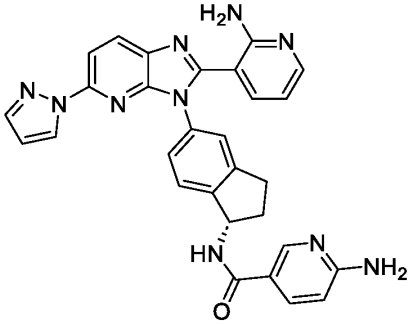
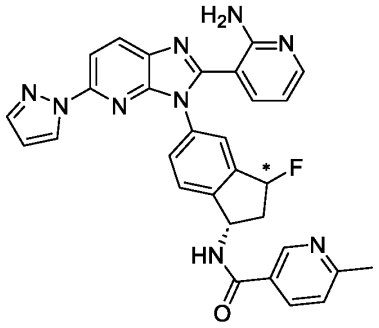
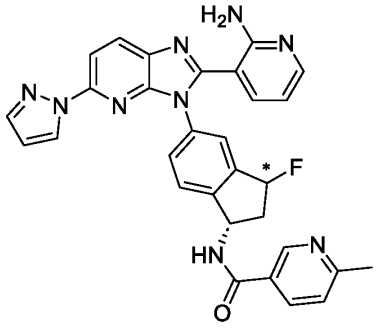
310	
311	
312	
313	

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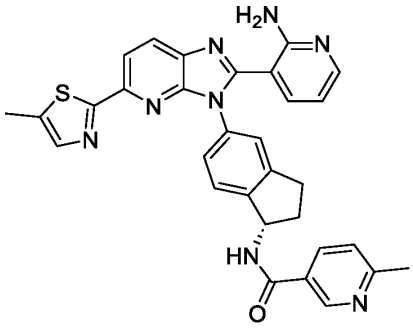
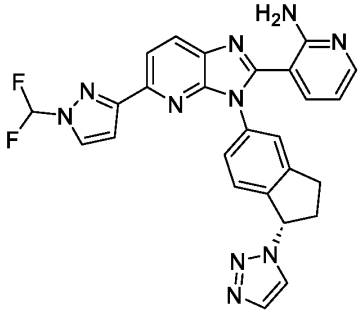
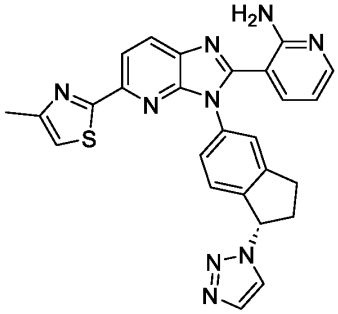
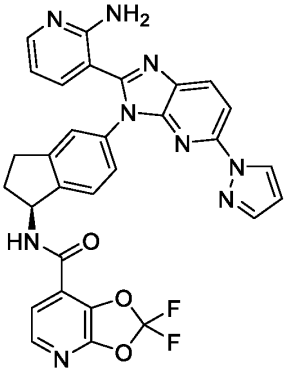
314	
315	
316	
317	

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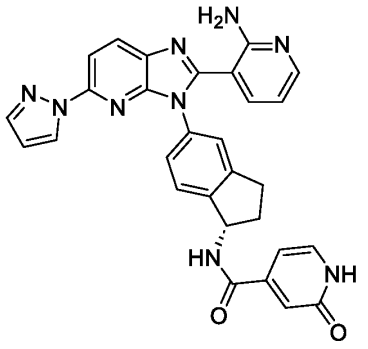
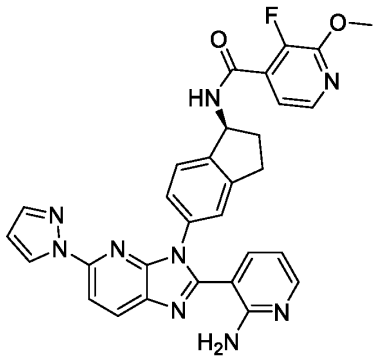
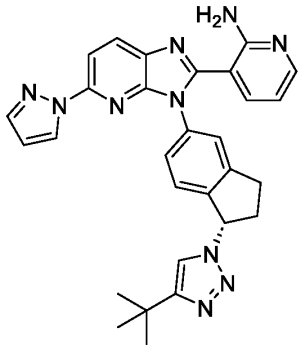
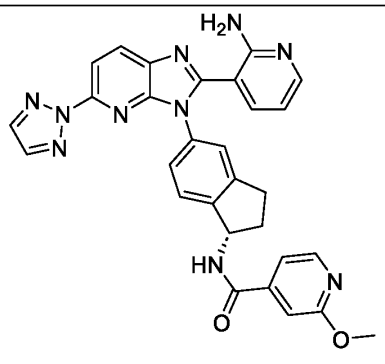
318	
319	
320	
321	

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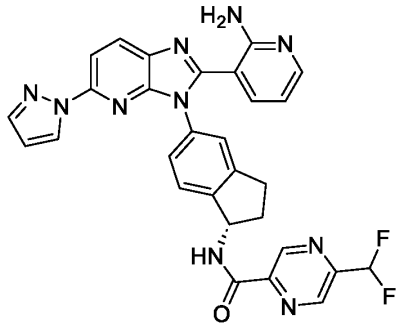
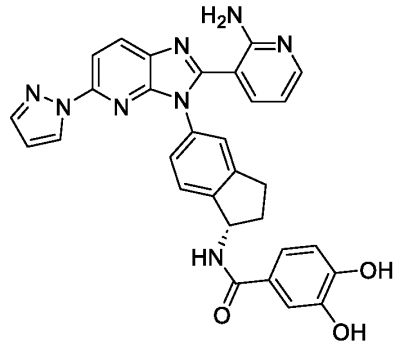
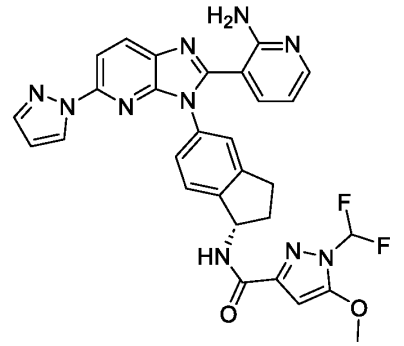
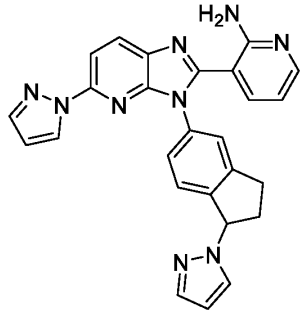
322	
323	
324	
325	

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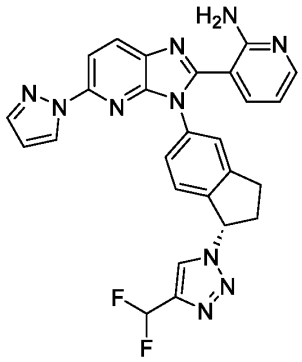
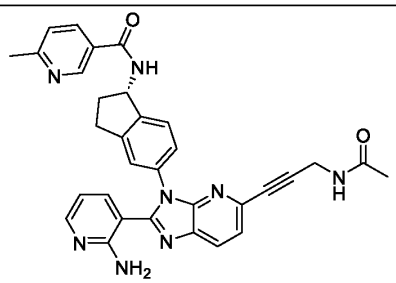
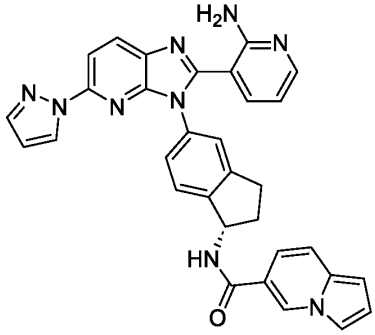
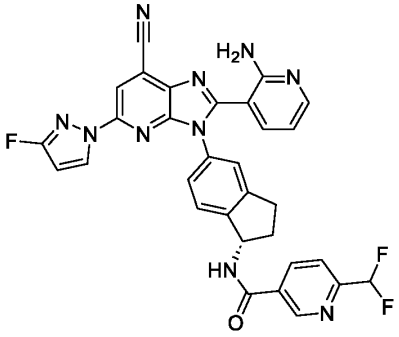
326	
327	
328	
329	

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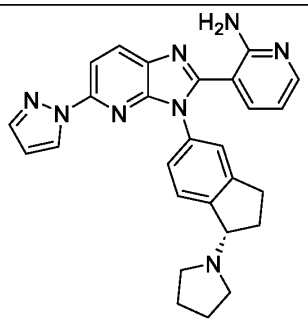
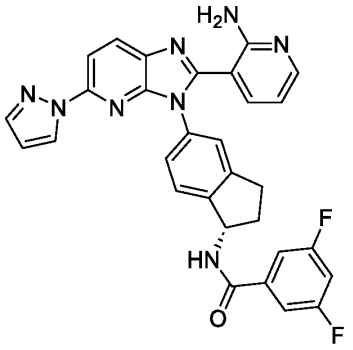
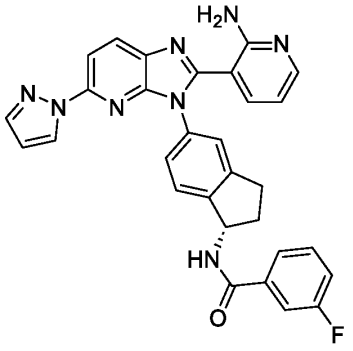
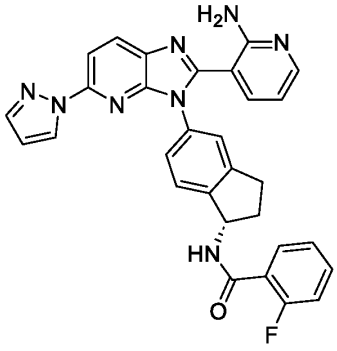
330	
331	
332	
333	

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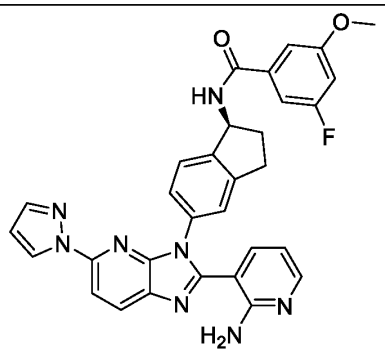
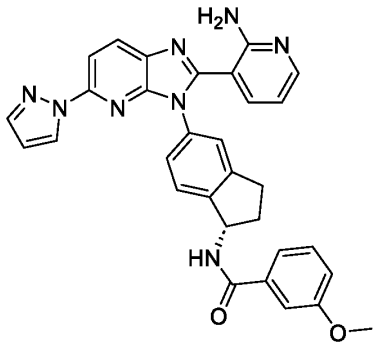
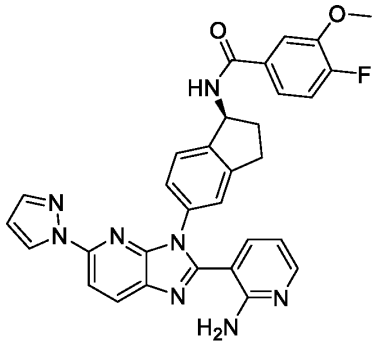
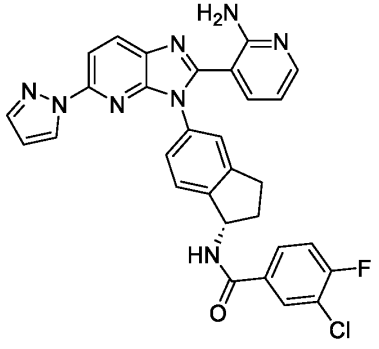
334	
335	
336	
337	

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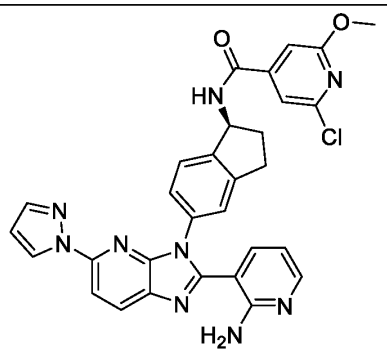
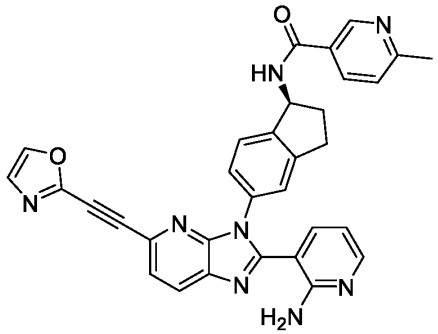
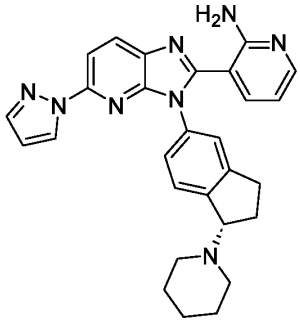
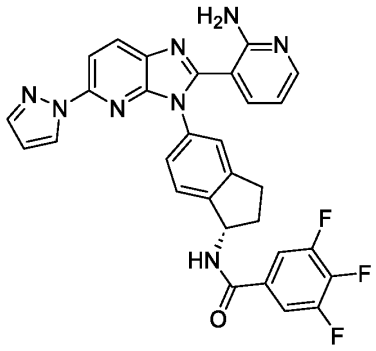
338	
341	
342	
343	

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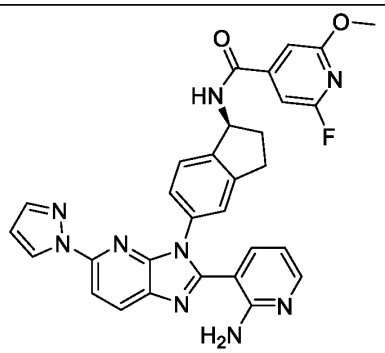
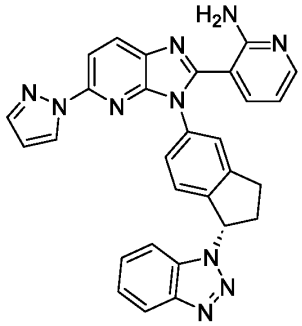
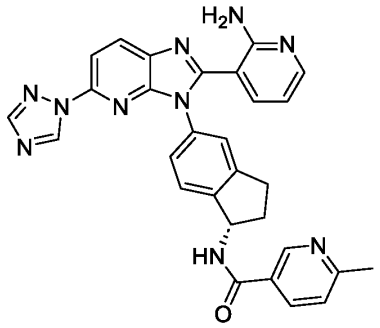
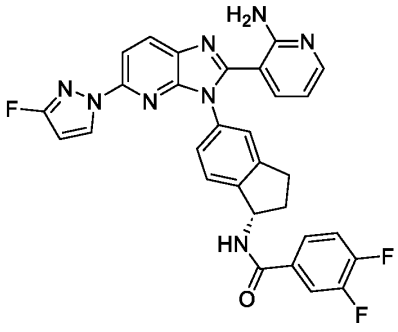
344	
345	
346	
347	

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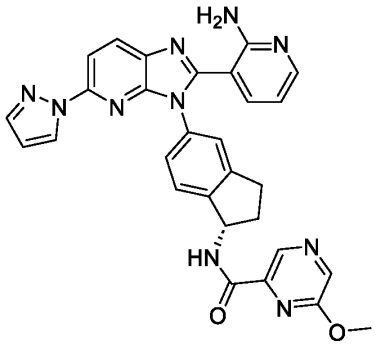
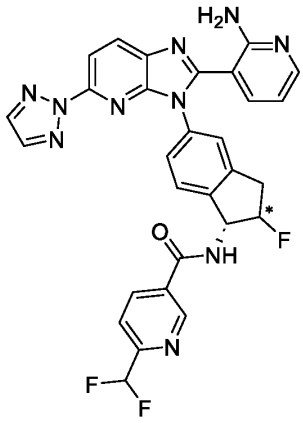
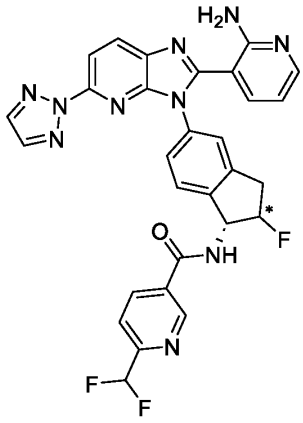
348	
349	
350	

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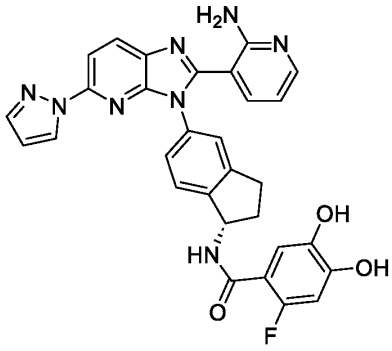
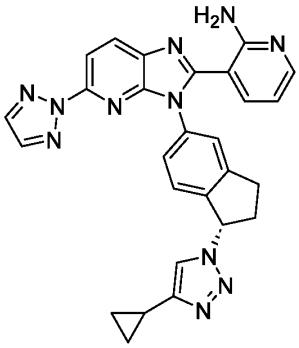
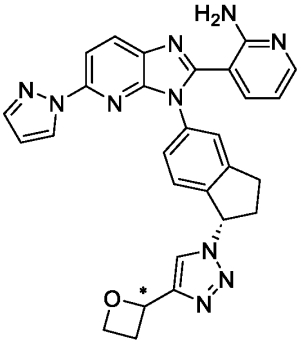
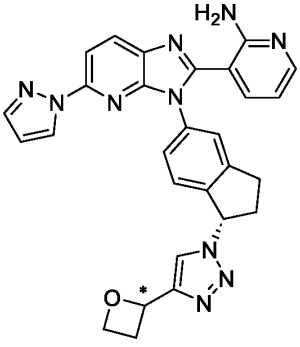
351	
352	
353	
354	

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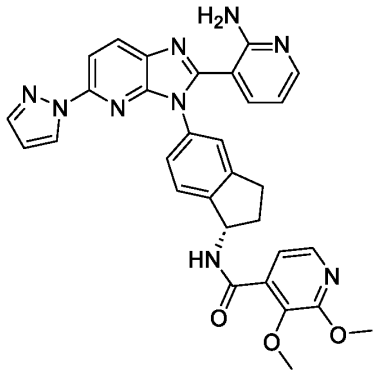
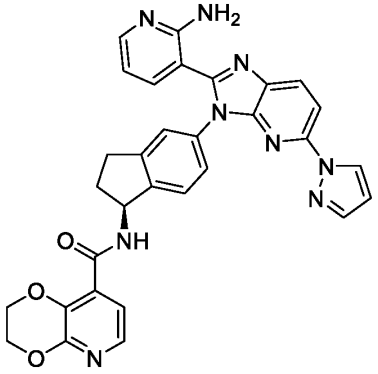
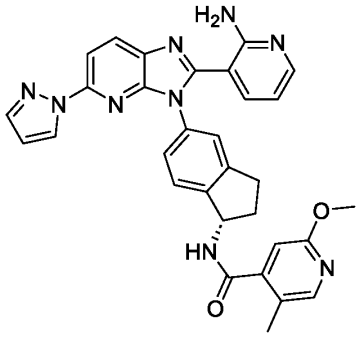
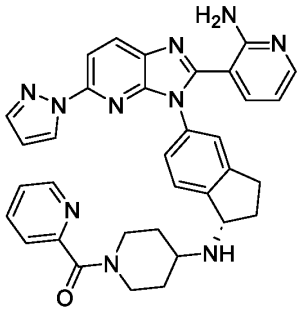
355	
356	
357	
358	

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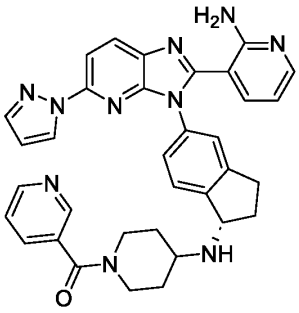
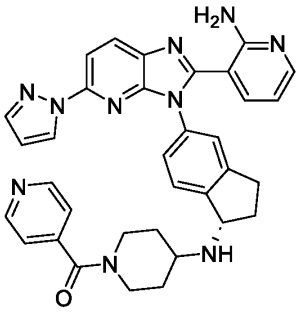
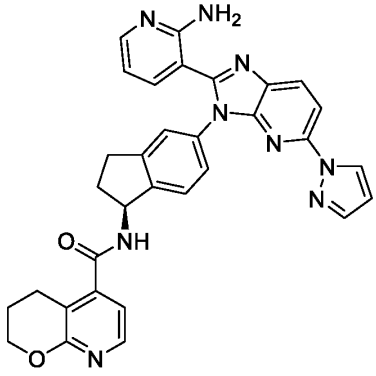
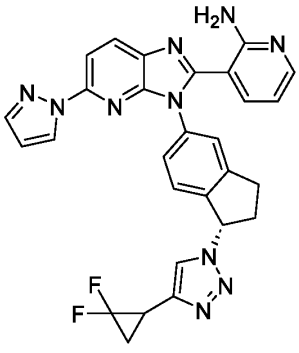
359	
360	
361	
362	

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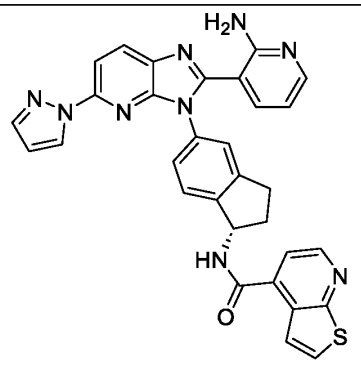
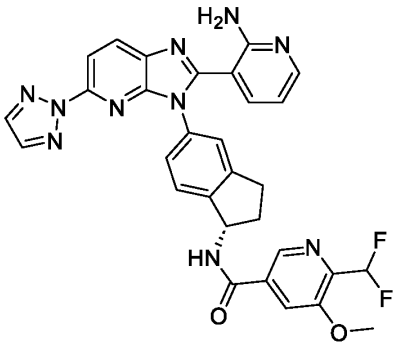
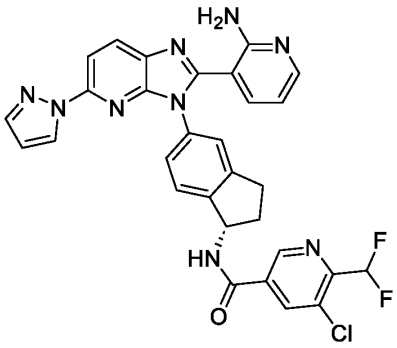
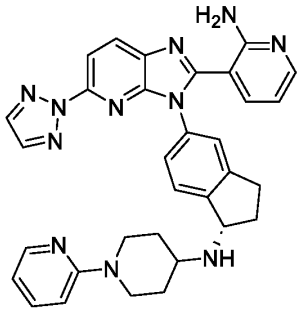
363	
364	
365	
366	

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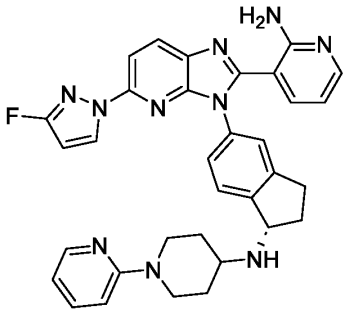
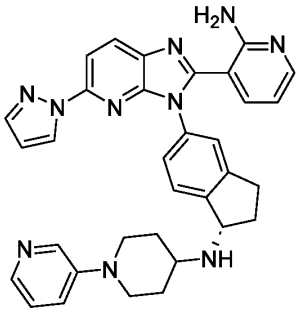
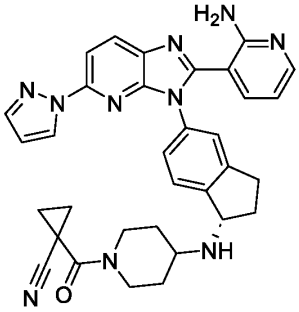
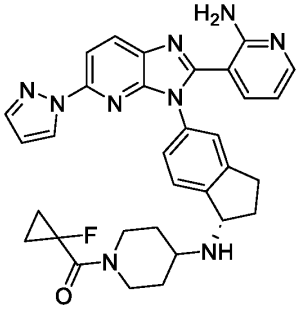
367	
368	
369	
370	

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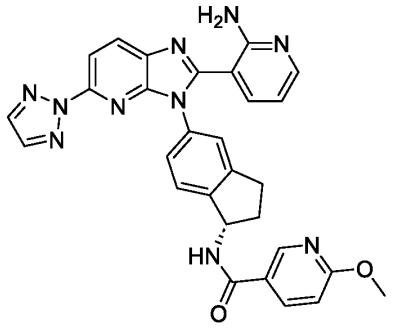
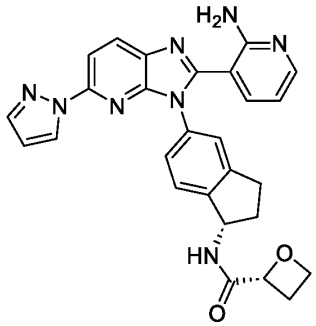
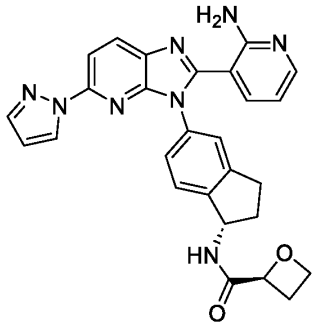
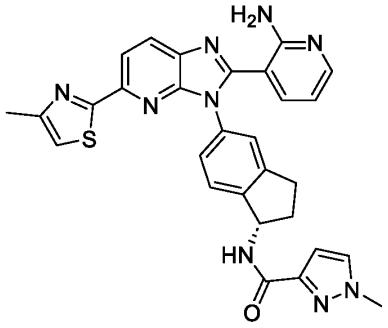
371	
372	
373	
374	

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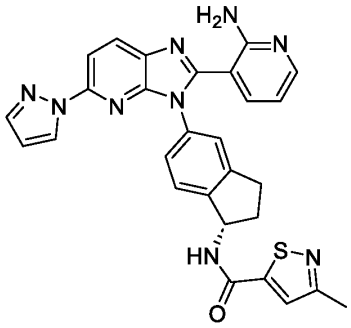
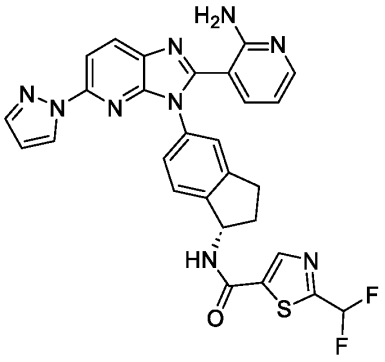
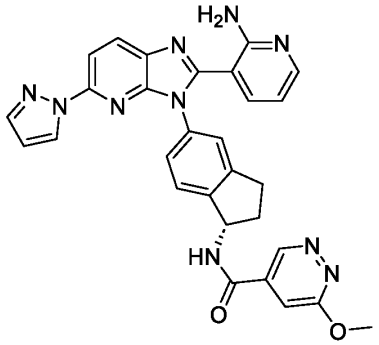
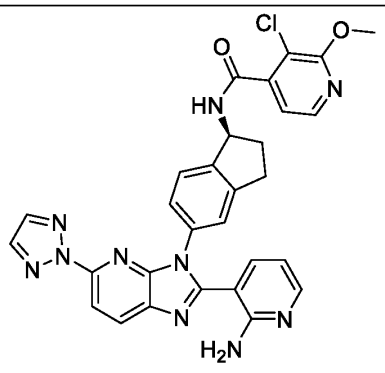
375	
376	
377	
378	

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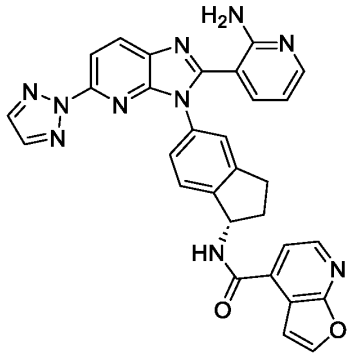
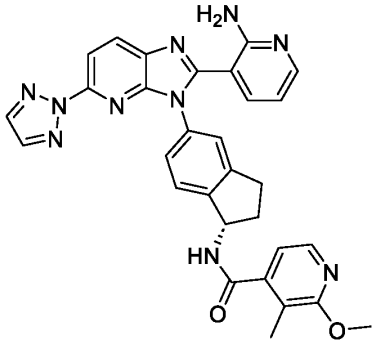
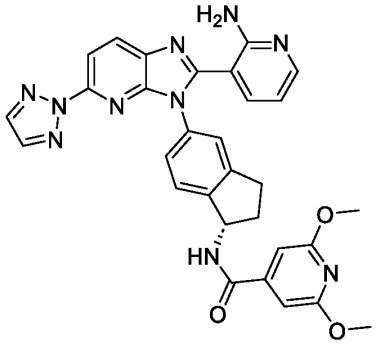
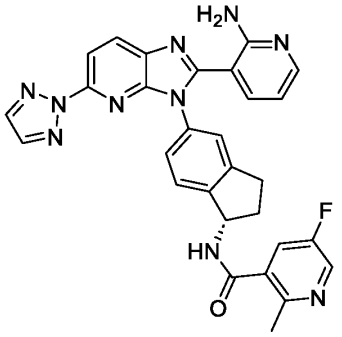
379	
380	
381	
382	

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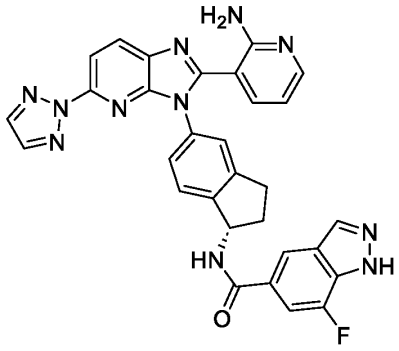
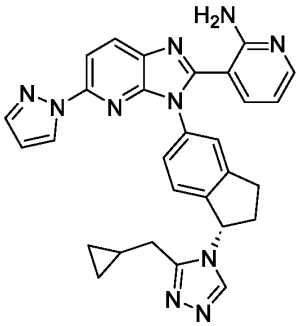
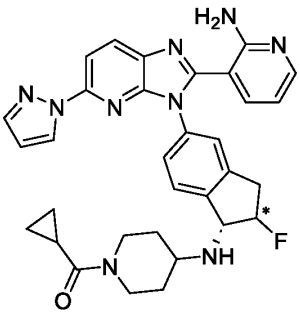
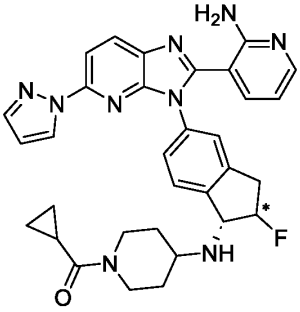
383	
384	
385	
386	

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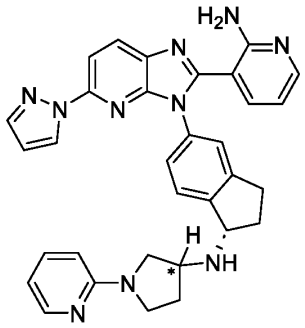
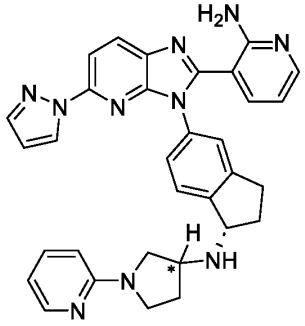
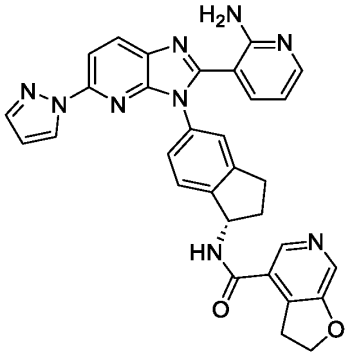
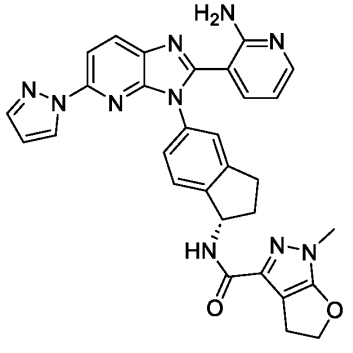
387	
388	
389	
390	

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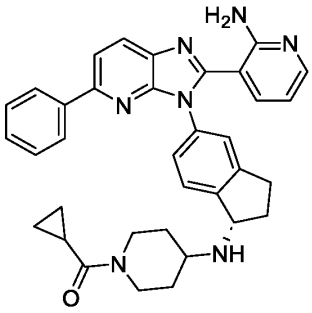
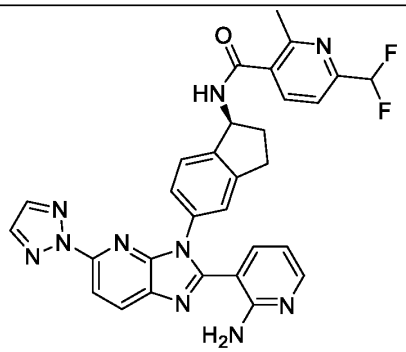
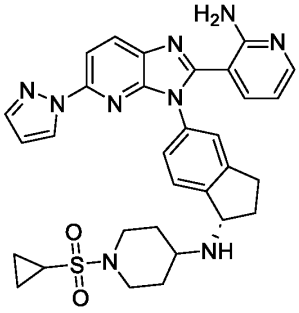
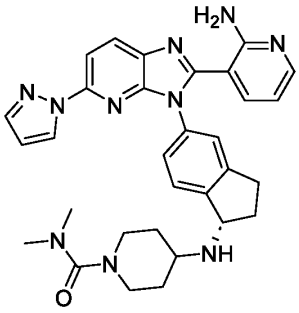
391	
392	
393	
394	

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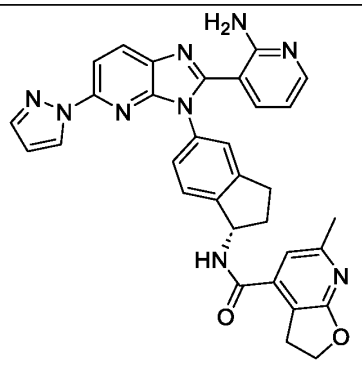
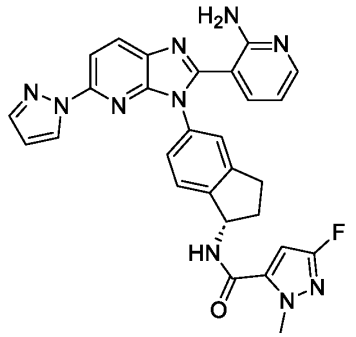
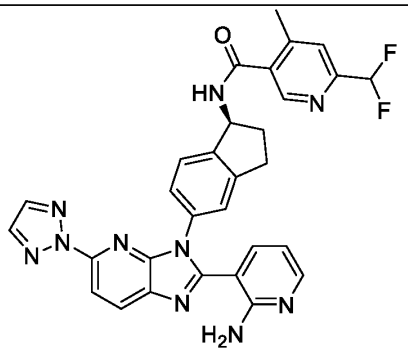
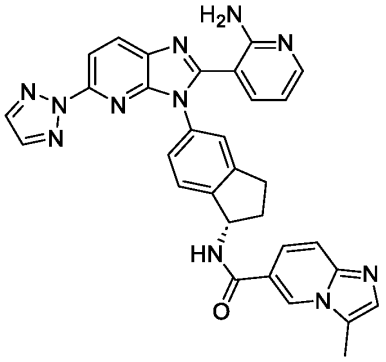
395	
396	
397	
398	

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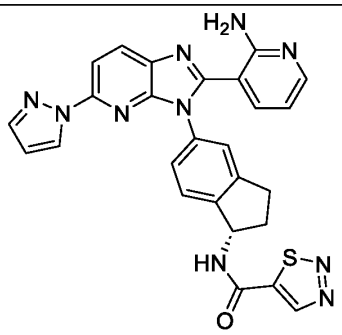
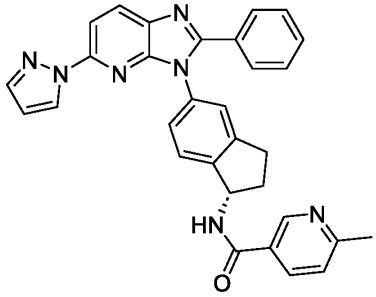
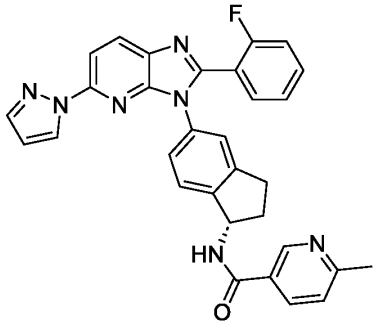
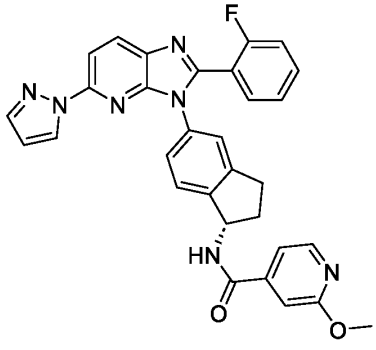
399	
400	
401	
402	

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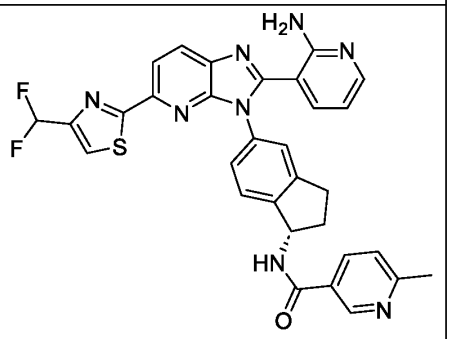
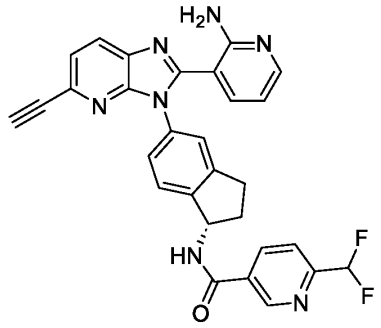
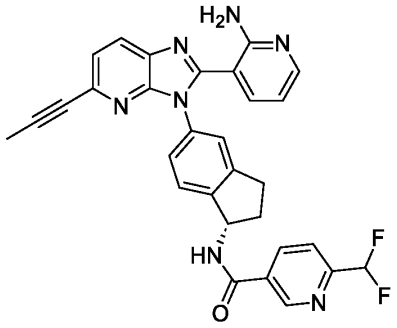
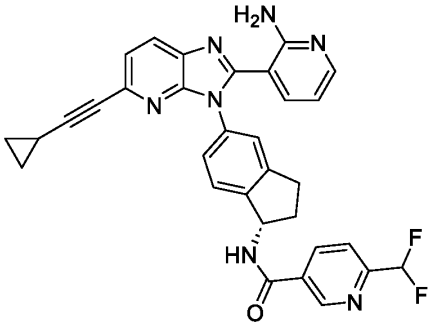
403	
404	
405	
406	

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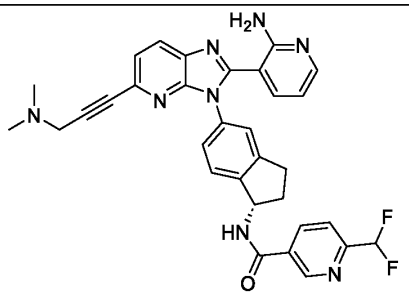
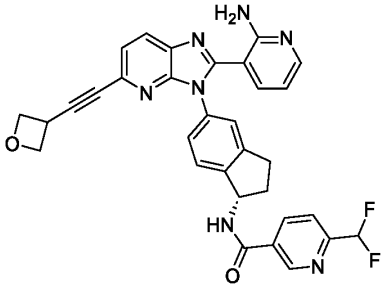
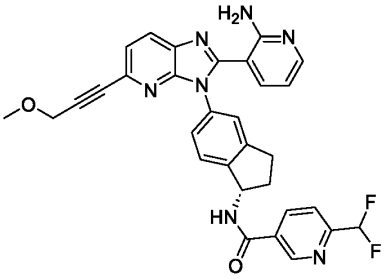
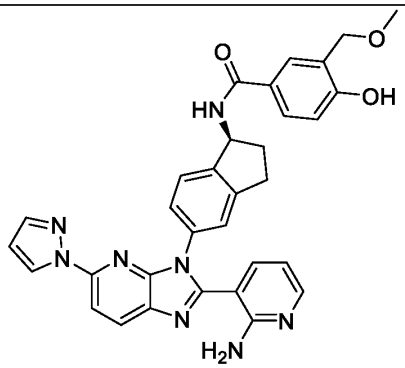
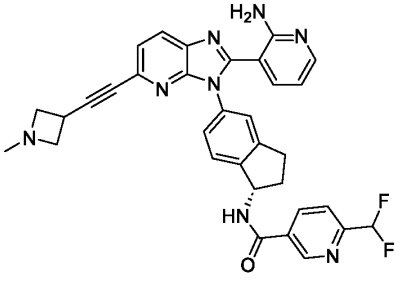
407	
408	
409	
410	
411	

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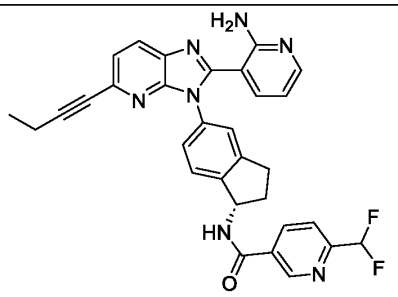
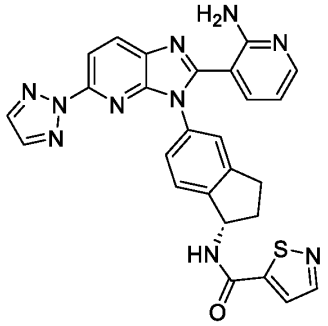
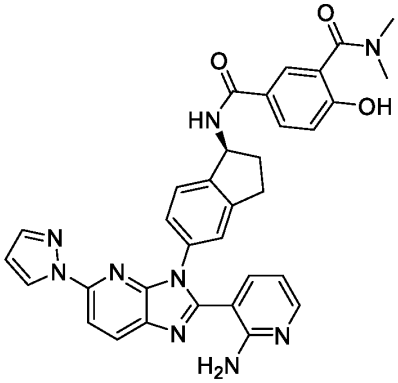
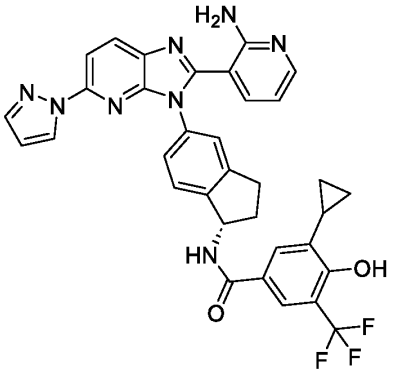
412	
413	
414	
415	

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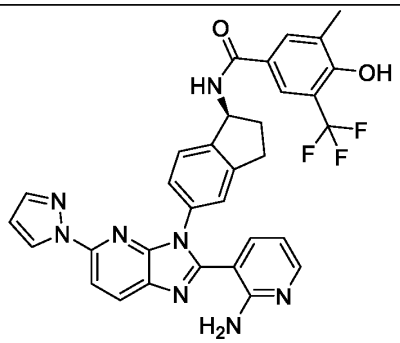
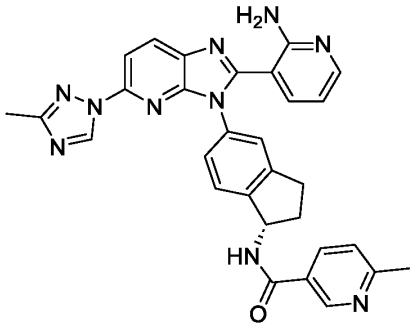
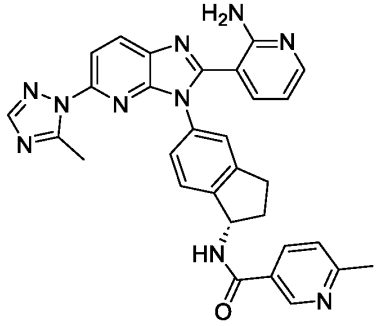
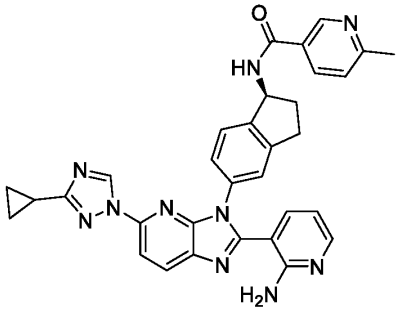
416	
417	
418	
419	

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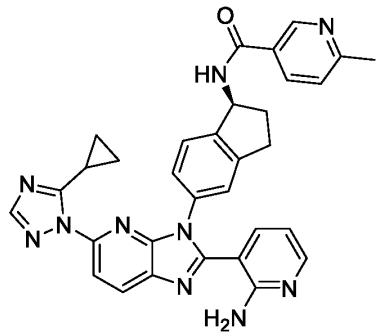
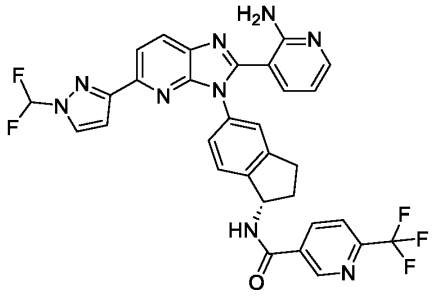
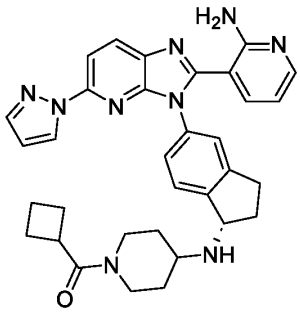
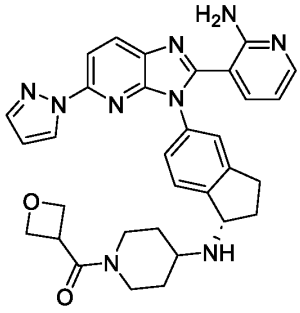
420	
421	
422	
423	

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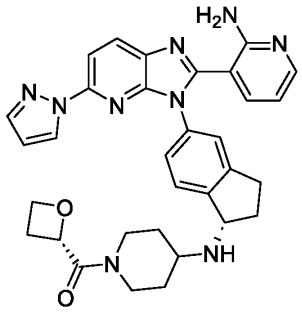
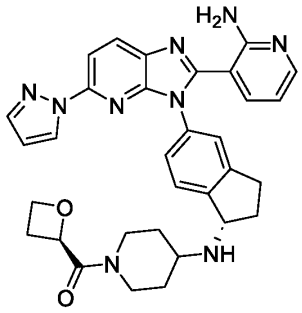
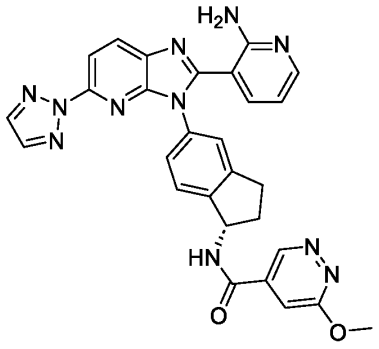
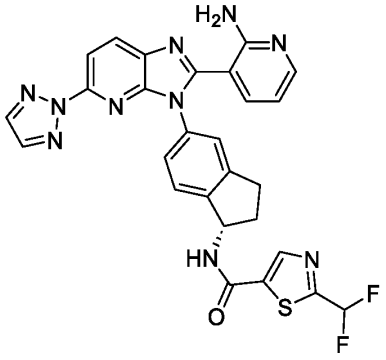
424	
425	
426	
427	

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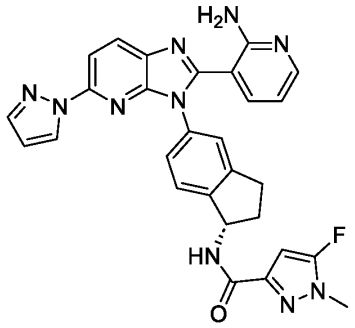
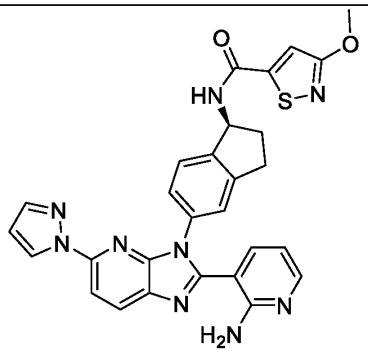
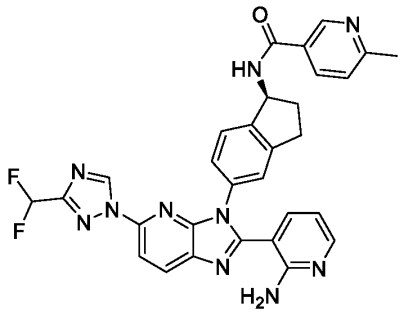
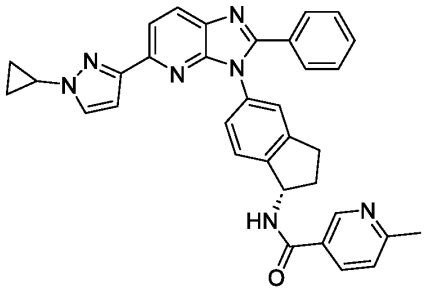
428	
429	
430	
431	

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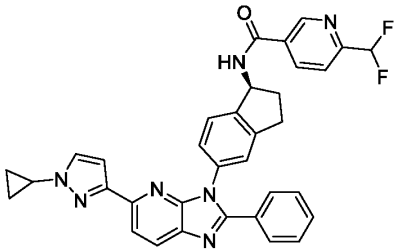
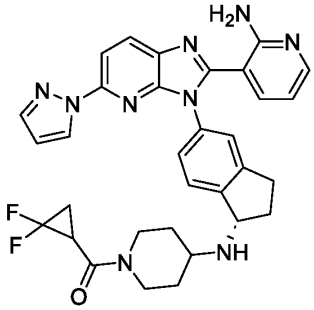
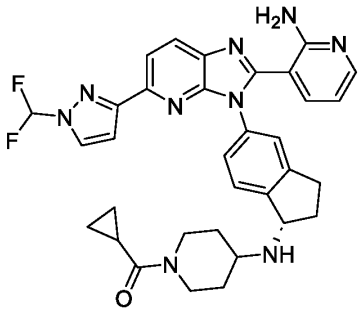
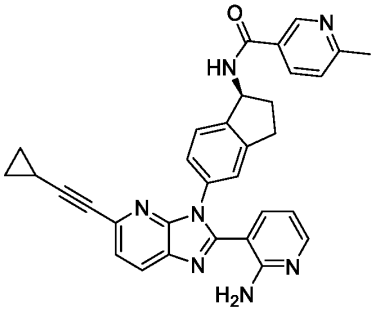
432	
433	
434	
435	

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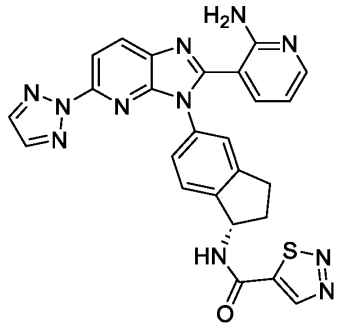
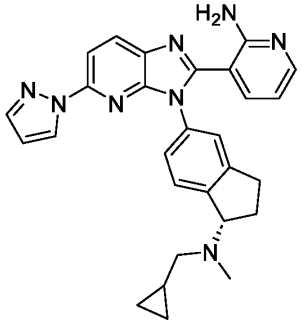
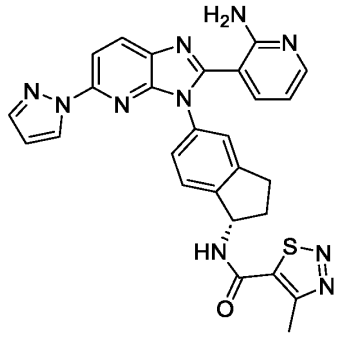
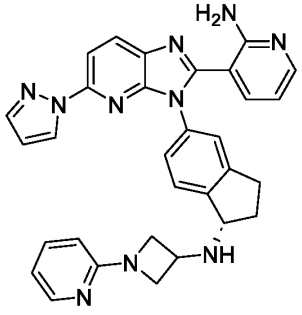
436	
437	
438	
439	

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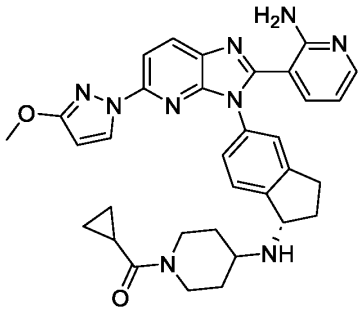
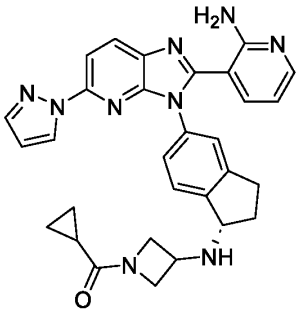
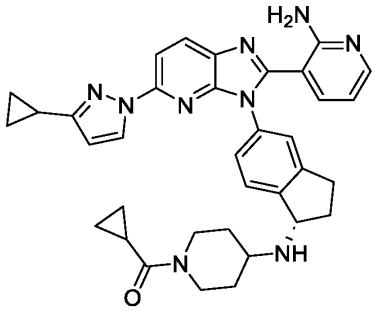
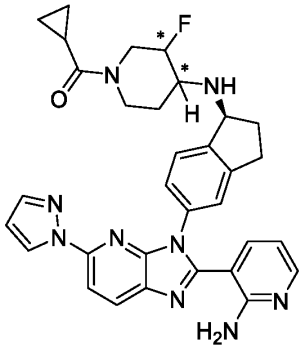
440	
441	
442	
443	

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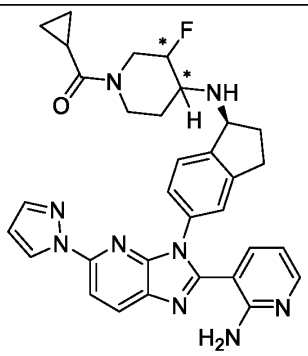
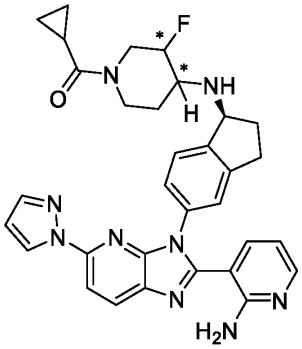
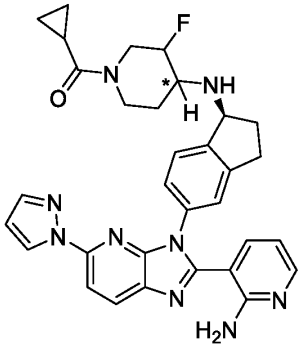
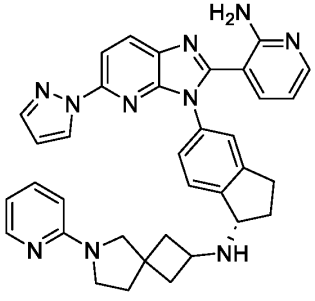
444	
445	
446	
447	

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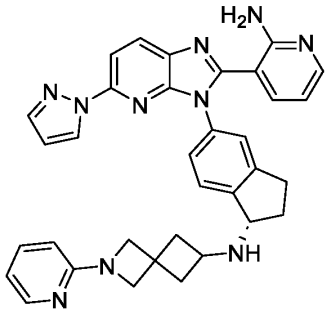
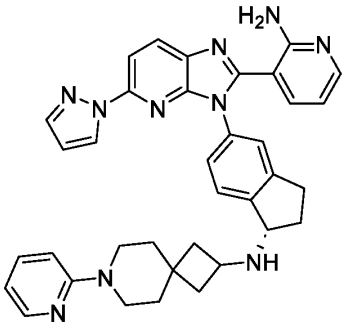
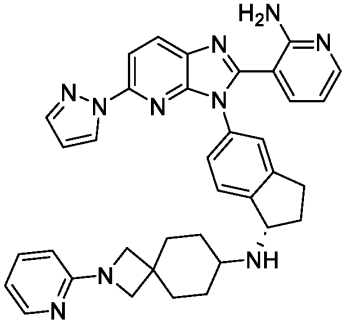
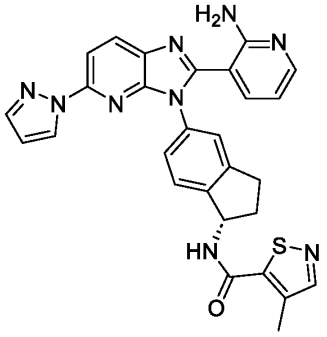
448	
449	
450	
451	

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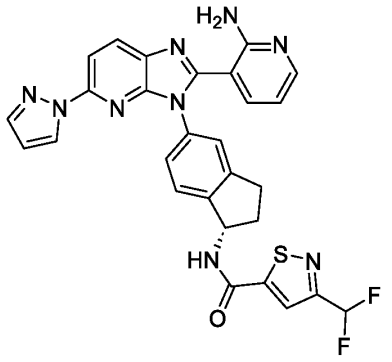
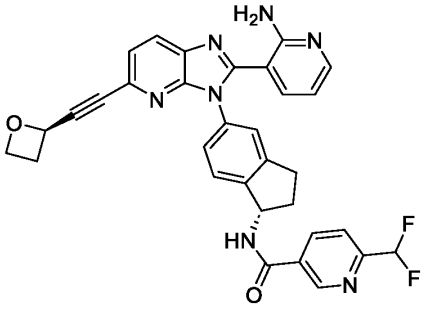
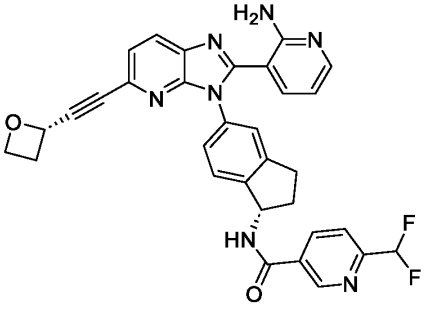
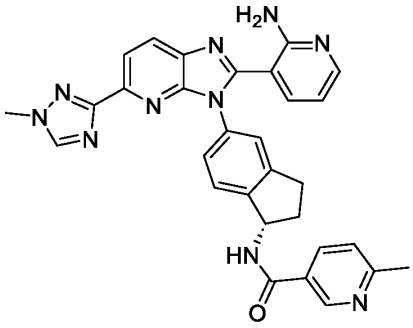
452	
453	
454	
455	

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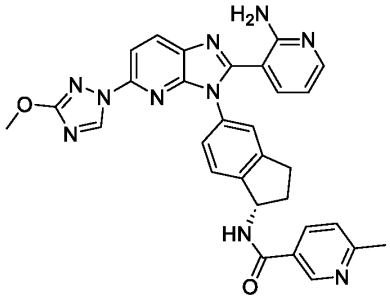
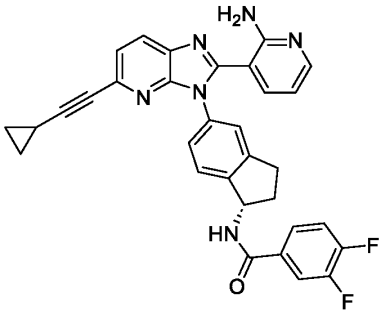
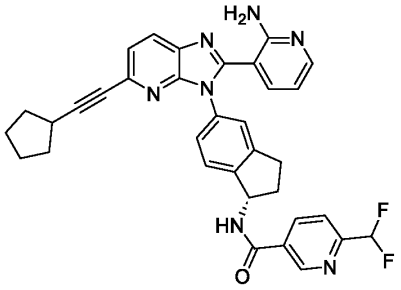
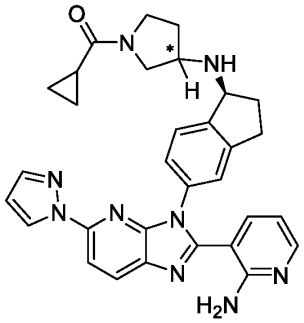
456	
459	
460	
461	

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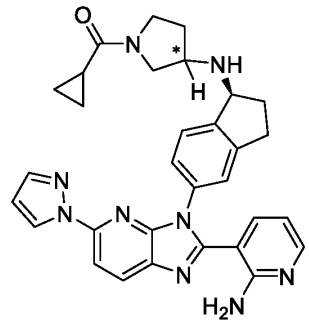
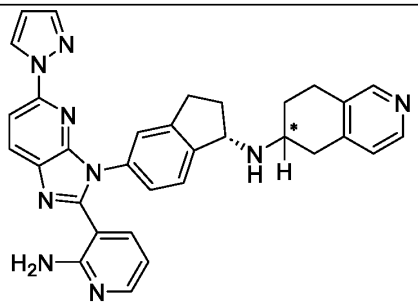
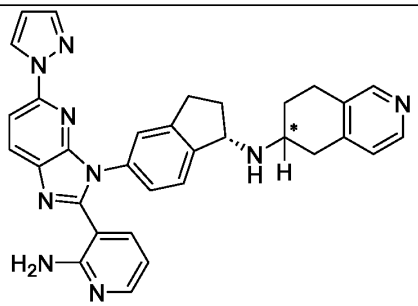
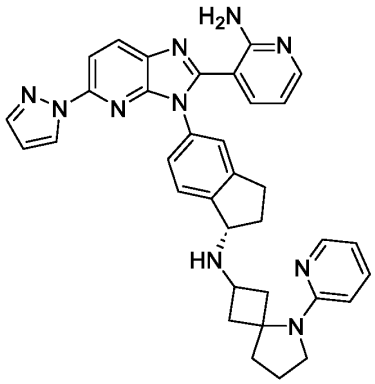
462	
463	
464	
465	

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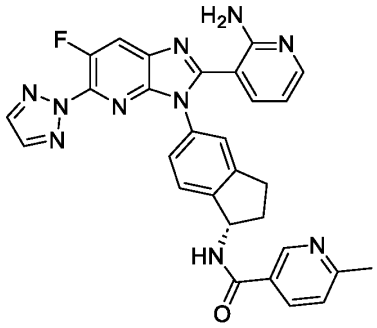
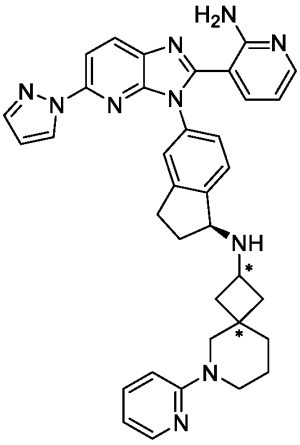
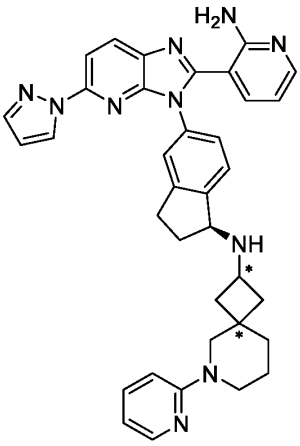
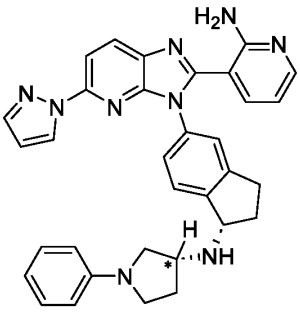
466	
467	
468	
469	

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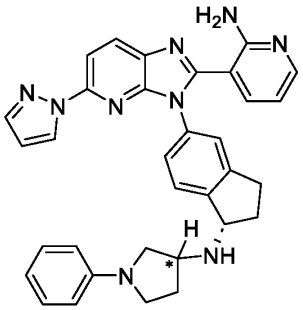
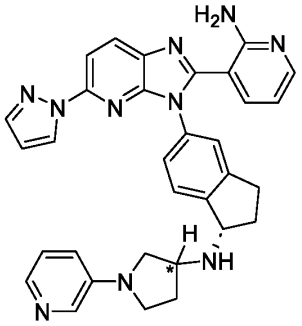
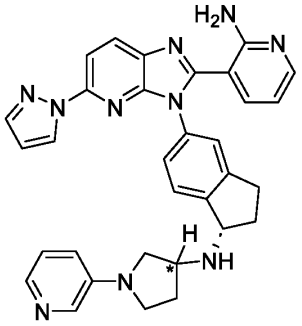
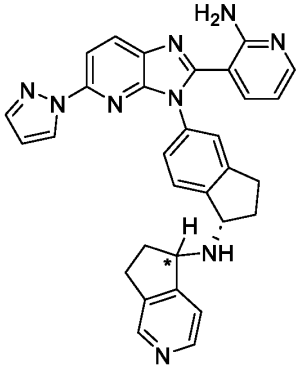
470	
471	
472	
473	

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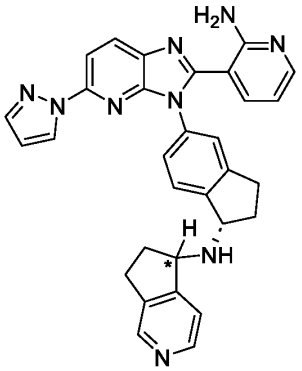
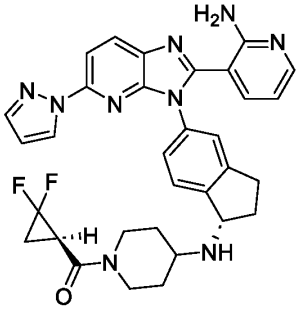
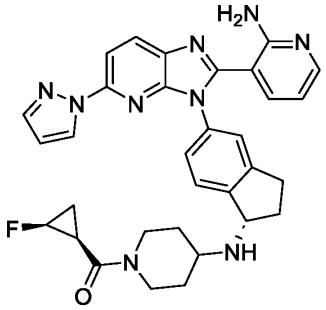
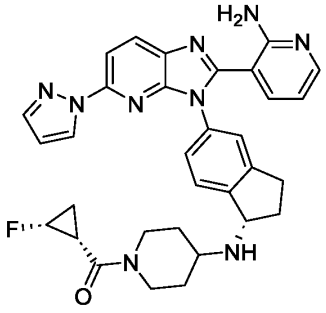
474	
476	
477	
478	

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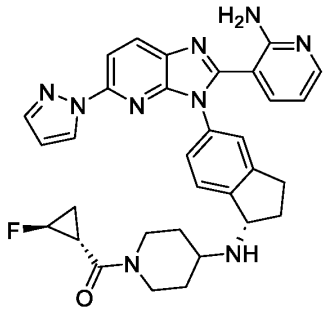
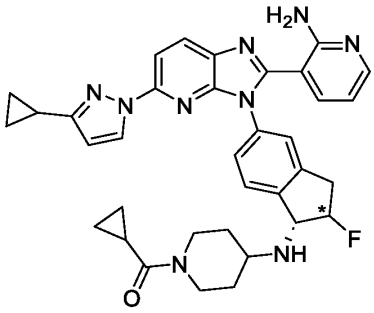
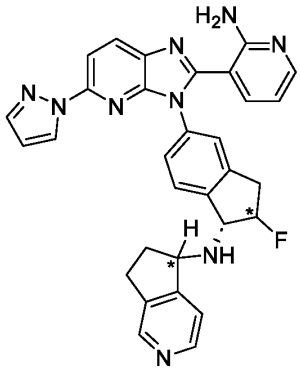
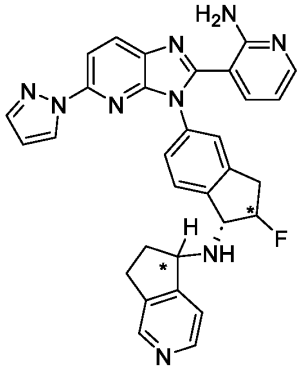
479	
480	
481	
482	

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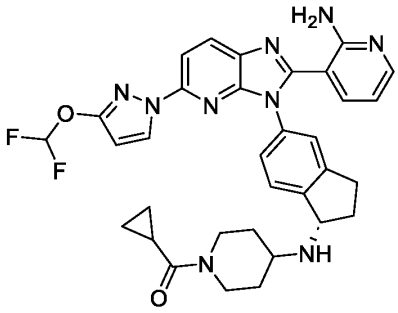
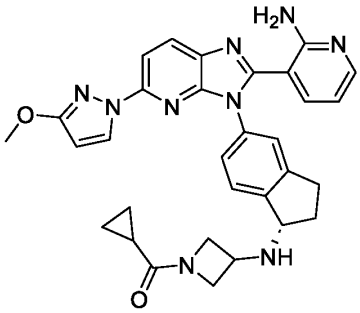
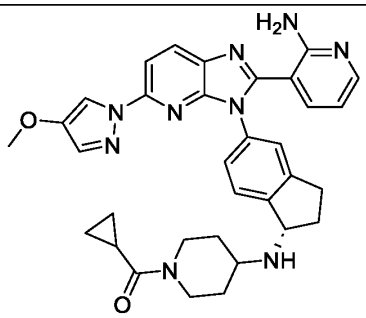
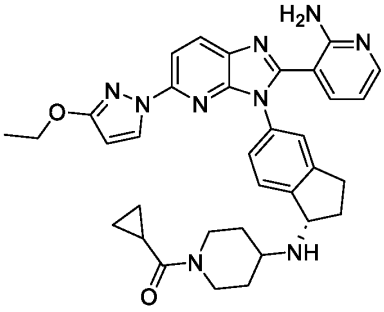
483	
484	
485	
486	

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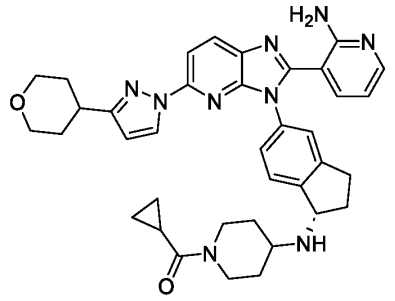
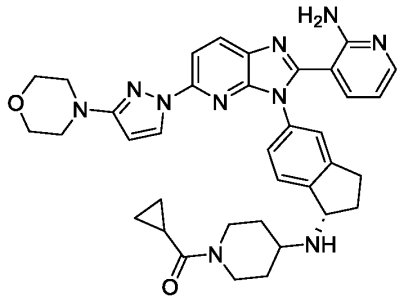
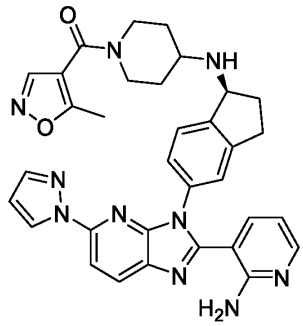
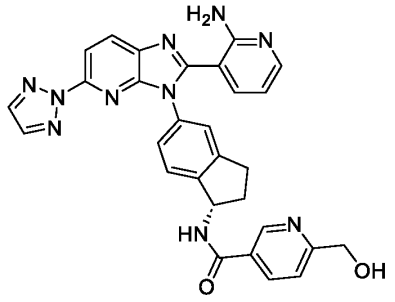
487	
488	
489	
490	

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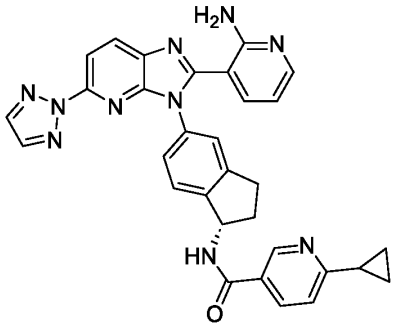
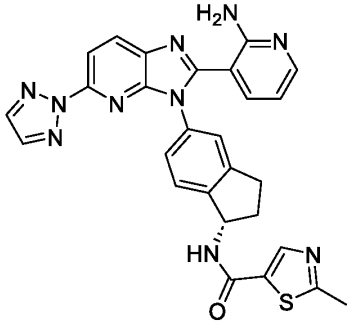
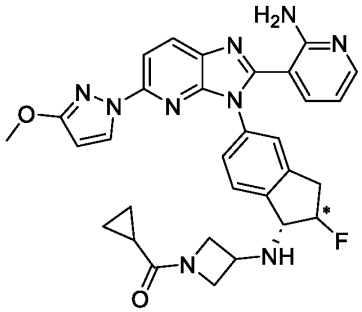
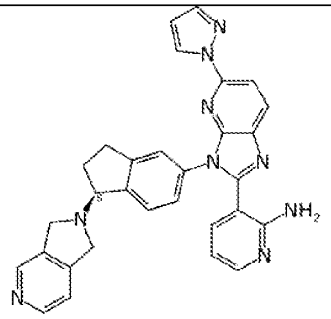
491	
492	
493	
494	

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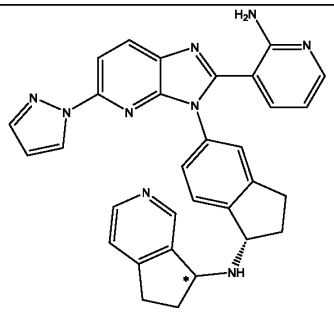
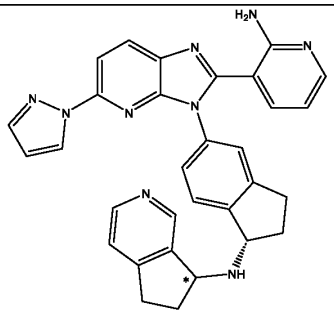
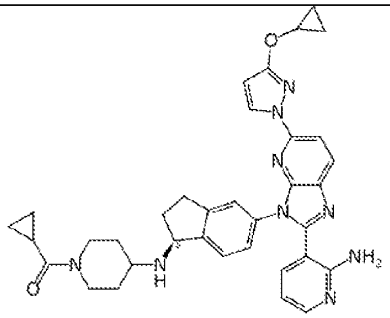
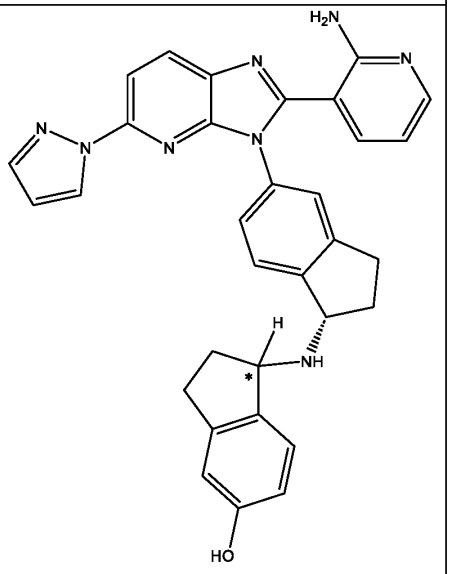
495	
496	
497	
499	

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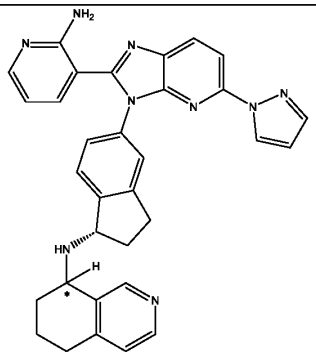
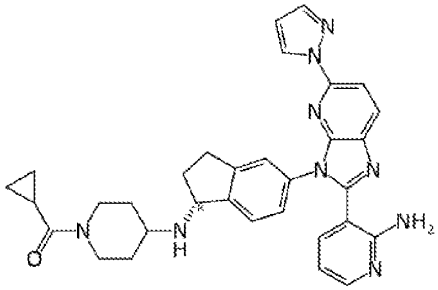
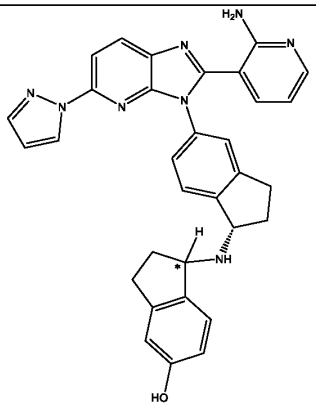
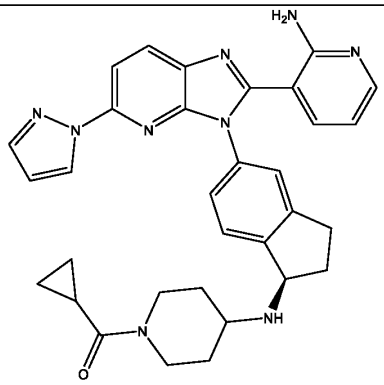
501	
503	
498	
500	

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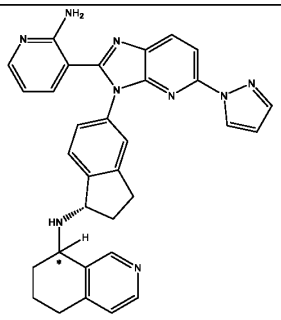
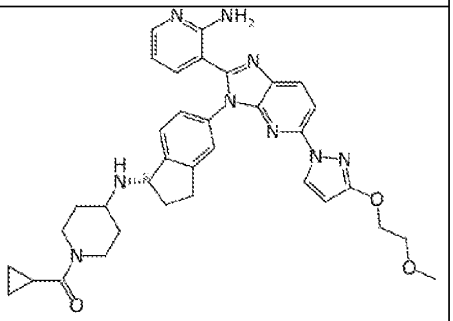
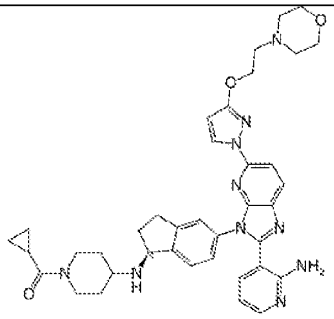
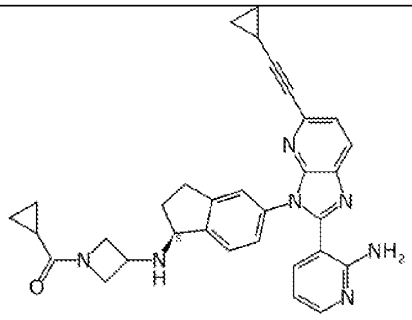
502	
504	
505	
506	

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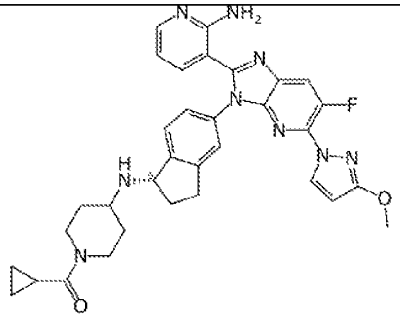
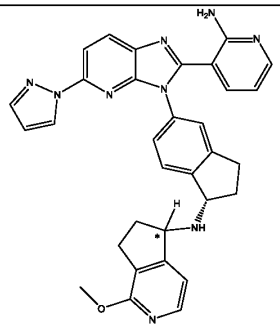
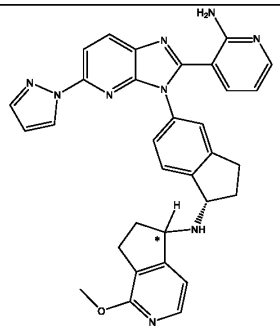
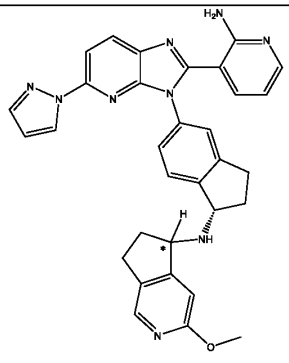
507	
508	
509	
510	

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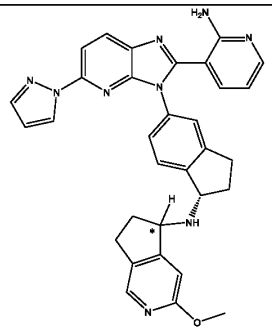
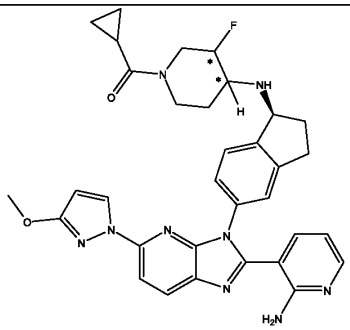
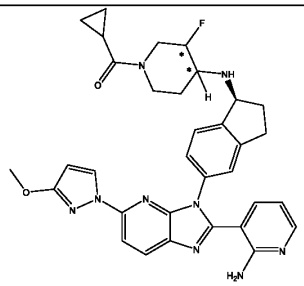
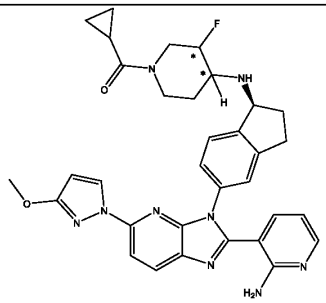
511	
512	
513	
514	

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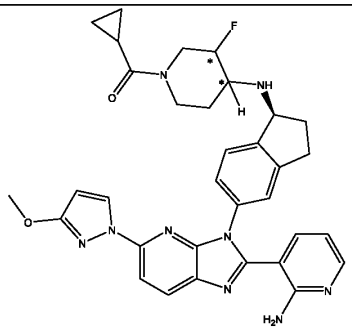
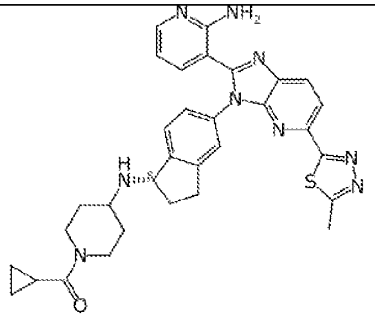
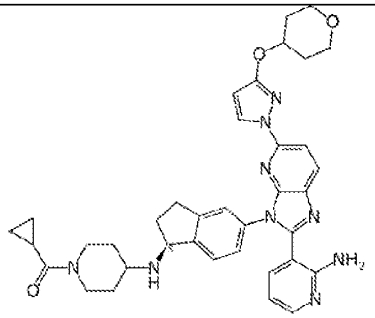
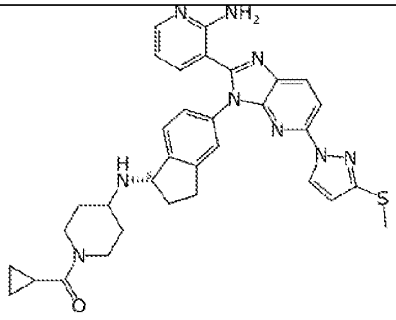
515	
516	
517	
518	

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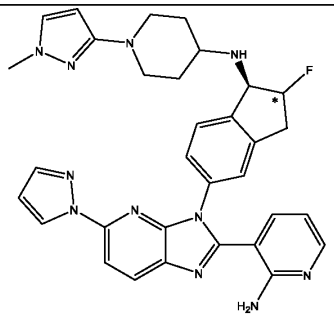
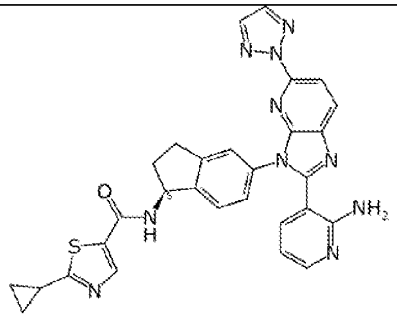
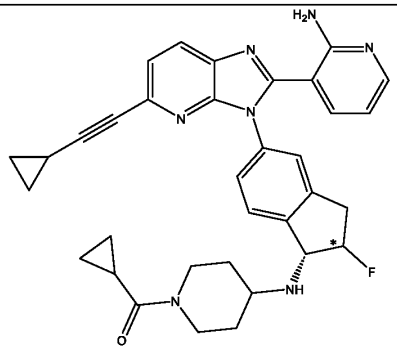
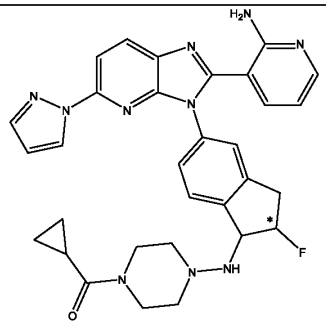
519	
520	
521	
522	

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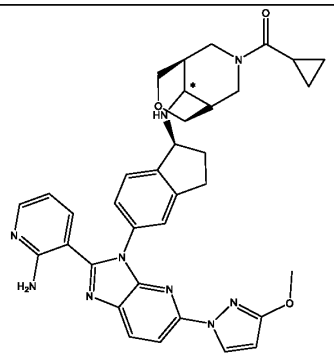
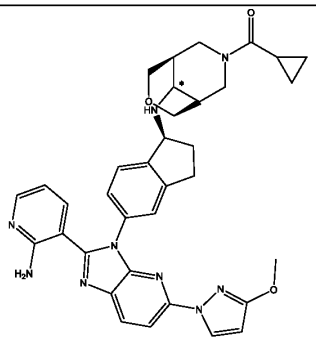
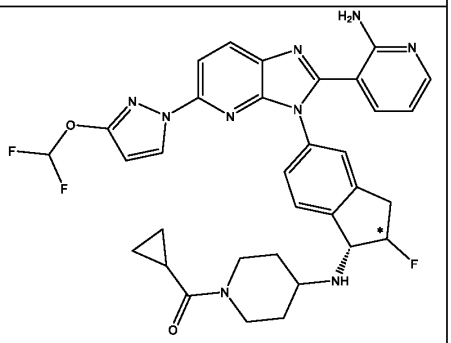
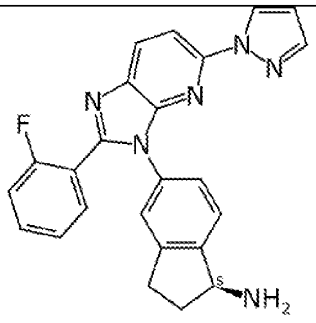
523	
524	
525	
527	

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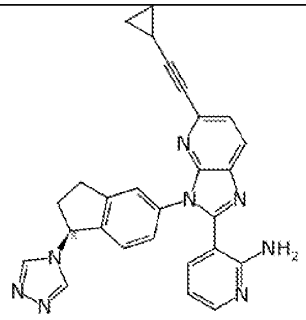
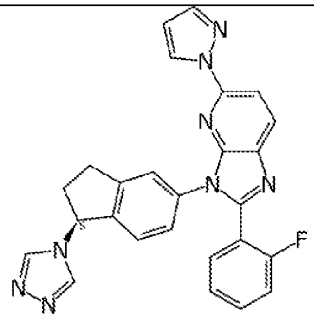
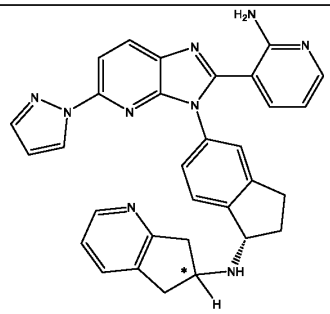
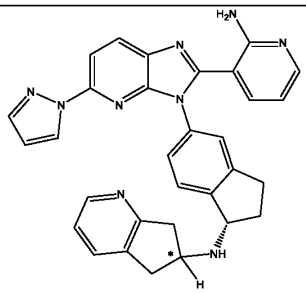
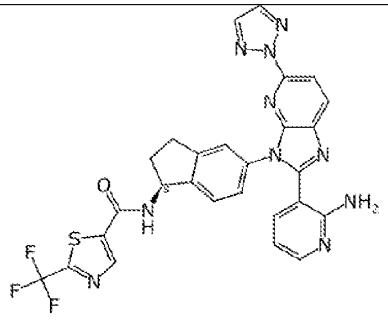
528	
529	
530	
531	
526	

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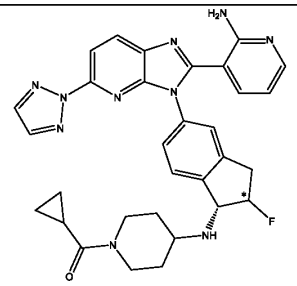
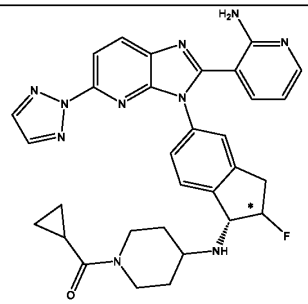
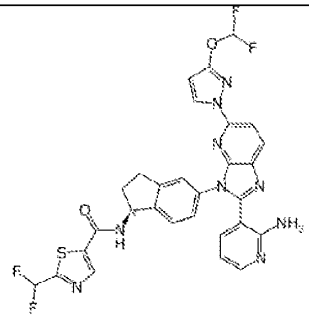
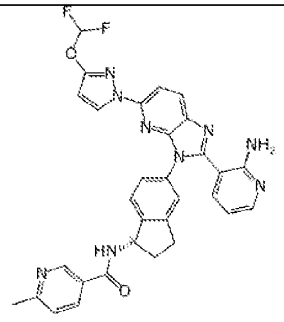
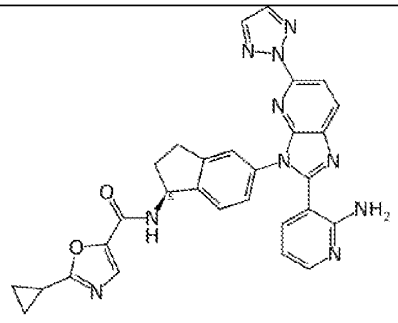
532	
533	
534	
535	
536	

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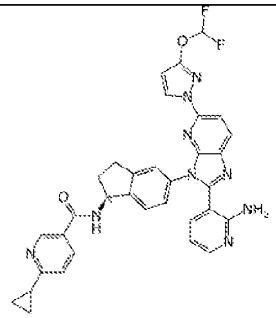
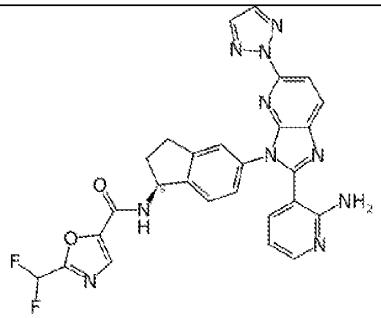
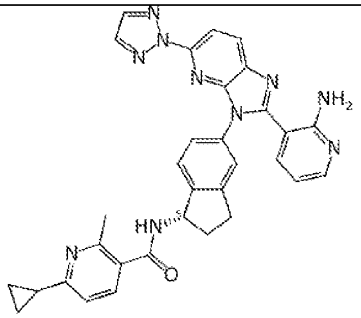
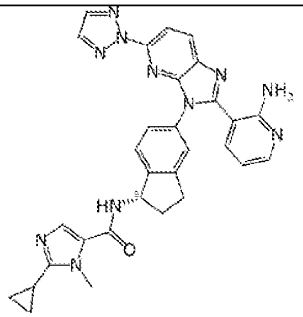
537	
538	
539	
540	

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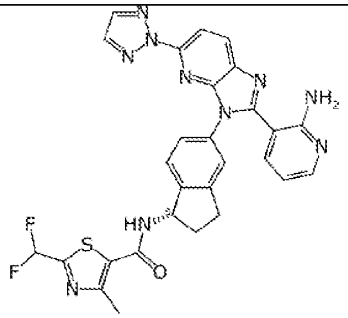
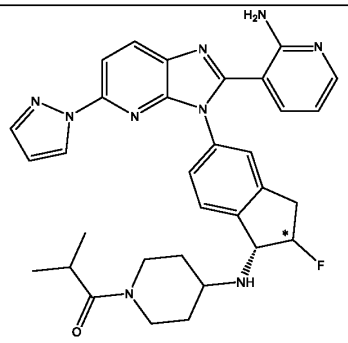
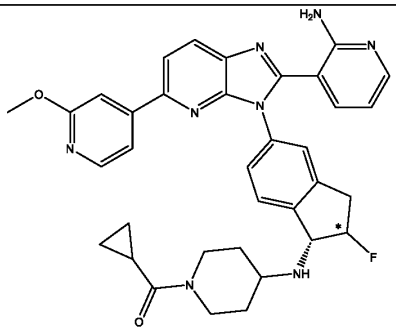
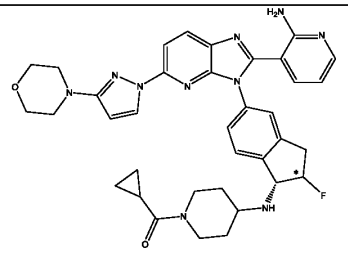
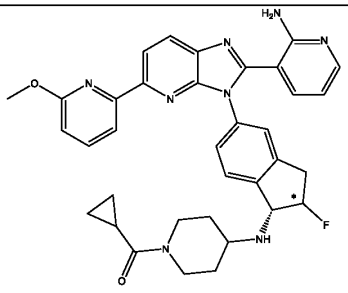
541	
542	
543	
544	
545	

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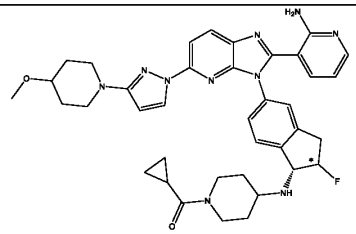
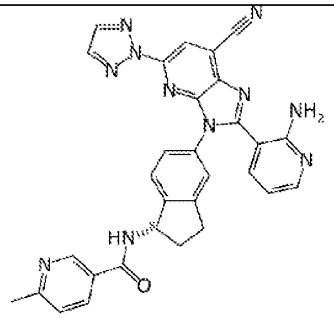
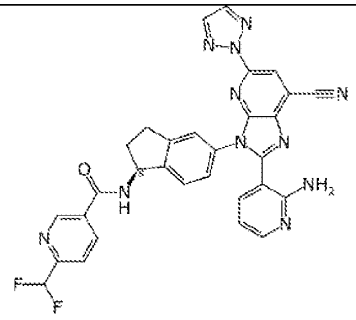
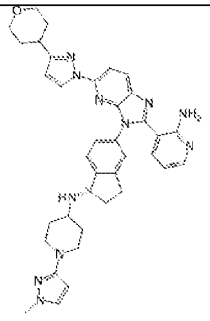
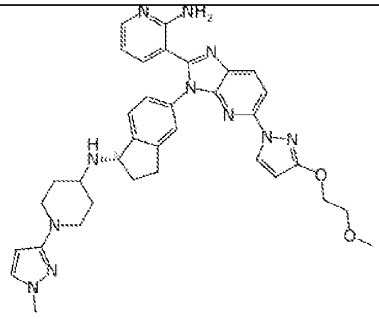
546	
547	
548	
549	
551	

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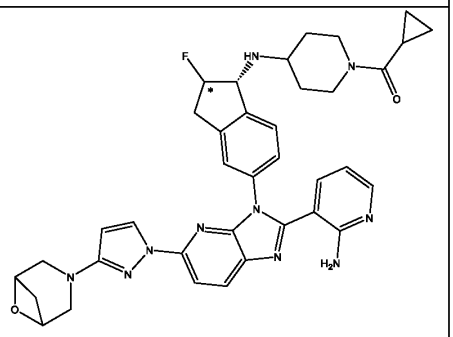
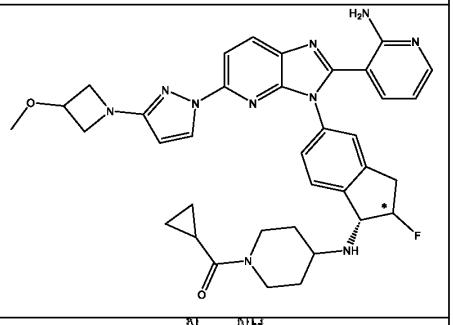
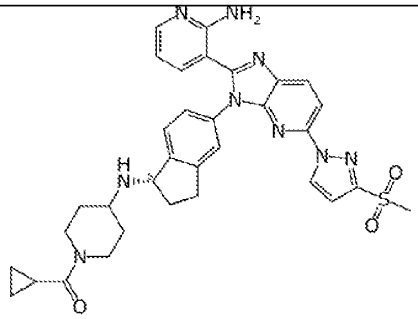
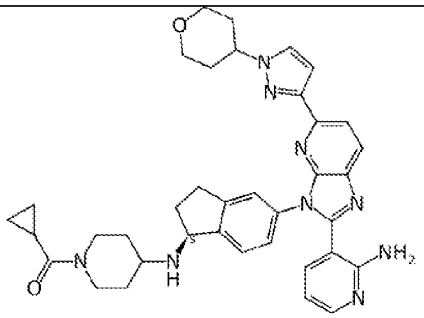
552	
553	
554	
555	

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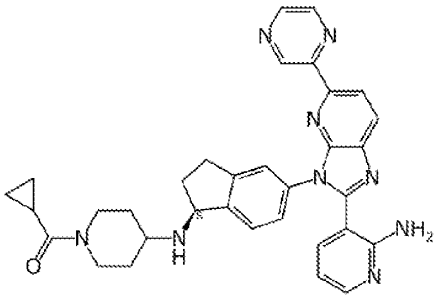
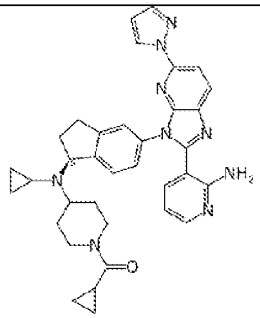
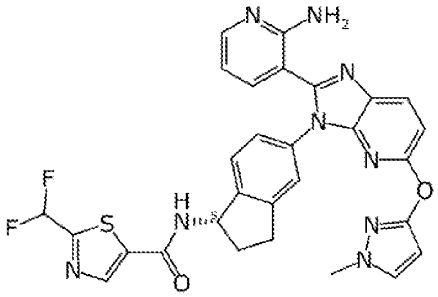
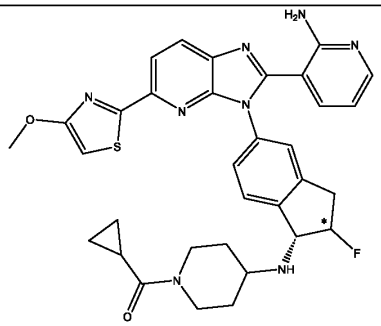
556	
557	
558	
559	

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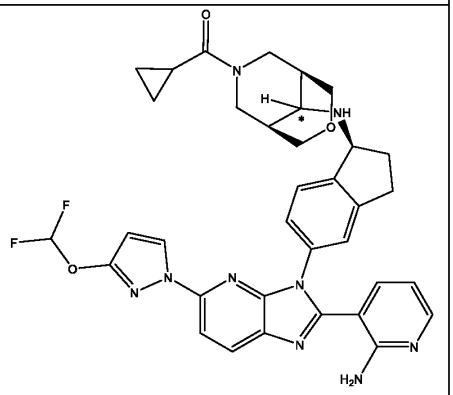
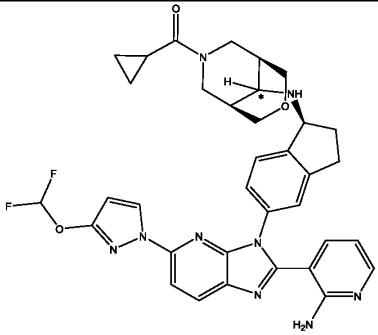
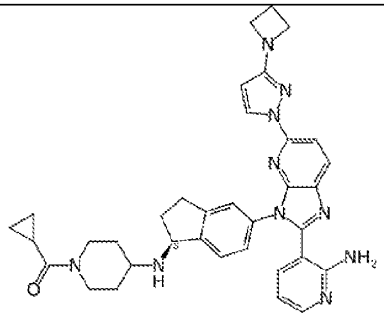
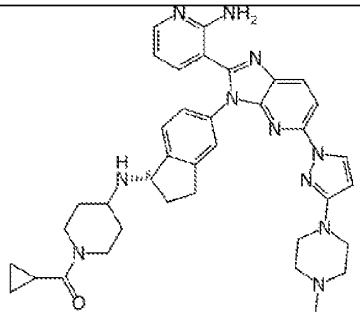
560	
561	
562	
563	

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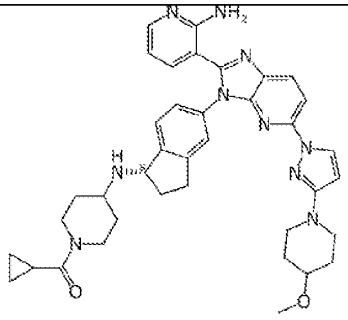
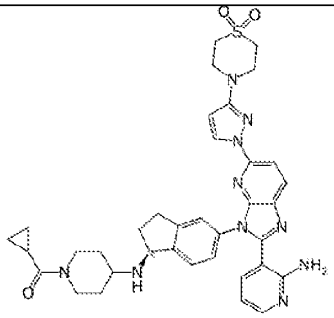
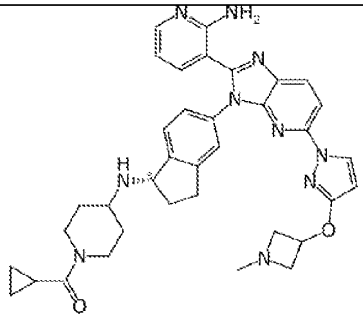
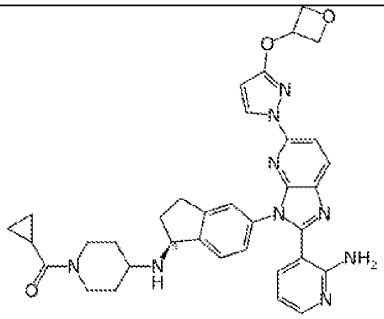
564	
565	
566	
567	

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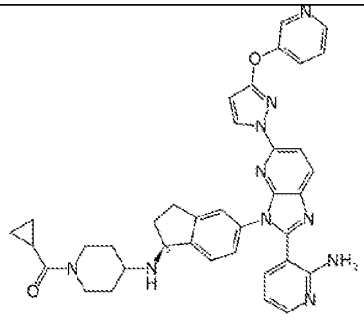
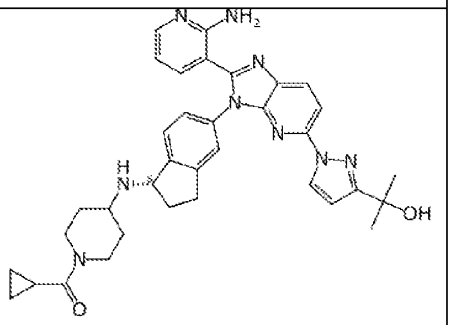
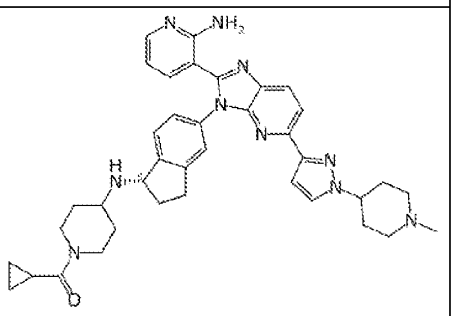
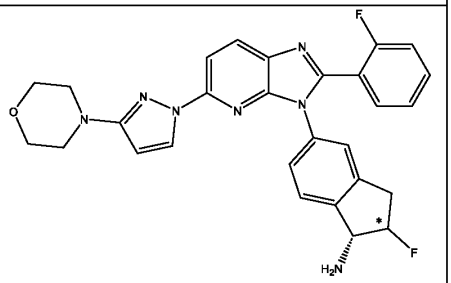
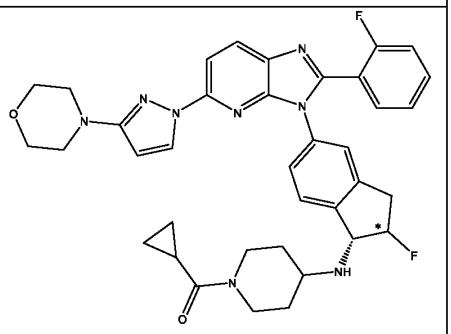
568	
569	
570	
571	
572	

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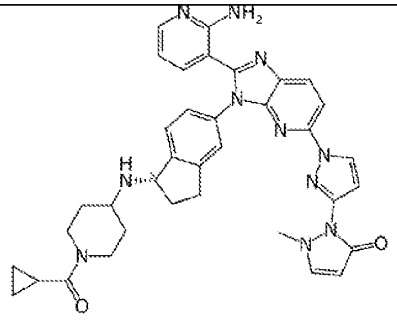
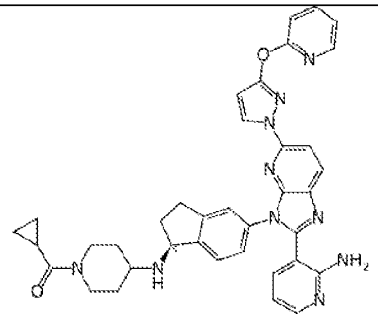
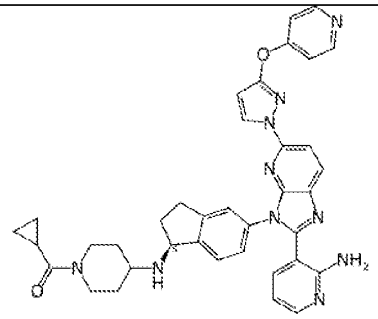
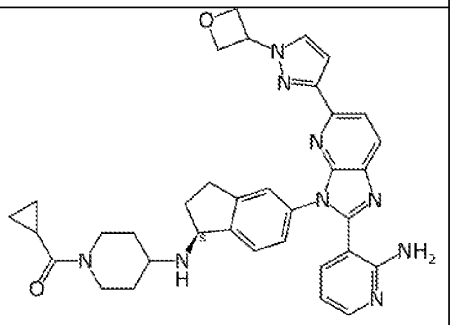
573	
574	
575	
576	

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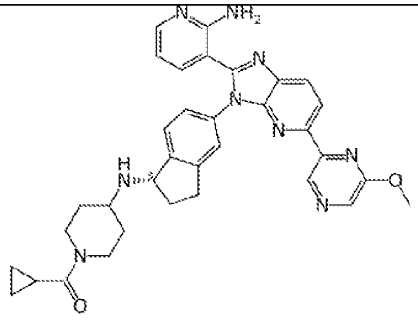
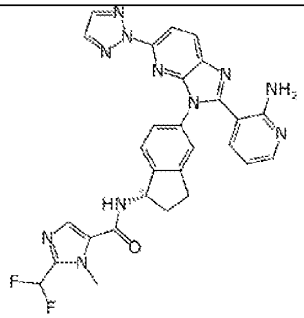
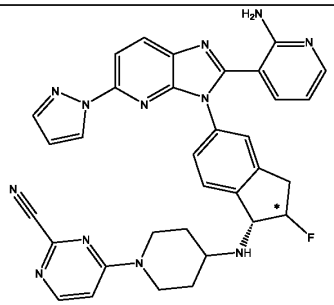
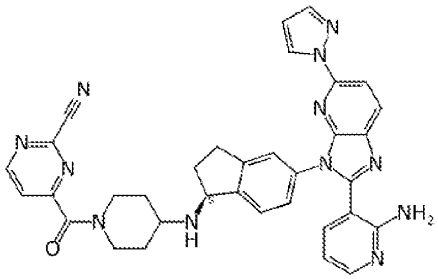
577	
578	
579	
580	

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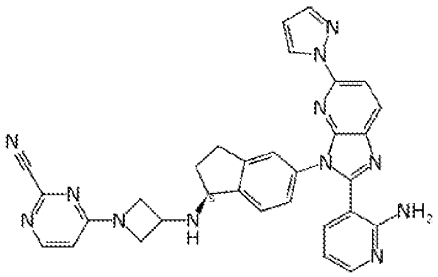
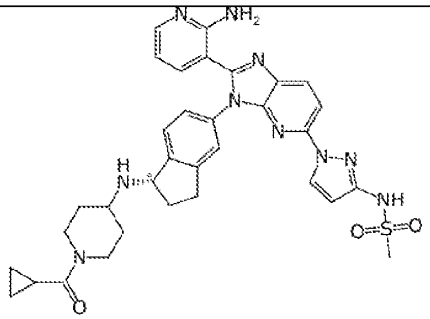
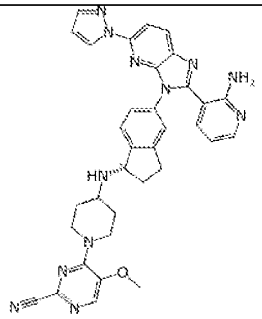
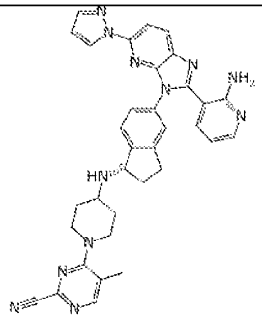
581	
582	
586	
584	

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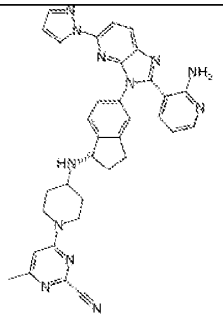
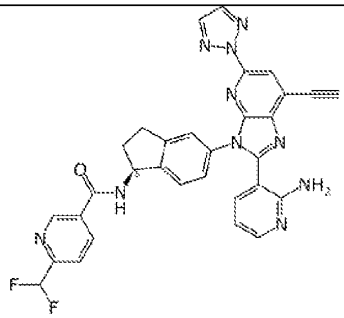
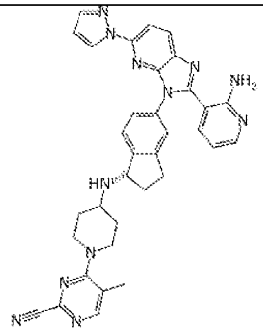
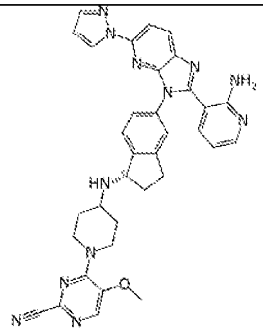
584	
583	
585	
586	

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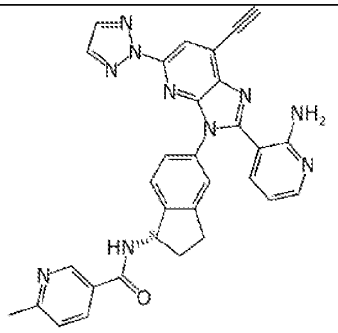
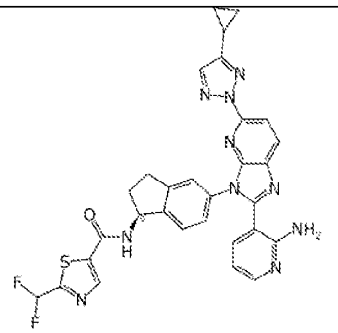
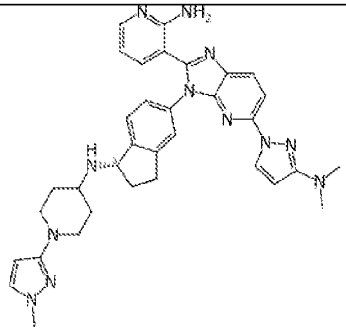
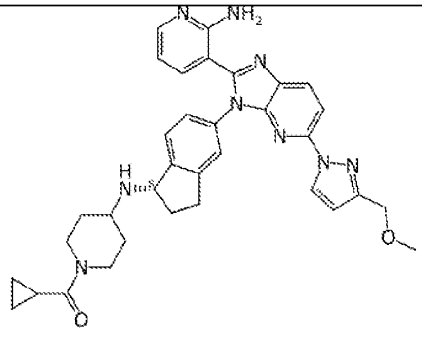
587	
588	
589	
590	

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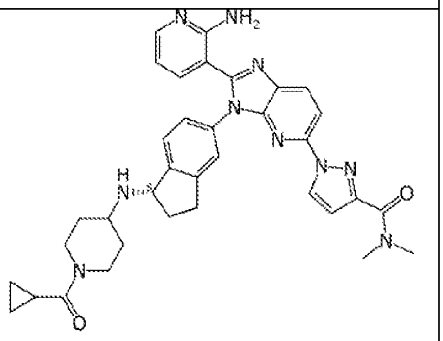
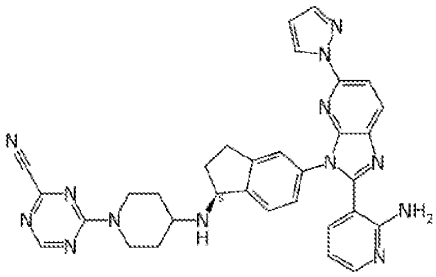
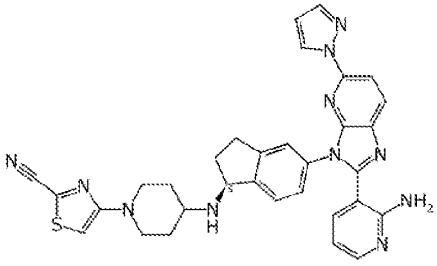
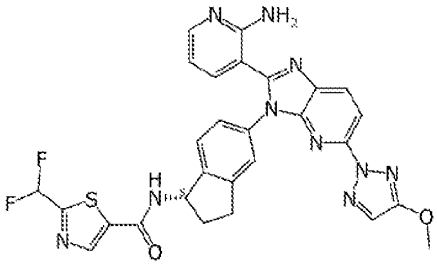
591	
592	
593	
594	

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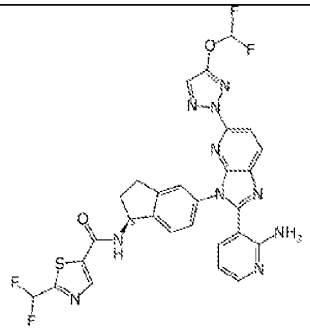
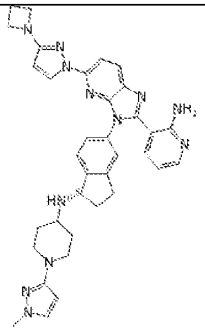
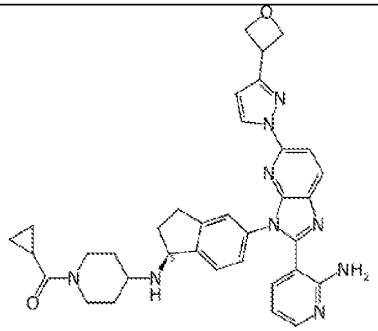
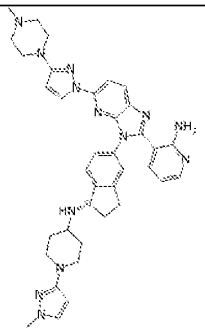
595	
596	
597	
598	

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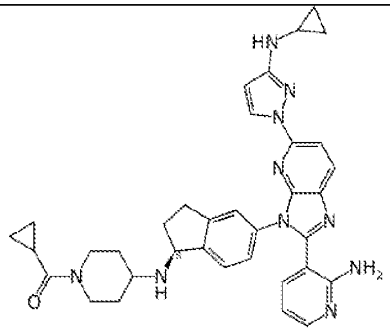
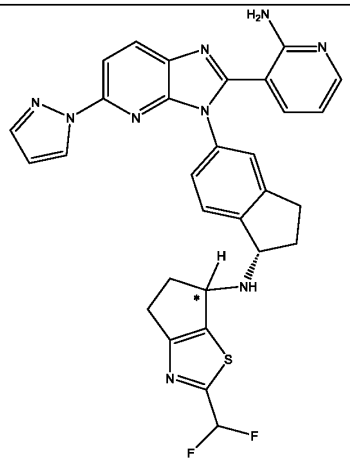
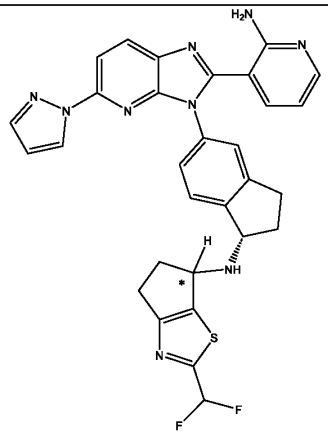
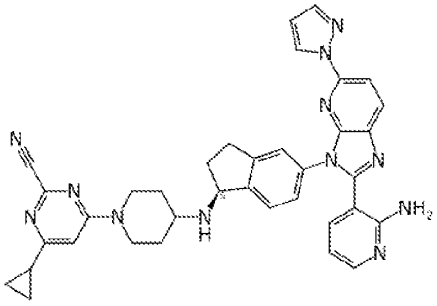
599	
600	
601	
602	

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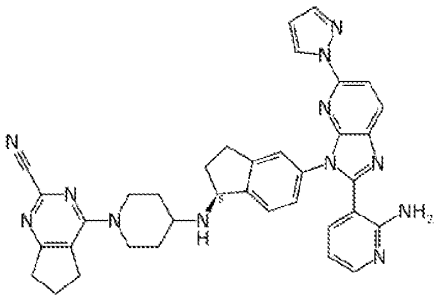
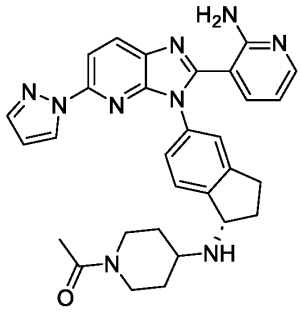
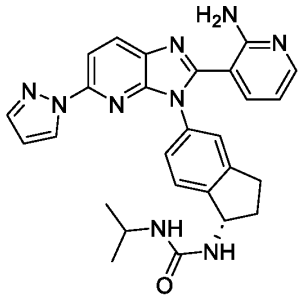
603	

[00209] In some aspects, the present disclosure provides a compound, wherein the compound is selected from a compound of Table 2, or a pharmaceutically acceptable salt thereof.

Table 2. Chemical structures of selected compounds.

Cpd ID	Structure
109	
134	

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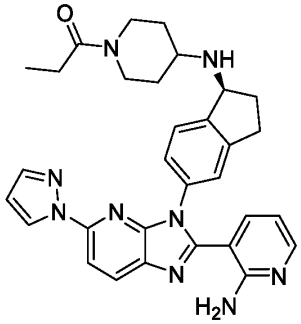
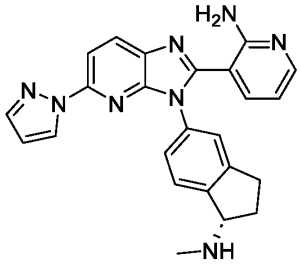
278	
339	

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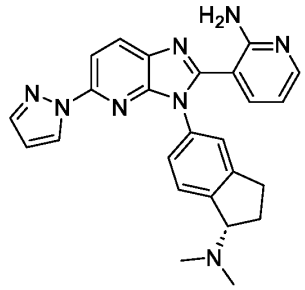
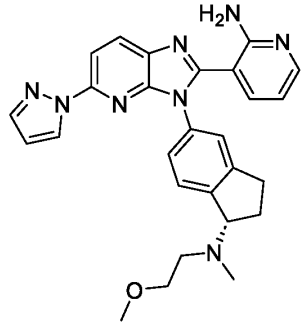
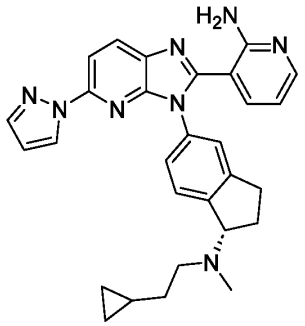
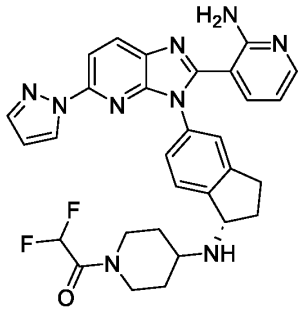
340	
457	

Cpd ID	Structure
458	
475	

[00210] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

[00211] Chemical entities having carbon-carbon double bonds or carbon-nitrogen double bonds may exist in *Z*- or *E*- form (or *cis*- or *trans*- form). Furthermore, some chemical entities may exist in various tautomeric forms. Unless otherwise specified, compounds or salts of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), are intended to include all *Z*-, *E*- and tautomeric forms as well.

[00212] "Isomers" are different compounds that have the same molecular formula. "Stereoisomers" are isomers that differ only in the way the atoms are arranged in space. "Enantiomers" are a pair of stereoisomers that are non-superimposable mirror images of each other. A 1:1 mixture of a pair of enantiomers is a "racemic" mixture. The term "(±)" is used to

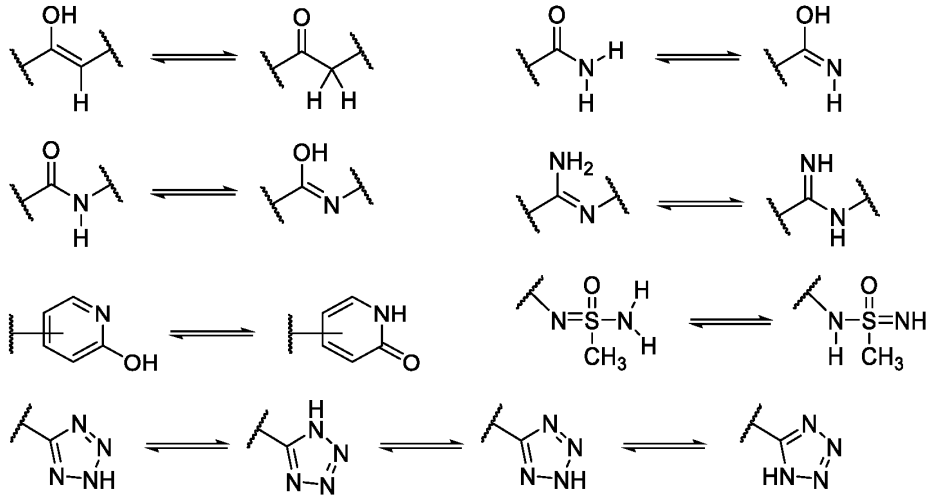
designate a racemic mixture where appropriate. “Diastereoisomers” or “diastereomers” are stereoisomers that have at least two asymmetric atoms but are not mirror images of each other. The absolute stereochemistry is specified according to the Cahn-Ingold-Prelog R-S system. When a compound is a pure enantiomer, the stereochemistry at each chiral carbon can be specified by either R or S. Resolved compounds whose absolute configuration is unknown can be designated (+) or (-) depending on the direction (dextro- or levorotatory) in which they rotate plane polarized light at the wavelength of the sodium D line. Certain compounds described herein contain one or more asymmetric centers and can thus give rise to enantiomers, diastereomers, and other stereoisomeric forms, the asymmetric centers of which can be defined, in terms of absolute stereochemistry, as (R)- or (S)-. The present chemical entities, pharmaceutical compositions and methods are meant to include all such possible stereoisomers, including racemic mixtures, optically pure forms, mixtures of diastereomers and intermediate mixtures. Optically active (R)- and (S)-isomers can be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. The optical activity of a compound can be analyzed via any suitable method, including but not limited to chiral chromatography and polarimetry, and the degree of predominance of one stereoisomer over the other isomer can be determined.

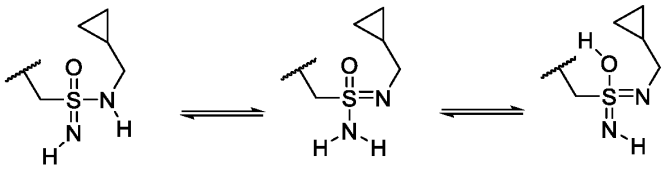
[00213] The compounds or salts for Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), herein may in some cases exist as diastereomers, enantiomers, or other stereoisomeric forms. The compounds presented herein include all diastereomeric, enantiomeric, and epimeric forms as well as the racemates, mixtures of diastereomers, and other mixtures thereof, to the extent they can be made by one of ordinary skill in the art by routine experimentation. Separation of stereoisomers may be performed by chromatography or by forming diastereomers and separating by recrystallization, or chromatography, or any combination thereof. (Jean Jacques, Andre Collet, Samuel H. Wilen, “Enantiomers, Racemates and Resolutions,” John Wiley And Sons, Inc., 1981, herein incorporated by reference for this disclosure). Stereoisomers may also be obtained by stereoselective synthesis. Furthermore, a mixture of two enantiomers enriched in one of the two can be purified to provide further optically enriched form of the major enantiomer by recrystallization and/or trituration.

[00214] In certain embodiments, compounds or salts for Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), may comprise two or more enantiomers or diatereomers of a compound wherein a single enantiomer or diastereomer accounts for at least about 70% by weight, at least about 80% by weight, at least about 90% by weight, at least about 98% by weight, or at least about 99% by weight or more of

the total weight of all stereoisomers. Methods of producing substantially pure enantiomers are well known to those of skill in the art. For example, a single stereoisomer, *e.g.*, an enantiomer, substantially free of its stereoisomer may be obtained by resolution of the racemic mixture using a method such as formation of diastereomers using optically active resolving agents (Stereochemistry of Carbon Compounds, (1962) by E. L. Eliel, McGraw Hill; Lochmuller (1975) *J. Chromatogr.*, 113(3): 283-302). Racemic mixtures of chiral compounds can be separated and isolated by any suitable method, including, but not limited to: (1) formation of ionic, diastereomeric salts with chiral compounds and separation by fractional crystallization or other methods, (2) formation of diastereomeric compounds with chiral derivatizing reagents, separation of the diastereomers, and conversion to the pure stereoisomers, and (3) separation of the substantially pure or enriched stereoisomers directly under chiral conditions. Another approach for separation of the enantiomers is to use a Diacel chiral column and elution using an organic mobile phase such as done by Chiral Technologies (www.chiraltech.com) on a fee for service basis.

[00215] A "tautomer" refers to a molecule wherein a proton shift from one atom of a molecule to another atom of the same molecule is possible. In certain embodiments, the compounds or salts for Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), exist as tautomers. In circumstances where tautomerization is possible, a chemical equilibrium of the tautomers may exist. The exact ratio of the tautomers depends on several factors, including physical state, temperature, solvent, and pH. Some non–limiting examples of tautomeric equilibrium include:





[00216] The compounds disclosed herein, in some embodiments, are used in different enriched isotopic forms, e.g., enriched in the content of ^{2}H, ^{3}H, ^{11}C, ^{13}C and/or ^{14}C. In one particular embodiment, the compound may be deuterated in at least one position. Such deuterated forms can be made by the procedure described in U.S. Patent Nos. 5,846,514 and 6,334,997. As described in U.S. Patent Nos. 5,846,514 and 6,334,997, deuteration can improve the metabolic stability and or efficacy, thus increasing the duration of action of drugs.

[00217] In certain embodiments, the compounds disclosed herein have some or all of the ^{1}H atoms replaced with ^{2}H atoms. The methods of synthesis for deuterium-containing compounds are known in the art and include, by way of non-limiting example only, the following synthetic methods.

[00218] Deuterium substituted compounds are synthesized using various methods such as described in: Dean, Dennis C.; Editor. Recent Advances in the Synthesis and Applications of Radiolabeled Compounds for Drug Discovery and Development. [In: Curr., Pharm. Des., 2000; 6(10)] 2000, 110 pp; George W.; Varma, Rajender S. The Synthesis of Radiolabeled Compounds via Organometallic Intermediates, Tetrahedron, 1989, 45(21), 6601-21; and Evans, E. Anthony. Synthesis of radiolabeled compounds, J. Radioanal. Chem., 1981, 64(1-2), 9-32.

[00219] Deuterated starting materials are readily available and are subjected to the synthetic methods described herein to provide for the synthesis of deuterium-containing compounds. Large numbers of deuterium-containing reagents and building blocks are available commercially from chemical vendors, such as Aldrich Chemical Co.

[00220] Unless otherwise stated, compounds described herein are intended to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by ^{13}C- or ^{14}C-enriched carbon are within the scope of the present disclosure.

[00221] The compounds of the present disclosure optionally contain unnatural proportions of atomic isotopes at one or more atoms that constitute such compounds. For example, the compounds may be labeled with isotopes, such as for example, deuterium (^{2}H), tritium (^{3}H), iodine-125 (^{125}I) or carbon-14 (^{14}C). Isotopic substitution with ^{2}H, ^{11}C, ^{13}C, ^{14}C, ^{15}C, ^{12}N, ^{13}N, ^{15}N, ^{16}N, ^{16}O, ^{17}O, ^{14}F, ^{15}F, ^{16}F, ^{17}F, ^{18}F, ^{33}S, ^{34}S, ^{35}S, ^{36}S, ^{35}Cl, ^{37}Cl, ^{79}Br, ^{81}Br, and ^{125}I are all

contemplated. All isotopic variations of the compounds of the present invention, whether radioactive or not, are encompassed within the scope of the present invention.

[00222] Included in the present disclosure are salts, particularly pharmaceutically acceptable salts, of the compounds of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B). The compounds of the present disclosure may possess a sufficiently acidic, a sufficiently basic, or both functional groups, can react with any of a number of inorganic bases, and inorganic and organic acids, to form a salt. Alternatively, compounds that are inherently charged, such as those with a quaternary nitrogen, can form a salt with an appropriate counterion, e.g., a halide such as bromide, chloride, or fluoride, particularly bromide.

[00223] The methods and compositions of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B) include the use of amorphous forms as well as crystalline forms (also known as polymorphs). The compounds described herein may be in the form of pharmaceutically acceptable salts. As well, in some embodiments, active metabolites of these compounds having the same type of activity are included in the scope of the present disclosure. In addition, the compounds described herein can exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like. The solvated forms of the compounds presented herein are also considered to be disclosed herein.

[00224] Compounds of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), also include crystalline and amorphous forms of those compounds, pharmaceutically acceptable salts, and active metabolites of these compounds having the same type of activity, including, for example, polymorphs, pseudopolymorphs, solvates, hydrates, unsolvated polymorphs (including anhydrates), conformational polymorphs, and amorphous forms of the compounds, as well as mixtures thereof.

[00225] Included in the present disclosure are salts, particularly pharmaceutically acceptable salts, of compounds represented by Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B). The compounds of the present invention that possess a sufficiently acidic, a sufficiently basic, or both functional groups, can react with any of a number of inorganic bases, and inorganic and organic acids, to form a salt. Alternatively, compounds that are inherently charged, such as those with a quaternary nitrogen, can form a salt with an appropriate counterion, e.g., a halide such as bromide, chloride, or fluoride, particularly bromide.

[00226] In certain embodiments, compounds or salts of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), may be prodrugs,

e.g., wherein a hydroxyl in the parent compound is presented as an ester or a carbonate, or carboxylic acid present in the parent compound is presented as an ester. The term "prodrug" is intended to encompass compounds which, under physiologic conditions, are converted into pharmaceutical agents of the present disclosure. One method for making a prodrug is to include one or more selected moieties which are hydrolyzed under physiologic conditions to reveal the desired molecule. In other embodiments, the prodrug is converted by an enzymatic activity of the host animal such as specific target cells in the host animal. For example, esters or carbonates (e.g., esters or carbonates of alcohols or carboxylic acids and esters of phosphonic acids) are preferred prodrugs of the present disclosure.

Pharmaceutical Formulations

[00227] In some aspects, the present disclosure provides a pharmaceutical composition comprising a compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B) and at least one pharmaceutically acceptable excipient.

[00228] In some aspects, the present disclosure provides a pharmaceutical composition comprising a compound of Table 2.

[00229] Pharmaceutical compositions can be formulated using one or more physiologically-acceptable carriers comprising excipients and auxiliaries. Formulation can be modified depending upon the route of administration chosen. Pharmaceutical compositions comprising a compound, salt or conjugate can be manufactured, for example, by lyophilizing the compound, salt or conjugate, mixing, dissolving, emulsifying, encapsulating or entrapping the conjugate. The pharmaceutical compositions can also include the compounds, salts or conjugates in a free-base form or pharmaceutically-acceptable salt form.

[00230] A compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B) may be formulated in any suitable pharmaceutical formulation. A pharmaceutical formulation of the present disclosure typically contains an active ingredient (e.g., compound or salt of any one of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B), and one or more pharmaceutically acceptable excipients or carriers, including but not limited to: inert solid diluents and fillers, diluents, sterile aqueous solution and various organic solvents, permeation enhancers, antioxidents, solubilizers, and adjuvants.

[00231] A compound or salt of Table 2 may be formulated in any suitable pharmaceutical formulation. A pharmaceutical formulation of the present disclosure typically contains an active ingredient (e.g., a compound or salt of Table 2), and one or more pharmaceutically acceptable

excipients or carriers, including but not limited to: inert solid diluents and fillers, diluents, sterile aqueous solution and various organic solvents, permeation enhancers, antioxidents, solubilizers, and adjuvants.

Methods of Treatment

[00232] The compounds described herein can be used in the preparation of medicaments for the prevention or treatment of diseases or conditions. In addition, a method for treating any of the diseases or conditions described herein in a subject in need of such treatment, involves administration of pharmaceutical compositions containing at least one compound described herein, or a pharmaceutically acceptable salt, pharmaceutically acceptable prodrug, or pharmaceutically acceptable solvate thereof, in therapeutically effective amounts to said subject.

[00233] The compositions containing the compound(s) described herein can be administered for prophylactic and/or therapeutic treatments. In therapeutic applications, the compositions are administered to a patient already suffering from a disease or condition, in an amount sufficient to cure or at least partially arrest the symptoms of the disease or condition. Amounts effective for this use will depend on the severity and course of the disease or condition, previous therapy, the patient's health status, weight, and response to the drugs, and the judgment of the treating physician.

[00234] In prophylactic applications, compositions containing the compounds described herein are administered to a patient susceptible to or otherwise at risk of a particular disease, disorder or condition. Such an amount is defined to be a “prophylactically effective amount or dose.” In this use, the precise amounts also depend on the patient's state of health, weight, and the like. When used in a patient, effective amounts for this use will depend on the severity and course of the disease, disorder or condition, previous therapy, the patient's health status and response to the drugs, and the judgment of the treating physician.

[00235] In some aspects, the present disclosure provides a method for treatment, comprising administering to a subject in need thereof an effective amount of a compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B). In some aspects, the present disclosure provides a method for treating cancer in a patient in need thereof, comprising administering to the subject an effective amount of a compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B). In some embodiments, the cancer is selected from breast cancer, colorectal cancer, and meningioma. In some embodiments, the cancer is breast cancer. In some embodiments, the cancer is colorectal cancer. In some embodiments, the cancer is meningioma.

[00236] In certain embodiments, the present disclosure can be used as a method of inhibiting an AKT1 protein in a subject in need thereof, comprising administering to the subject a compound or salt of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B) or a pharmaceutical composition of Formula (I), (II), (II-A), (III), (III-A), (III-B), (IV), (IV-A), (IV-B), (V), (V-A), (V-B), (VI), (VI-A), or (VI-B). In some embodiments, the AKT protein is wild-type AKT1. In some embodiments, the AKT protein is a mutant AKT1 protein. In some embodiments, the mutant AKT1 protein comprises an E17K mutant. In some embodiments, the administrating modulates the activity of mutant AKT1. In some embodiments, the administrating modulates the activity of wild-type AKT1.

[00237] In some aspects, the present disclosure provides a method for treatment, comprising administering to a subject in need thereof an effective amount of a compound or salt of Table 2. In some aspects, the present disclosure provides a method for treating cancer in a patient in need thereof, comprising administering to the subject an effective amount of a compound or salt of Table 2. In some embodiments, the cancer is selected from breast cancer, colorectal cancer, and meningioma. In some embodiments, the cancer is breast cancer. In some embodiments, the cancer is colorectal cancer. In some embodiments, the cancer is meningioma.

[00238] In certain embodiments, the present disclosure can be used as a method of inhibiting an AKT1 protein in a subject in need thereof, comprising administering to the subject a compound or salt of Table 2 or a pharmaceutical composition comprising a compound or salt of Table 2. In some embodiments, the AKT protein is wild-type AKT1. In some embodiments, the AKT protein is a mutant AKT1 protein. In some embodiments, the mutant AKT1 protein comprises an E17K mutant. In some embodiments, the administrating modulates the activity of mutant AKT1. In some embodiments, the administrating modulates the activity of wild-type AKT1.

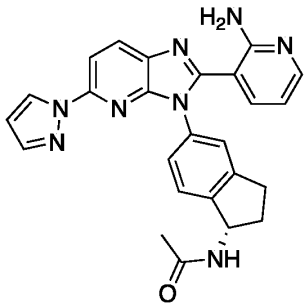
EXAMPLES

[00239] The invention now being generally described, it will be more readily understood by reference to the following examples which are included merely for purposes of illustration of certain aspects and embodiments of the present invention and are not intended to limit the invention in any way.

Chemical Synthesis

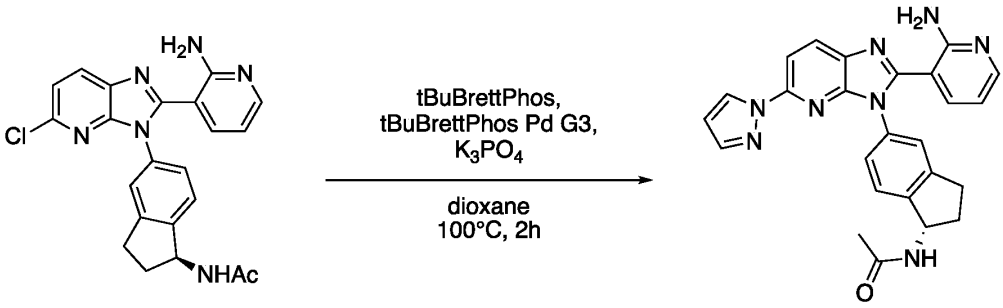
[00240] The following examples describe illustrate various methods of preparation of compounds described herein. Examples are exemplary and not exhaustive. It is understood that one skilled in the art may be able to synthesize described compounds by similar methods.

[00241] Compound 1: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (Compound 1)



Compound 1

[00242] Synthetic Route:



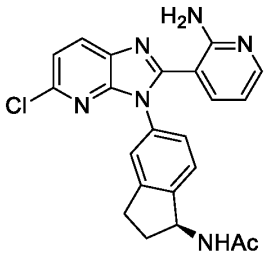
Intermediate 1-1 **Compound 1**

[00243] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (Compound 1)

[00244] To a mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-chloro-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (**Intermediate 1-1**) (200 mg, 0.477 mmol, 1 equiv), pyrazole (39 mg, 0.57 mmol, 1.5 equiv), t-BuBrettPhos Pd G3 (41 mg, 0.048 mmol, 0.1 equiv), t-BuBrettPhos (23 mg, 0.048 mmol, 0.1 equiv) and K_3PO_4 (304 mg, 1.43 mmol, 3 equiv) was added 1,4-dioxane (5 mL) under N_2 at room temperature. The resulting mixture was stirred at 100 °C for 2 h under nitrogen atmosphere. Brine was added and the mixture was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using a gradient of methanol in ethyl acetate. The material obtained at this stage was used in subsequent transformations *vide infra*. The material was further purified for characterization and assaying by preparative HPLC on a XSelect CSH Prep C18 OBD Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (TFA salt) (**Compound 1**) (84 mg, 39%) as a white solid. MS (ESI) calcd.

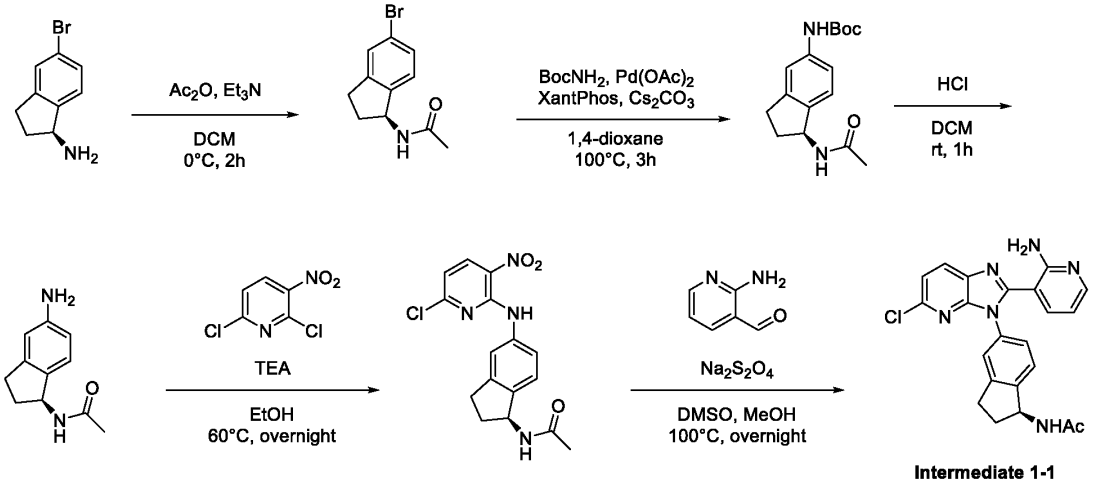
for $C_{25}H_{22}N_8O$: 450.19 m/z, found 451.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.40 - 8.50 (m, 1H), 8.33 - 8.40 (m, 1H), 8.02 - 8.10 (m, 1H), 7.95 - 8.02 (m, 1H), 7.78 - 7.88 (m, 1H), 7.72 - 7.78 (m, 1H), 7.40 - 7.51 (m, 1H), 7.26 - 7.40 (m, 2H), 6.78 - 6.90 (m, 1H), 6.55 - 6.65 (m, 1H), 5.22 - 5.40 (m, 1H), 2.80 - 3.10 (m, 2H), 2.35 - 2.50 (m, 1H), 1.91 - 2.00 (m, 3H), 1.78 - 1.90 (m, 1H).

[00245] Intermediate 1-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-chloro-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)acetamide



Intermediate 1-1

[00246] Synthetic route:



Intermediate 1-1

[00247] Step 1: Synthesis of (*S*)-*N*-(5-bromo-2,3-dihydro-1*H*-inden-1-yl)acetamide

[00248] To a mixture of (S)-5-bromo-2,3-dihydro-1H-inden-1-amine (74 g, 350 mmol, 1 equiv) and triethylamine (106 g, 1.05 mol, 3 equiv) in dichloromethane (1.5 L) was added acetic anhydride (55.2 g, 526 mmol, 1.5 equiv) at 0 °C and the mixture was stirred at 0 °C for 2 h. The reaction mixture was quenched by addition of water and extracted 3 times with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was re-crystallized from petroleum ether to afford (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)acetamide (90 g, 83% yield) as a white solid. MS (ESI) calculated for $C_{11}H_{12}BrNO$: 253.01, found 254.00 $[M+H]^+$, 256.00 $[M+H+2]^+$.

[00249] Step 2: Synthesis of *tert*-butyl (*S*)-(1-acetamido-2,3-dihydro-1*H*-inden-5-yl)carbamate

[00250] To a mixture of *N*-[(1S)-5-bromo-2,3-dihydro-1*H*-inden-1-yl]acetamide (40 g, 157 mmol, 1 equiv), *tert*-butyl carbamate (27.66 g, 236 mmol, 1.5 equiv), XantPhos (9.11 g, 15.7 mmol, 10 mol%), palladium (II) acetate (3.54 g, 15.7 mmol, 10 mol%), and cesium carbonate (154 g, 472 mmol, 10 mol%) was added 1,4-dioxane (300 mL) under nitrogen atmosphere. The resulting mixture was stirred for 3 h at 100 °C. The reaction mixture was quenched by addition of water and extracted 3 times with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using an eluent of petroleum ether/dichloromethane/methanol (70:27:3) to afford *tert*-butyl *N*-[(1S)-1-acetamido-2,3-dihydro-1*H*-inden-5-yl]carbamate (43.1 g, 48%). MS (ESI) calculated for $C_{16}H_{22}N_2O_3$: 290.16 m/z, found 289.05 $[M-H]^-$.

[00251] Step 3: Synthesis of (S)-*N*-(5-amino-2,3-dihydro-1*H*-inden-1-yl)acetamide

[00252] To a stirred solution of *tert*-butyl *N*-[(1S)-1-acetamido-2,3-dihydro-1*H*-inden-5-yl]carbamate (43.1 g, 148 mmol, 1 equiv) in dichloromethane (180 mL) was added 4N hydrochloric acid in 1,4-dioxane (185 mL, 742 mmol, 5 equiv). The reaction mixture was stirred for 1 h at room temperature. The reaction mixture was concentrated *in vacuo* and re-crystallized from ethyl acetate to afford *N*-[(1S)-5-amino-2,3-dihydro-1*H*-inden-1-yl]acetamide (hydrochloride salt) (23 g, 81%) as a white solid. MS (ESI) calculated for $C_{11}H_{14}N_2O$: 190.11 m/z, found 191.15 $[M+H]^+$.

[00253] Step 4: Synthesis of *N*-[(1S)-5-[(6-chloro-3-nitropyridin-2-yl)amino]-2,3-dihydro-1*H*-inden-1-yl]acetamide

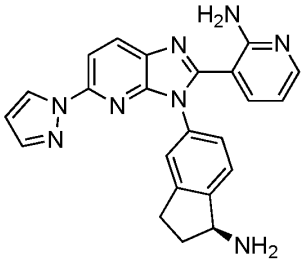
[00254] To a solution of *N*-[(1S)-5-amino-2,3-dihydro-1*H*-inden-1-yl]acetamide (100 g, 526 mmol, 1 equiv) in ethanol (2 L) was added triethylamine (160 g, 1.58 mol, 3 equiv) and 2,6-dichloro-3-nitropyridine (122 g, 631 mmol, 1.2 equiv). The resulting mixture was stirred at 60 °C overnight. The mixture was then cooled to room temperature and quenched with water. The resulting precipitate was collected by filtration and rinsed with ethanol/water to afford *N*-[(1S)-5-[(6-chloro-3-nitropyridin-2-yl)amino]-2,3-dihydro-1*H*-inden-1-yl]acetamide (100 g, 49%) as a red solid. MS (ESI) calculated for $C_{16}H_{15}ClN_4O_3$: 346.08 m/z, found 345.00 $[M-H]^-$.

[00255] Step 5: Synthesis of *N*-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-chloroimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1*H*-inden-1-yl]acetamide (Intermediate 1-1)

[00256] To a solution of *N*-[(1S)-5-[(6-chloro-3-nitropyridin-2-yl)amino]-2,3-dihydro-1*H*-inden-1-yl]acetamide (100 g, 288 mmol, 1 equiv) in dimethyl sulfoxide (1.8 L) and methanol (300 mL) was added 2-aminopyridine-3-carbaldehyde (38.74 g, 317.2 mmol, 1.1

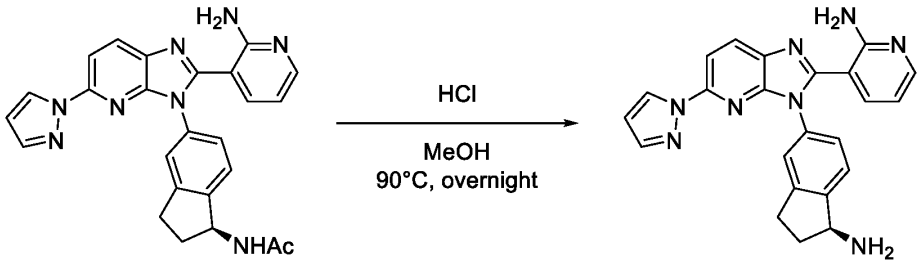
equiv) and sodium dithionite (110 g, 634 mmol, 2.2 equiv). The resulting mixture was stirred at 100 °C overnight. Water was added and the precipitated solids were collected by filtration, rinsing with water. The solid collected was purified by silica gel column chromatography eluting with dichloromethane / methanol (10:1) to afford *N*-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-chloroimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1*H*-inden-1-yl]acetamide (**Intermediate 1-1**) (43.2 g, 31%) as a yellow solid. MS (ESI) calculated for $C_{22}H_{19}ClN_6O$: 418.13 m/z, found 419.10 $[M+H]^+$.

[00257] Example 2: (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 2)



Compound 2

[00258] Synthetic Route:



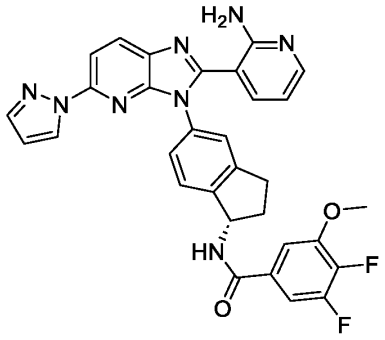
Compound 1 **Compound 2**

[00259] Step 1: Synthesis of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 2)

[00260] To a stirred suspension of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (**Compound 1**) (1.00 g, 2.22 mmol, 1 equiv) in methanol (5 mL) was added HCl (5 mL, concentrated) and the resulting solution was stirred at 90 °C overnight under nitrogen atmosphere. The solution was cooled to room temperature and diluted with dichloromethane. The solution was concentrated to dryness under reduced pressure. The crude solid was taken up into DMSO and pyrrolidine (395 mg, 5.55 mmol, 2.5 equiv) was added. The solution was stirred for 2 min followed by addition of TFA (959 mg, 6.66 mmol, 3 equiv). The solution was purified by preparative HPLC on a Phenomenex Gemini C18 Column using a gradient of acetonitrile in water (+ 0.05% TFA) to

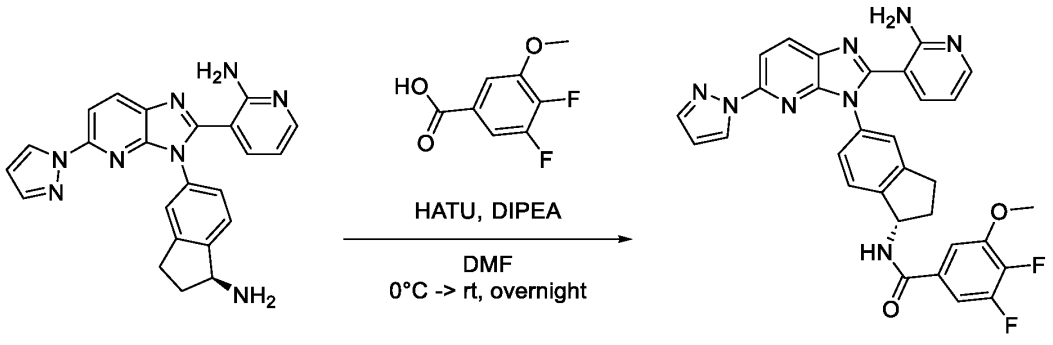
afford (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (TFA salt) (**Compound 2**) (869 mg, 75%) as a yellow solid. MS (ESI) calcd. for $C_{23}H_{20}N_8$: 408.08 m/z, found 409.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.40 - 8.43 (m, 1H), 8.32 - 8.40 (m, 1H), 8.02 - 8.10 (m, 1H), 7.95 - 8.02 (m, 1H), 7.78 - 7.85 (m, 1H), 7.61 - 7.75 (m, 2H), 7.48 - 7.58 (m, 1H), 7.36 - 7.45 (m,1H), 6.72 - 6.82 (m, 1H), 6.51 - 6.69 (m, 1H), 4.72 - 4.82 (m, 1H), 3.05 - 3.30 (m, 1H), 2.88 - 3.05 (m, 1H), 2.55 - 2.68 (m, 1H), 2.01 - 2.18 (m, 1H).

[00261] Example 3: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-3,4-difluoro-5-methoxybenzamide (Compound 3)



Compound 3

[00262] Synthetic Route:



Compound 2 **Compound 3**

[00263] Step 1: Synthesis of (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-3,4-difluoro-5-methoxybenzamide (Compound 3)

[00264] A dry vial was charged with 3,4-difluoro-5-anisic acid (37 mg, 0.20 mmol, 1 equiv) under nitrogen atmosphere. A solution of HATU (79 mg, 0.20 mmol, 1.05 equiv) in N,N-dimethylformamide (0.8 mL) was added and the solution was cooled to 0 °C. N,N-diisopropylethylamine (26 mg, 0.20 mmol, 1 equiv) was added and the solution was stirred at 0

°C for 1 h. A solution of (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (126 mg, 0.24 mmol, 1.2 equiv) and N,N-diisopropylethylamine (64 mg, 0.5 mmol, 2.5 equiv) in N,N-dimethylformamide (1.2 mL) was added and the solution was stirred overnight at room temperature. The reaction mixture was purified by preparative HPLC on a Phenomenex Gemini C18 column using a gradient of acetonitrile in water (+ 0.05% TFA (or formic acid for the formic acid salts obtained using an analogous procedure or ammonium bicarbonate for free bases obtained using an analogous procedure)) to afford (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-3,4-difluoro-5-methoxybenzamide (TFA salt) (**Compound 3**) (78 mg, 69%). MS (ESI) calculated for $C_{31}H_{24}F_2N_8O_2$: 578.20 m/z, found 579.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.00 (d, J = 8.2 Hz, 1H), 8.43 (d, J = 8.7 Hz, 1H), 8.38 (dd, J = 2.6, 0.7 Hz, 1H), 8.09 (dd, J = 5.9, 1.7 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.83 (dd, J = 1.8, 0.7 Hz, 1H), 7.76 (dd, J = 7.5, 1.7 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.49 – 7.46 (m, 1H), 7.42 – 7.35 (m, 2H), 6.79 (dd, J = 7.6, 5.9 Hz, 1H), 6.57 (dd, J = 2.6, 1.7 Hz, 1H), 5.64 (dd, J = 8.2, 8.2 Hz, 1H), 3.95 (s, 3H), 3.07 (ddd, J = 16.3, 8.9, 2.7 Hz, 1H), 2.93 (ddd, J = 16.2, 8.4, 8.4 Hz, 1H), 2.59 – 2.53 (m, 1H), 2.17 – 2.02 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm) -137.55 (d, J = 21.1 Hz), -156.31 (d, J = 21.3 Hz).

[00265] The following compounds were prepared analogously to the synthetic preparation in Example 3 (Compound 3).

[00266] **Table 3.** Characterization data of compounds prepared analogously to compound 3.

Cpd ID	Characterization Data
66	MS (ESI) calcd. for $C_{32}H_{25}F_2N_9O$, 589.22 m/z, found 590.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.98 - 9.13 (m, 1H), 8.27 - 8.43 (m, 3H), 7.99 - 8.09 (m, 1H), 7.90 - 7.98 (m, 1H), 7.77 - 7.86 (m, 1H), 7.35 - 7.47 (m, 2H), 7.20 - 7.34 (m, 2H), 6.52 - 6.61 (m, 1H), 6.38 - 6.51 (m, 1H), 5.56 - 5.74 (m, 1H), 2.96 - 3.18 (m, 3H), 2.83 - 2.95 (m, 1H), 2.53 - 2.80 (m, 3H), 2.02 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -90.75.
67	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found 529.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.05 (s, 1H), 8.50 - 8.57 (m, 2H), 8.11 - 8.18 (m, 3H), 8.07 - 8.10 (m, 1H), 7.85 - 7.90 (m, 1H), 7.68 - 7.71 (m, 1H), 7.47 - 7.51 (m, 2H), 7.39 - 7.42 (m, 1H), 6.85 - 6.91 (m, 1H), 5.61 - 5.69 (m, 1H), 2.99 - 3.14 (m, 1H), 2.87 - 2.98 (m, 1H), 2.63 (s, 3H), 2.55 - 2.60 (m, 1H), 2.09 - 2.18 (m, 1H). (2,2,2-trifluoroacetic acid salt)
68	MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O_2$ 597.18 m/z, found 598.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.85 (s, 1H), 8.41 - 8.48 (m, 1H), 8.37 - 8.40 (m, 1H), 8.33 - 8.36 (m, 1H), 8.00 - 8.05 (m, 1H), 7.95 - 7.99 (m, 1H), 7.81 - 7.83 (m, 1H), 7.39 - 7.45 (m, 3H), 7.30 - 7.33 (m, 2H), 6.60 - 6.62 (m, 1H), 6.50 - 6.57 (m, 1H), 5.59 - 5.67 (m, 1H), 2.99 - 3.14 (m, 1H), 2.87 - 2.98 (m, 1H), 2.55 - 2.60 (m, 1H), 2.01 - 2.13 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -55.21. (formic acid salt)

Cpd ID	Characterization Data
69	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found 542.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.26 - 8.34 (m, 2H), 7.99 - 8.07 (m, 1H), 7.89 - 7.97 (m, 1H), 7.74 - 7.80 (m, 1H), 7.64 - 7.71 (m, 1H), 7.37 - 7.41 (m, 1H), 7.30 - 7.36 (m, 1H), 7.19 - 7.29 (m, 2H), 7.08 - 7.16 (m, 1H), 6.56 - 6.64 (m, 1H), 6.41 - 6.50 (m, 1H), 5.47 - 5.58 (m, 1H), 2.79 - 3.06 (m, 2H), 2.54 - 2.59 (m, 1H), 2.47 - 2.53 (m, 3H), 2.37 - 2.46 (m, 3H), 1.92 - 2.08 (m, 1H).
71	MS (ESI) calcd. for $C_{32}H_{26}N_{10}O$, 566.23 m/z, found 567.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.13 - 9.20 (m, 1H), 8.30 - 8.44 (m, 3H), 7.94 - 8.08 (m, 4H), 7.78 - 7.83 (m, 1H), 7.66 - 7.76 (m, 1H), 7.40 - 7.51 (m, 2H), 7.31 - 7.39 (m, 1H), 6.70 - 6.81 (m, 1H), 6.52 - 6.60 (m, 1H), 5.61 - 5.73 (m, 1H), 3.05 - 3.16 (m, 1H), 2.87 - 3.05 (m, 1H), 2.54 - 2.63 (m, 4H), 2.02 - 2.22 (m, 1H).
72	MS (ESI) calcd. for $C_{32}H_{26}ON_{10}$ 566.23 m/z, found, 567.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.33 - 9.40 (m, 1H), 8.40 - 8.45 (m, 1H), 8.34 - 8.38 (m, 1H), 8.20 - 8.35 (m, 1H), 8.14 (s, 1H), 8.04 - 8.10 (m, 1H), 7.98 - 8.03 (m, 1H), 7.87 - 7.95 (m, 1H), 7.79 - 7.85 (m, 1H), 7.68 - 7.77 (m, 1H), 7.46 - 7.50 (m, 1H), 7.43 (s, 1H), 7.31 - 7.41 (m, 1H), 6.72 - 6.81 (m, 1H), 6.52 - 6.60 (m, 1H), 5.59 - 5.71 (m, 1H), 3.02 - 3.16 (m, 1H), 2.86 - 3.01 (m, 1H), 2.54 - 2.66 (m, 1H), 2.52 (s, 3H), 2.04 - 2.20 (m, 1H).
73	MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$, 577.22 m/z, found 578.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.83 - 8.95 (m, 1H), 8.19 - 8.30 (m, 2H), 8.10 - 8.20 (m, 1H), 7.78 - 8.10 (m, 3H), 7.31 - 7.42 (m, 3H), 7.21 - 7.31 (m, 2H), 6.89 - 6.98 (m, 1H), 6.45 - 6.55 (m, 1H), 5.54 - 5.67 (m, 1H), 3.02 - 3.10 (m, 1H), 2.90 - 3.00 (m, 1H), 2.55 - 2.65 (m, 3H), 2.50 - 2.54 (m, 1H), 2.05 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -94.15. (formic acid salt)
74	MS (ESI) calcd. for $C_{31}H_{23}F_4N_9O$, 613.20 m/z, found 614.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.10 - 9.21 (m, 1H), 8.39 - 8.53 (m, 1H), 8.18 - 8.35 (m, 2H), 7.36 - 8.12 (m, 6H), 7.23 - 7.35 (m, 2H), 6.80 - 7.22 (m, 2H), 6.39 - 6.53 (m, 1H), 5.58 - 5.75 (m, 1H), 2.81 - 3.18 (m, 2H), 2.53 - 2.69 (m, 1H), 1.97 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -94.22, -116.04.
75	MS (ESI) calcd. for $C_{30}H_{25}N_9O$, 527.22 m/z, found 528.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.68 - 8.83 (m, 1H), 8.40 - 8.52 (m, 1H), 8.32 - 8.39 (m, 1H), 8.06 - 8.15 (m, 1H), 7.98 - 8.05 (m, 2H), 7.86 - 7.97 (m, 1H), 7.73 - 7.85 (m, 2H), 7.46 - 7.55 (m, 1H), 7.40 - 7.45 (m, 1H), 7.30 - 7.39 (m, 1H), 6.78 - 6.92 (m, 1H), 6.50 - 6.61 (m, 1H), 5.54 - 5.70 (m, 1H), 2.85 - 3.20 (m, 2H), 2.65 (s, 3H), 2.53 - 2.62 (m, 1H), 2.01 - 2.21 (m, 1H). (TFA salt)
76	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found, 542.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.43 - 8.48 (m, 1H), 8.37 - 8.41 (m, 1H), 8.05 - 8.11 (m, 1H), 8.01 - 8.04 (m, 1H), 7.95 - 7.99 (m, 2H), 7.86 - 7.90 (m, 1H), 7.80 - 7.83 (m, 1H), 7.48 - 7.51 (m, 1H), 7.43 - 7.47 (m, 1H), 7.39 - 7.41 (m, 1H), 6.81 - 6.88 (m, 1H), 6.60 - 6.63 (m, 1H), 5.60 - 5.68 (m, 1H), 3.05 - 3.14 (m, 1H), 2.90 - 3.02 (m, 1H), 2.71 (s, 6H), 2.55 - 2.60 (m, 1H), 2.03 - 2.15 (m, 1H). (TFA salt)
77	MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O$, 581.19 m/z, found 582.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.11 - 9.25 (m, 1H), 8.48 - 8.60 (m, 1H), 8.42 - 8.47 (m, 1H), 8.33 - 8.41 (m, 1H), 7.95 - 8.15 (m, 3H), 7.77 - 7.90 (m, 2H), 7.40 - 7.55 (m, 2H), 7.30 - 7.39 (m, 1H), 6.77 - 6.92 (m, 1H), 6.50 - 6.63 (m, 1H), 5.57 - 5.73 (m, 1H), 3.02 - 3.18 (m, 1H), 2.85 - 3.01 (m, 1H), 2.55 - 2.68 (m, 1H), 2.01 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -66.59. (TFA salt)

Cpd ID	Characterization Data
78	MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O_2$ 597.18 m/z, found, 598.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.16 - 9.20 (m, 1H), 8.42 - 8.46 (m, 1H), 8.33 - 8.41 (m, 2H), 8.13 - 8.16 (m, 1H), 7.92 - 8.06 (m, 2H), 7.79 - 7.82 (m, 1H), 7.53 - 7.57 (m, 1H), 7.45 - 7.49 (m, 1H), 7.25 - 7.41 (m, 3H), 6.55 - 6.58 (m, 1H), 6.48 - 6.50 (m, 1H), 5.50 - 5.65 (m, 1H), 2.88 - 3.09 (m, 2H), 2.55 - 2.60 (m, 1H), 1.91 - 2.10 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -54.65. (formic acid salt)
79	MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O$, 563.20 m/z, found, 564.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.80 - 8.82 (m, 1H), 8.42 - 8.47 (m, 1H), 8.39 - 8.41 (m, 1H), 8.03 - 8.11 (m, 3H), 7.84 - 7.88 (m, 1H), 7.81 - 7.83 (m, 1H), 7.68 - 7.73 (m, 1H), 7.50 - 7.57 (m, 2H), 7.15 - 7.42 (m, 2H), 6.80 - 6.88 (m, 1H), 6.59 - 6.61 (m, 1H), 5.59 - 5.63 (m, 1H), 2.90 - 3.11 (m, 2H), 2.55 - 2.60 (m, 1H), 2.00 - 2.13 (m, 1H). (TFA salt)
80	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found, 542.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.06 - 9.12 (m, 1H), 8.95 - 9.00 (m, 1H), 8.33 - 8.40 (m, 2H), 8.15 - 8.22 (m, 1H), 8.00 - 8.06 (m, 1H), 7.92 - 7.98 (m, 1H), 7.79 - 7.82 (m, 1H), 7.33 - 7.43 (m, 3H), 7.22 - 7.33 (m, 2H), 6.52 - 6.56 (m, 1H), 6.42 - 6.48 (m, 1H), 5.56 - 5.71 (m, 1H), 2.95 - 3.08 (m, 2H), 2.80 - 2.88 (m, 2H), 2.53 - 2.60 (m, 1H), 1.98 - 2.18 (m, 1H), 1.20 - 1.30 (m, 3H). (formic acid salt)
85	MS (ESI) calcd. for $C_{32}H_{30}N_{10}O$, 570.26 m/z, found, 571.20 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.12 - 9.18 (m, 1H), 8.34 - 8.48 (m, 3H), 8.06 - 8.12 (m, 1H), 8.01 - 8.05 (m, 1H), 7.83 - 7.88 (m, 1H), 7.71 - 7.80 (m, 1H), 7.60 - 7.70 (m, 1H), 7.46 - 7.50 (m, 1H), 7.42 - 7.45 (m, 1H), 7.35 - 7.39 (m, 1H), 6.80 - 6.85 (m, 1H), 6.53 - 6.62 (m, 1H), 5.60 - 5.70 (m, 1H), 4.54 (s, 2H), 3.07 - 3.11 (m, 1H), 2.90 - 3.00 (m, 1H), 2.83 (s, 6H), 2.58 - 2.62 (m, 1H), 2.05 - 2.20 (m, 1H). (TFA salt)
86	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found 542.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.52 - 8.60 (m, 1H), 8.30 - 8.40 (m, 2H), 8.00 - 8.05 (m, 1H), 7.90 - 8.00 (m, 1H), 7.80 - 7.83 (m, 1H), 7.75 - 7.80 (m, 1H), 7.40 - 7.48 (m, 1H), 7.35 - 7.40 (m, 1H), 7.20 - 7.35 (m, 3H), 6.52 - 6.60 (m, 1H), 6.38 - 6.50 (m, 1H), 5.50 - 5.68 (m, 1H), 2.98 - 3.08 (m, 1H), 2.82 - 2.98 (m, 3H), 2.52 - 2.62 (m, 1H), 1.91 - 2.10 (m, 1H), 1.15 - 1.25 (m, 3H). (formic acid salt)
90	MS (ESI) calcd. for $C_{32}H_{25}N_{11}O$, 579.22 m/z, found 580.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.52 - 8.60 (m, 1H), 8.40 - 8.50 (m, 2H), 8.32 - 8.40 (m, 1H), 7.95 - 8.10 (m, 3H), 7.82 - 7.90 (m, 1H), 7.75 - 7.82 (m, 1H), 7.65 - 7.75 (m, 2H), 7.46 - 7.58 (m, 1H), 7.32 - 7.46 (m, 2H), 6.75 - 6.90 (m, 1H), 6.49 - 6.65 (m, 2H), 5.42 - 5.58 (m, 1H), 2.85 - 3.15 (m, 2H), 2.45 - 2.50 (m, 1H), 1.90 - 2.10 (m, 1H). (TFA salt)
92	MS (ESI) calcd. for $C_{29}H_{25}N_{11}O$, 543.22 m/z, found, 544.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.66 (s, 1H), 8.50 - 8.53 (m, 1H), 8.15 - 8.19 (m, 2H), 8.11 - 8.13 (m, 1H), 8.05 - 8.10 (m, 1H), 7.85 - 7.88 (m, 1H), 7.51 - 7.53 (m, 1H), 7.47 - 7.50 (m, 1H), 7.38 - 7.42 (m, 1H), 6.80 - 6.90 (m, 1H), 5.59 - 5.64 (m, 1H), 2.90 - 3.10 (m, 2H), 2.61 (s, 3H), 2.58 - 2.60 (m, 4H), 1.94 - 2.09 (m, 1H). (TFA salt)
93	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found, 529.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.01 - 9.08 (m, 1H), 8.46 - 8.52 (m, 1H), 8.40 - 8.43 (m, 1H), 8.07 - 8.12 (m, 2H), 8.04 - 8.07 (m, 1H),7.95 - 8.04 (m, 1H), 7.77 - 7.82 (m, 1H), 7.46 - 7.51 (m, 1H), 7.38 - 7.42 (m, 1H), 7.29 - 7.35 (m, 3H), 6.44 - 6.50 (m, 1H), 5.57 - 5.65 (m, 1H), 2.80 - 3.09 (m, 2H), 2.55 - 2.58 (m, 4H), 1.95 - 2.10 (m, 1H). (formic acid salt)

Cpd ID	Characterization Data
94	MS (ESI) calcd. for $C_{32}H_{27}N_9O$, 553.63 m/z, found 554.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.70 - 8.95 (m, 1H), 8.20 - 8.55 (m, 2H), 8.10 - 8.15 (m, 1H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H), 7.80 - 7.90 (m, 1H), 7.35 - 7.45 (m, 2H), 7.25 - 7.35 (m, 2H), 6.55 - 6.65 (m, 1H), 6.45 - 6.55 (m, 1H), 5.50 - 5.85 (m, 1H), 2.85 - 3.18 (m, 6H), 2.55 - 2.65 (m, 1H), 2.00 - 2.25 (m, 3H). (formic acid salt)
95	MS (ESI) calcd. for $C_{33}H_{30}N_{10}O_2$, 598.26 m/z, found 599.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.58 - 8.90 (m, 2H), 8.30 - 8.40 (m, 2H), 7.89 - 8.22 (m, 3H), 7.70 - 7.85 (m, 1H), 7.25 - 7.40 (m, 4H), 6.80 - 6.96 (m, 1H), 6.55 - 6.60 (m, 1H), 6.42 - 6.50 (m, 1H), 5.50 - 5.70 (m, 1H), 3.68 - 3.70 (m, 5H), 3.52 - 3.55 (m, 3H), 2.85 - 3.08 (m, 2H), 2.55 - 2.62 (m, 1H), 1.90 - 2.25 (m, 1H).
96	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found 543.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.66 (s, 1H), 8.49 (s, 1H), 8.38 - 8.39 (m, 1H), 8.04 - 8.05 (m, 1H), 8.01 - 8.03 (m, 1H), 7.80 - 7.83 (m, 2H), 7.48 - 7.52 (m, 2H), 7.36 - 7.39 (m, 1H), 6.84 - 6.86 (m, 1H), 6.57 - 6.59 (m, 1H), 5.54 - 5.59 (m, 1H), 2.85 - 3.10 (m, 2H), 2.60 (s, 3H), 2.55 (s, 3H), 2.52 - 2.53 (m, 1H), 2.05 - 2.20 (m, 1H). (TFA salt)
98	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$, 545.21 m/z, found 546.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.98 - 9.13 (m, 1H), 8.26 - 8.47 (m, 3H), 7.99 - 8.10 (m, 1H), 7.90 - 7.98 (m, 1H), 7.75 - 7.87 (m, 1H), 7.56 - 7.70 (m, 1H), 7.34 - 7.46 (m, 2H), 7.18 - 7.33 (m, 2H), 6.53 - 6.61 (m, 1H), 6.38 - 6.52 (m, 1H), 5.58 - 5.72 (m, 2H), 5.46 (s, 1H), 2.83 - 3.18 (m, 2H), 2.55 - 2.64 (m, 1H), 2.00 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -217.94.
99	MS (ESI) calcd. for $C_{28}H_{23}N_9OS$ 533.17 m/z, found, 534.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.07 (s, 1H), 8.44 - 8.51 (m, 1H), 8.38 - 8.42 (m, 1H), 8.08 - 8.12 (m, 1H), 8.01 - 8.06 (m, 1H), 7.84 - 7.90 (m, 2H), 7.46 - 7.52 (m, 1H), 7.40 - 7.43 (m, 1H), 7.35 - 7.39 (m, 1H), 6.82 - 6.91 (m, 1H), 6.56 - 6.61 (m, 1H), 5.55 (s, 1H), 3.01 - 3.12 (m, 1H), 2.85 - 2.98 (m, 1H), 2.60 - 2.65 (m, 3H), 2.49 - 2.52 (m, 1H), 2.01 -2.15 (m, 1H).
100	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found 542.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.46 - 8.53 (m, 1H), 8.32 - 8.39 (m, 1H), 7.98 - 8.09 (m, 1H), 7.78 - 7.85 (m, 3H), 7.21 - 7.52 (m, 5H), 6.53 - 6.60 (m, 1H), 6.45 - 6.51 (m, 1H), 5.51 - 5.62 (m, 1H), 2.88 - 3.09 (m, 2H), 2.72 - 2.81 (m, 3H), 2.49 - 2.58 (m, 3H), 2.59 - 2.62 (m, 1H), 1.98 - 2.16 (m, 1H).
101	MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$, 577.22 m/z, found, 578.10$[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.08 - 9.15 (m, 1H), 8.38 - 8.47 (m, 1H), 8.28 - 8.35 (m, 1H), 7.94 - 8.03 (m, 1H), 7.81 - 7.89 (m, 1H), 7.74 - 7.81 (m, 2H), 7.32 - 7.37 (m, 1H), 7.38 - 7.43 (m, 1H), 7.20 - 7.31 (m, 2H), 6.79 - 7.20 (m, 1H), 6.50 - 6.56 (m, 1H), 6.39 - 6.49 (m, 1H), 5.57 - 5.68 (m, 1H), 2.99 - 3.10 (m, 1H), 2.82 - 2.98 (m, 1H), 2.68 - 2.74 (m, 3H), 2.52 - 2.62 (m, 1H), 1.98 - 2.17 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.01, -116.05.
103	MS (ESI) calcd. for $C_{32}H_{27}N_9O$, 553.23 m/z, found 554.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.45 (m, 1H), 8.33 - 8.39 (m, 2H), 8.01 - 8.09 (m, 1H), 7.95 - 7.99 (m, 1H), 7.81 - 7.89 (m, 1H), 7.71 - 7.78 (m, 1H), 7.46 - 7.52 (m, 1H), 7.40 - 7.44 (m, 1H), 7.25 - 7.31 (m, 2H), 7.19 - 7.23 (m, 1H), 6.55 - 6.66 (m, 1H), 6.44 - 6.54 (m, 1H), 5.60 - 5.80 (m, 1H), 3.02 - 3.10 (m, 1H), 2.91 - 2.96 (m, 1H), 2.52 - 2.58 (m, 1H), 2.37 - 2.48 (m, 1H), 2.01 - 2.03 (m, 1H), 0.88 - 1.10 (m, 4H).

Cpd ID	Characterization Data
104	MS (ESI) calcd. for $C_{32}H_{30}N_{10}O$, 570.26 m/z, found 571.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.59 - 8.60 (m, 1H), 8.29 - 8.40 (m, 2H), 8.11 - 8.15 (m, 1H), 8.01 - 8.06 (m, 1H), 7.95 - 7.99 (m, 1H), 7.81 - 7.92 (m, 1H), 7.54 - 7.65(m, 1H), 7.48 - 7.50 (m, 1H), 7.42 - 7.44 (m, 1H), 7.32 - 7.39 (m, 1H), 7.25 - 7.28 (m, 1H), 6.55 - 6.75 (m, 1H), 6.40 - 6.50 (m, 1H), 5.55 - 5.68 (m, 1H), 3.70 - 3.75 (m, 1H), 3.49 - 3.60 (m, 1H), 2.88 - 3.09 (m, 2H), 2.61 - 2.68 (m, 1H), 1.96 - 2.05 (m, 7H).
105	MS (ESI) calcd. for $C_{31}H_{23}N_9O$, 537.20 m/z, found 538.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.20 - 9.30 (m, 1H), 8.72 - 8.73 (m, 1H), 8.35 - 8.37 (m, 2H), 8.05 - 8.07 (m, 2H), 7.93 - 7.96 (m, 1H), 7.87 - 7.89 (m, 1H), 7.79 - 7.82 (m, 1H), 7.47 - 7.52 (m, 2H), 7.40 - 7.46 (m, 1H), 7.35 - 7.40 (m, 1H), 6.85 - 6.90 (m, 2H), 6.56 - 6.57 (m, 1H), 6.43 - 6.46 (m, 1H), 5.61 - 5.65 (m, 1H), 4.45 (s, 1H), 3.03 - 3.05 (m, 1H), 2.94 - 2.96 (m, 1H), 2.50 - 2.51 (m, 1H), 2.10 - 2.12 (m, 1H).
106	MS (ESI) calcd. for $C_{31}H_{25}N_9O_2$, 555.21 m/z, found 556.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.91 - 8.97 (m, 1H), 8.29 - 8.38 (m, 2H), 8.16 - 8.21 (m, 1H), 8.02 - 8.06 (m, 1H), 7.93 - 8.00 (m, 1H), 7.75 - 7.82 (m, 1H), 7.34 - 7.42 (m, 2H), 7.25 - 7.32 (m, 2H), 6.53 - 6.57 (m, 1H), 6.39 - 6.49 (m, 1H), 5.58 - 5.64 (m, 1H), 5.11 (s, 2H), 4.93 (s, 2H), 2.85 - 3.15 (m, 2H), 2.51 - 2.60 (m, 1H), 1.97 - 2.16 (m, 1H).
107	MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$, 564.19 m/z, found 565.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.20 - 9.35 (m, 1H), 8.70 - 8.90 (m, 1H), 8.32 - 8.55 (m, 1H), 8.00 - 8.15 (m, 5H), 7.62 - 7.72 (m, 1H), 7.42 - 7.55 (m, 1H), 7.38 - 7.42 (m, 1H), 7.25 - 7.38 (m, 2H), 7.00 - 7.25 (m, 1H), 6.40 - 6.51 (m, 1H), 5.50 - 5.70 (m, 1H), 2.80 - 3.10 (m, 2H), 2.55 - 2.65 (m, 1H), 2.00 - 2.15 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm); -115.30.
108	MS(ESI) calcd. for $C_{29}H_{22}ClN_9O$, 547.16 m/z, found 548.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.48 - 8.56 (m, 1H), 8.31 - 8.43 (m, 2H), 7.99 - 8.06 (m, 1H), 7.91 - 7.98 (m, 2H), 7.81 - 7.90 (m, 1H), 7.49 - 7.52 (m, 2H), 7.38 - 7.42 (m, 1H), 7.26 - 7.37 (m, 2H), 6.61 - 6.68 (m, 1H), 6.51 - 6.59 (m, 1H), 5.53 - 5.66 (m, 1H), 2.94 - 3.15 (m, 2H), 2.56 - 2.64 (m, 1H), 1.96 - 2.08 (m, 1H).
110	MS(ESI) calcd. for $C_{30}H_{22}F_3N_9O$, 581.19 m/z, found 582.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.78 - 8.85 (m, 1H), 8.31 - 8.42 (m, 2H), 8.08 - 8.13 (m, 1H), 7.99 - 8.06 (m, 1H), 7.91 - 7.98 (m, 1H), 7.78 - 7.86 (m, 2H), 7.49 - 7.52 (m, 1H), 7.38 - 7.43 (m, 1H), 7.29 - 7.37 (m, 2H), 6.58 - 6.60 (m, 1H), 6.49 - 6.57 (m, 1H), 5.51 - 5.60 (m, 1H), 2.92 - 3.14 (m, 2H), 2.53 - 2.66 (m, 1H), 1.98 - 2.06 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -62.79, -62.84.
112	MS (ESI) calcd. for $C_{32}H_{28}N_{10}O$, 568.24 m/z, found 569.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.83 (s, 1H), 8.30 - 8.39 (m, 2H), 8.09 (s, 1H), 7.92 - 8.00 (m, 2H), 7.79 (s, 1H), 7.32 - 7.40 (m, 2H), 7.22 - 7.28 (m, 2H), 6.41 - 6.56 (m, 2H), 5.61 (s, 1H), 3.84 - 3.92 (m, 4H), 2.84 - 3.05 (m, 2H), 2.38 - 2.46 (m, 4H), 1.93 - 2.12 (m, 1H).
113	MS (ESI) calcd. for $C_{31}H_{23}N_9O$, 537.20 m/z, found 538.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 8.58 - 8.63 (m, 1H), 8.30 - 8.40 (m, 2H), 7.88 - 8.02 (m, 3H), 7.78 - 7.84 (m, 1H), 7.45 - 7.55 (m, 2H), 7.38 (s, 1H), 7.19 - 7.32 (m, 2H), 6.50 - 6.58 (m, 1H), 6.38 - 6.46 (m, 1H), 5.35 - 5.53 (m, 1H), 4.37 (s, 1H), 2.81 - 3.03 (m, 2H), 2.51 - 2.63 (m, 1H), 1.94 - 2.10 (m, 1H)

Cpd ID	Characterization Data
114	MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$, 564.19 m/z, found 565.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.46 (s, 2H), 8.38 - 8.43 (m, 2H), 8.01 -8.09 (m, 2H), 7.79 - 8.84 (m, 2H), 7.49 - 7.51 (m, 2H), 7.36 - 7.39 (m, 1H), 7.01 - 7.26 (m, 1H), 6.81 - 6.88 (m, 1H), 6.58 - 6.59 (m, 1H), 5.62 - 5.67 (m, 1H), 2.90 - 3.12 (m, 2H), 2.60 - 2.65 (m, 1H), 2.05 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -119.00. (TFA salt)
115	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found, 542.15 $[M+H]^+$. ^1HNMR (400 MHz, DMSO-d_6) δ (ppm); 8.83 (s, 1H), 8.40 - 8.47 (m, 2H), 8.35 - 8.39 (m, 1H), 7.97 - 8.02 (m, 2H), 7.79 - 7.82 (m, 1H), 7.75 - 7.78 (m, 1H), 7.44 - 7.47 (m, 1H), 7.38 - 7.42 (m, 1H), 7.30 - 7.35 (m, 1H), 6.76 - 6.81 (m, 1H), 6.53 - 6.57 (m, 1H), 5.59 - 5.64 (m, 1H), 3.00 - 3.10 (m, 1H), 2.89 - 2.98 (m, 1H), 2.61 (s, 3H), 2.58 - 2.60 (m, 1H), 2.38 (s, 3H), 2.00 - 2.09 (m, 1H). (TFA salt)
116	MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$, 564.19 m/z, found 565.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ(ppm); 9.44 (s, 1H), 9.16 (s, 1H), 8.38 - 8.47 (m, 2H), 7.98 - 8.11 (m, 2H), 7.78 - 7.86 (m, 1H), 7.50 - 7.59 (m, 1H), 7.12 - 7.49 (m, 4H), 6.49 - 6.64 (m, 2H), 5.57 - 5.69 (m, 1H), 2.96 - 3.14 (m, 2H), 2.61 - 2.67 (m, 1H), 1.99 - 2.17 (m, 1H).
117	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found 529.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.09 (s, 1H), 8.77 - 8.80 (m, 1H), 8.32 - 8.40 (m, 2H), 7.90 - 8.08 (m, 2H), 7.75 - 7.85 (m, 1H), 7.46 - 7.55 (m, 1H), 7.40 - 7.46 (m, 1H), 7.36 - 7.40 (m, 1H), 7.28 - 7.35 (m, 1H), 6.55 - 6.68 (m, 1H), 6.34 - 6.55 (m, 1H), 5.50 - 5.70 (m, 1H), 3.00 - 3.20 (m, 1H), 2.80 - 3.00 (m, 1H), 2.59 - 2.62 (m, 4H), 1.90 - 2.20 (m, 1H). (formic acid salt)
118	MS(ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found 529.25 $[M+H]^+$. ^1HNMR (300 MHz, DMSO-d_6) δ (ppm); 8.64 - 8.73 (m, 1H), 8.52 - 8.60 (m, 1H), 8.36 - 8.45 (m, 2H), 8.02 - 8.11 (m, 1H), 7.93 - 8.01 (m, 1H), 7.78 - 7.88 (m, 1H), 7.38 - 7.47 (m, 2H), 7.23 - 7.32 (m, 2H), 6.55 - 6.62 (m, 1H), 6.49 - 6.54 (m, 1H), 5.56 - 5.68 (m, 1H), 3.03 - 3.16 (m, 1H), 2.88 - 3.02 (m, 1H), 2.71 - 2.80 (m, 3H), 2.57 - 2.64 (m, 1H), 2.07 - 2.20 (m, 1H). (formic acid salt)
119	MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$, 564.19 m/z, found 565.10 $[M+H]^+$. ^1HNMR (300 MHz, DMSO-d_6) δ (ppm); 8.97 - 8.98 (m, 1H), 8.90 (s, 1H), 8.39 - 8.46 (m, 2H), 8.01 -8.08 (m, 2H), 7.45 - 7.55 (m, 3H), 7.37 - 7.43 (m, 2H), 7.34 - 7.35 (m, 1H), 6.83 - 6.87 (m, 1H), 6.57 - 6.58 (m, 1H), 5.61 - 5.66 (m, 1H), 3.01 - 3.13 (m, 1H), 2.85 - 2.95 (m, 1H), 2.54 - 2.58 (m, 1H), 2.17 - 2.27 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); 117.49. (TFA salt)
120	MS (ESI) calcd. for $C_{28}H_{23}N_9OS$, 533.17 m/z, found 534.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.49 (m, 2H), 8.15 - 8.30 (m, 1H), 8.00 - 8.15 (m, 1H), 7.90 - 8.00 (m, 1H), 7.71 - 7.90 (m, 1H), 7.32 - 7.45 (m, 2H), 7.22 - 7.32 (m, 2H), 6.55 - 6.70 (m, 1H), 6.35 - 6.55 (m, 1H), 5.42 - 5.70 (m, 1H), 2.85 - 3.10 (m, 2H), 2.68 (s, 3H), 2.58 - 2.60 (m, 1H), 1.90 - 2.20 (m, 1H). (formic acid salt)
126	MS (ESI) calcd. for $C_{29}H_{26}N_{10}O$, 530.23 m/z, found, 531.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.40 - 8.48 (m, 2H), 8.00 - 8.08 (m, 2H), 7.84 (s, 1H), 7.76 - 7.79 (m, 1H), 7.44 (s, 1H), 7.30 - 7.34 (m, 2H), 6.80 - 6.84 (m, 1H), 6.56 - 6.59 (m, 1H), 6.53 - 6.55 (m, 1H), 5.50 - 5.57 (m, 1H), 3.77 (s, 3H), 3.00 - 3.12 (m, 1H), 2.85 - 2.96 (m, 1H), 2.58 - 2.60 (m, 1H), 2.28 (s, 3H), 2.03 - 2.15 (m, 1H). (TFA salt)

Cpd ID	Characterization Data
127	MS (ESI) calcd. for $C_{29}H_{22}FN_9O$, 531.19 m/z, found 532.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.40 (m, 3H), 8.15 - 8.28 (m, 1H), 8.00 - 8.10 (m, 1H), 7.92 - 8.00 (m, 1H), 7.78 - 7.90 (m, 1H), 7.35 - 7.55 (m, 3H), 7.21 - 7.35 (m, 2H), 6.55 - 6.62 (m, 1H), 6.42 - 6.55 (m, 1H), 5.51 - 5.65 (m, 1H), 3.00 - 3.10 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.65 (m, 1H), 1.95 - 2.12 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm); -68.42. (formic acid salt)
128	MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$ 543.21 m/z, found, 544.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.44 - 8.48 (m, 1H), 8.34 - 8.44 (m, 1H), 8.28 - 8.34 (m, 1H), 8.11 - 8.15 (m, 1H), 8.05 - 8.09 (m, 1H), 7.99 - 8.05 (m, 1H), 7.76 - 7.86 (m, 2H), 7.41 - 7.51 (m, 2H), 7.33 - 7.40 (m, 1H), 7.12 - 7.19 (m, 1H), 6.80 - 6.90 (m, 1H), 6.55 - 6.61 (m, 1H), 5.53 - 5.63 (m, 1H), 3.95 (s, 3H), 2.88 - 3.11 (m, 2H), 2.53 - 2.63 (m, 1H), 1.97 - 2.15 (m, 1H). (TFA salt)
129	MS (ESI) calcd. for $C_{30}H_{27}N_7O$, 501.23 m/z, found 502.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.50 - 8.52 (m, 1H), 8.03 - 8.05 (m, 1H), 7.97 - 7.99 (m, 1H), 7.78 - 7.82 (m, 1H), 7.42 - 7.53 (m, 1H), 7.26 - 7.33 (m, 2H), 7.22 - 7.24 (m, 2H), 7.15 -7.18 (m, 1H), 6.40 - 6.53 (m, 1H), 5.56 - 5.64 (m, 1H), 2.80 - 3.03 (m, 1H), 2.84 - 2.95 (m, 1H), 2.56 (s, 3H), 2.10 - 2.21 (m, 1H), 1.98 - 2.02 (m, 1H), 1.23 (s, 1H), 0.88 - 0.98 (m, 2H), 0.77 - 0.88 (m, 2H).
130	MS (ESI) calcd. for $C_{30}H_{25}F_2N_7O$, 537.21 m/z, found 538.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.13 (s, 1H), 8.42 - 8.44 (m, 1H), 8.01 - 8.15 (m, 1H), 7.97 - 7.99 (m, 1H), 7.83 - 7.85 (m, 1H), 7.37 - 7.41 (m, 1H), 7.28 - 7.31 (m, 1H), 7.13 - 7.25 (m, 4H), 6.42 - 6.55 (m, 1H), 5.62 - 5.71 (m, 1H), 2.95 - 3.05 (m, 1H), 2.88 - 2.92 (m, 1H), 2.51 - 2.53 (m, 1H), 2.00 - 2.20 (m, 2H), 0.93 - 1.05 (m, 2H), 0.80 - 0.88 (m, 2H). ^{19}F NMR (400 MHz, DMSO-d_6) δ (ppm); -116.06.
135	MS (ESI) calcd. for $C_{31}H_{30}N_8O_2$, 546.25 m/z, found 547.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.59 - 8.50 (m, 1H), 7.94 - 7.99 (m, 2H), 7.77 - 7.79 (m, 1H), 7.42 -7.44 (m, 1H), 7.32- 7.33 (m, 1H), 7.20 - 7.28 (m, 2H), 7.12 - 7.19 (m, 1H), 6.88 - 6.90 (m, 1H), 6.40 - 6.42 (m, 1H), 5.52 - 5.56 (m, 1H), 3.81 - 3.83 (m, 4H), 3.38 - 3.41 (m, 4H), 2.95 - 3.08 (m, 1H), 2.86 - 2.88 (m, 1H), 2.54 - 2.56 (m, 4H), 1.98 - 2.05 (m, 1H).
136	MS (ESI) calcd. for $C_{31}H_{28}F_2N_8O_2$, 582.23 m/z, found 583.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.13 (m, 1H), 8.43 - 8.46 (m, 1H), 7.94 - 8.02 (m, 2H), 7.84 - 7.86 (m, 1H), 7.37 -7.39 (m, 1H), 7.32- 7.33 (m, 1H), 7.27- 7.30 (m, 1H),7.21 - 7.25 (m, 2H), 6.88 - 6.90 (m, 1H), 6.40 - 6.43 (m, 1H), 5.60 - 5.64 (m, 1H), 3.79 - 3.81 (m, 4H), 3.40 - 3.41 (m, 4H), 2.91 - 3.98 (m, 1H), 2.86 - 2.88 (m, 1H), 2.54 - 2.55 (m, 1H), 2.05 - 2.15 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.05.
137	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found, 542.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.58 (s, 1H), 8.43 -8.49 (m, 1H), 8.40 - 8.42 (m, 1H), 8.25 - 8.27 (m, 1H), 8.01 - 8.09 (m, 2H), 7.80 - 7.85 (m, 2H), 7.52 - 7.54 (m, 1H), 7.49 - 7.51 (m, 1H), 7.36 - 7.39 (m, 1H), 6.85 - 6.88 (m, 1H), 6.57 - 6.59 (m, 1H), 5.54 - 5.59 (m, 1H), 2.90 - 3.15 (m, 2H), 2.69 (s, 3H), 2.52 - 2.53 (m, 1H), 2.44 (s, 3H), 2.01 - 2.11 (m, 1H). (TFA salt)
138	MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O_2$, 597.18 m/z, found 598.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.10 - 9.19 (m, 1H), 8.84 - 8.90 (m, 1H), 8.32 - 8.41 (m, 2H), 8.28 - 8.31 (m, 1H), 8.03 - 8.10 (m, 1H), 7.97 - 8.02 (m, 1H), 7.80 - 7.87 (m, 1H), 7.39 - 7.51 (m, 2H), 7.27 - 7.38 (m, 2H), 6.57 - 6.62 (m, 1H), 6.47 - 6.56 (m, 1H), 5.61 - 5.72 (m, 1H), 2.88 - 3.16 (m, 2H), 2.61 - 2.68 (m, 1H), 1.99 - 2.17 (m, 1H).

Cpd ID	Characterization Data
143	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found, 529.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.96 - 9.08 (m, 2H), 8.27 - 8.41 (m, 2H), 7.88 - 7.98 (m, 2H), 7.69 - 7.78 (m, 2H), 7.38 - 7.43 (m, 2H), 7.20 - 7.30 (m, 1H), 6.72 - 6.84 (m, 1H), 6.45 - 6.55 (m, 1H), 5.50 - 5.60 (m, 1H), 2.94 - 3.06 (m, 1H), 2.82 - 2.93 (m, 1H), 2.64 (s, 3H), 2.38 - 2.45 (m, 1H), 1.95 - 2.09 (m, 1H). (TFA salt)
144	MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$, 516.21 m/z, found 517.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.85 - 9.00 (m, 1H), 8.32 - 8.40 (m, 2H), 8.02 - 8.10 (m, 1H), 7.95 - 8.02 (m, 1H), 7.80 - 7.85 (m, 1H), 7.45 - 7.50 (m, 1H), 7.33 - 7.42 (m, 2H), 7.22 - 7.33 (m, 2H), 6.93 (s, 1H), 6.53 - 6.58 (m, 1H), 6.40 - 6.53 (m, 1H), 5.50 - 5.70 (m, 1H), 4.11 (s, 3H), 2.85 - 3.15 (m, 2H), 2.46 - 2.48 (m, 1H), 2.00 - 2.20 (m, 1H). (formic acid salt)
145	MS (ESI) calcd. for $C_{38}H_{25}N_7O$, 475.21 m/z, found 476.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.69 (s, 1H), 8.04 - 8.28 (m, 3H), 7.62 - 7.79 (m, 2H), 7.32 - 7.50 (m, 4H), 6.82 (s, 1H), 5.57 (s, 1H), 2.85 - 3.12 (m, 2H), 2.60 - 2.71 (m, 3H), 2.52 - 2.53 (m, 1H), 2.49 - 2.51 (m, 3H), 1.98 - 2.08 (m, 1H). (TFA salt)
146	MS (ESI) calcd. for $C_{28}H_{23}F_2N_7O$, 511.19 m/z, found 512.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.13 (m, 1H), 8.43 - 8.46 (m, 1H), 8.14 - 8.17 (m, 1H), 8.01 - 8.04 (m, 1H), 7.79 - 7.87 (m, 2H), 7.42 - 7.45 (m, 2H), 7.34 -7.37 (m, 1H), 7.30- 7.33 (m, 1H), 6.80-7.20 (m, 2H), 5.61 - 5.66 (m, 1H), 3.02 - 3.14 (m, 1H), 2.86 - 2.95 (m, 1H), 2.54 - 2.55 (m, 1H), 2.50 (s, 3H), 2.05 - 2.15 (m, 1H). (TFA salt)
147	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$, 545.21 m/z, found, 546.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.59 - 8.69 (m, 1H), 8.32 - 8.51 (m, 2H), 7.96 - 8.18 (m, 3H), 7.73 - 7.89 (m, 2H), 7.50 - 7.62 (m, 3H), 7.39 - 7.49 (m, 1H), 6.76 - 6.87 (m, 1H), 6.53 - 6.63 (m, 1H), 5.31 - 5.69 (m, 2H), 3.41 - 3.62 (m, 1H), 3.04 - 3.31 (m, 1H), 2.66 (s, 3H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -179.18. (TFA salt)
148	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$, 545.21 m/z, found, 546.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.58 - 8.73 (m, 1H), 8.27 - 8.53 (m, 2H), 7.92 - 8.24 (m, 3H), 7.68 - 7.91 (m, 2H), 7.29 - 7.65 (m, 4H), 6.69 - 6.89 (m, 1H), 6.43 - 6.65 (m, 1H), 5.68 - 5.87 (m, 1H), 5.36 - 5.66 (m, 1H), 3.03 - 3.46 (m, 2H), 2.69 (s, 3H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -192.55. (TFA salt)
149	MS (ESI) calcd. for $C_{31}H_{27}N_9O_2$, 557.23 m/z, found 558.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.59 - 8.60 (m, 1H), 8.35 - 8.37 (m, 2H), 8.01 - 8.02 (m, 1H), 7.97 - 8.00 (m, 1H), 7.80 -7.95 (m, 1H), 7.78 - 7.80 (m, 1H), 7.51 - 7.54 (m, 1H), 7.48 - 7.51 (m, 1H), 7.44 - 7.47 (m, 1H), 7.29 - 7.39 (m, 2H), 6.56 - 6.57 (m, 1H), 6.46 - 6.55 (m, 1H), 5.53 - 7.59 (m, 1H), 4.71 - 4.75 (m, 1H), 4.40 - 4.46 (m, 1H), 3.22 - 3.23 (m, 3H), 2.95 - 3.10 (m, 2H), 2.50 - 2.52 (m, 1H), 1.98 - 2.08 (m, 1H).
150	MS (ESI) calcd. for $C_{32}H_{29}N_9O$, 555.25 m/z, found 556.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ(ppm); 8.36 - 8.48 (m, 2H), 8.23 - 8.35 (m, 1H), 7.98 - 8.07 (m, 2H), 7.82 - 7.89 (m, 1H), 7.74 - 7.81 (m, 1H), 7.51 - 7.60 (m, 1H), 7.42 - 7.50 (m, 1H), 7.32 - 7.41 (m, 1H), 6.77 - 6.89 (m, 1H), 6.59 - 6.63 (m, 1H), 5.52 - 5.64 (m, 1H), 2.91 - 3.15 (m, 2H), 2.71 (s, 3H), 2.52 - 2.61 (m, 4H), 2.33 - 2.42 (m, 3H), 2.01 - 2.17 (m, 1H). (TFA salt)
157	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$ 544.21 m/z, found, 545.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.83 - 8.90 (m, 1H), 8.74 - 8.80 (m, 1H), 8.41 - 8.47 (m, 1H), 8.34 - 8.40 (m, 1H), 7.97 - 8.09 (m, 2H), 7.77 - 7.86 (m, 2H), 7.39 - 7.49 (m, 2H), 7.30 - 7.39 (m, 1H), 6.79 - 6.89 (m, 1H), 6.53 - 6.61 (m, 1H), 5.50 - 5.62 (m, 1H), 4.00 (s, 3H), 2.85 - 3.02 (m, 2H), 2.53 - 2.61 (m, 1H), 1.98 - 2.14 (m, 1H). (TFA salt)

Cpd ID	Characterization Data
158	MS (ESI) calcd. for $C_{29}H_{26}N_{10}O_2$, 546.22 m/z, found 547.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.80 - 8.90 (m, 1H), 8.32 - 8.40 (m, 2H), 8.00 - 8.10 (m, 1H), 7.92 - 8.00 (m, 1H), 7.81 (s, 1H), 7.35 - 7.45 (m, 2H), 7.25 - 7.35 (m, 2H), 6.55 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 6.36 (s, 1H), 5.50 - 5.66 (m, 1H), 3.96 (s, 3H), 3.77 (s, 3H), 2.85 - 3.15 (m, 2H), 2.45 - 2.50 (m, 1H), 2.00 - 2.20 (m, 1H). (formic acid salt)
159	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$, 545.21 m/z, found 546.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.51 - 8.59 (m, 1H), 8.34 - 8.42 (m, 2H), 8.02 - 8.09 (m, 1H), 7.95 - 8.01 (m, 1H), 7.81 - 7.86 (m, 1H), 7.71 - 7.80 (m, 1H), 7.51 - 7.60 (m, 1H), 7.39 - 7.50 (m, 1H), 7.29 - 7.38 (m, 2H), 6.57 - 6.63 (m, 1H), 6.48 - 6.56 (m, 1H), 5.59 - 5.66 (m, 1H), 2.92 - 3.13 (m, 2H), 2.58 - 2.67 (m, 4H), 1.98 - 2.14 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -131.47. (TFA salt)
160	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found 554.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.49 - 9.56 (m, 1H), 8.97 - 9.08 (m, 1H), 8.36 - 8.45 (m, 2H), 8.02 - 8.09 (m, 2H), 7.95 - 8.01 (m, 1H), 7.79 - 7.88 (m, 2H), 7.51 - 7.58 (m, 1H), 7.41 - 7.50 (m, 1H), 7.27 - 7.36 (m, 2H), 6.59 - 6.68 (m, 1H), 6.47 - 6.55 (m, 1H), 5.67 - 5.75 (m, 1H), 2.89 - 3.15 (m, 2H), 2.56 - 2.63 (m, 1H), 2.01 - 2.16 (m, 1H).
161	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found, 553.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.79 - 8.83 (m, 1H), 8.36 - 8.43 (m, 2H), 8.10 - 8.18 (m, 2H), 8.02 - 8.09 (m, 1H), 7.95 - 8.01 (m, 1H), 7.85 - 7.88 (m, 1H), 7.71 - 7.73 (m, 1H), 7.41 - 7.50 (m, 2H), 7.27 - 7.36 (m, 2H), 7.15 - 7.21 (m, 1H), 6.57 - 6.60 (m, 1H), 6.47 - 6.55 (m, 1H), 5.67 - 5.75 (m, 1H), 2.93 - 3.15 (m, 2H), 2.69 - 2.80 (m, 1H), 2.01 - 2.13 (m, 1H).
162	MS (ESI) calcd. for $C_{30}H_{24}FN_9O_2$561.20 m/z, found, 562.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.52 - 8.56 (m, 1H), 8.31 - 8.40 (m, 2H), 8.07 - 8.12 (m, 2H), 7.96 - 8.00 (m, 1H), 7.80 - 7.86 (m, 1H), 7.25 - 7.45 (m, 4H), 6.50 - 6.62 (m, 2H), 5.55 - 5.65 (m, 1H), 4.01 (s, 3H), 3.00 - 3.09 (m, 1H), 2.82 - 3.00 (m, 1H), 2.59 - 2.64 (m, 1H), 2.00 - 2.11 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -139.38.
163	MS (ESI) calcd. for $C_{31}H_{25}N_{11}O$, 567.22 m/z, found 568.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.66 - 8.74 (m, 1H), 8.59 - 8.65 (m, 1H), 8.32 - 8.40 (m, 2H), 8.02 - 8.10 (m, 1H), 7.96 - 8.01 (m, 1H), 7.83 - 7.89 (m, 1H), 7.41 - 7.52 (m, 3H), 7.25 - 7.36 (m, 2H), 6.58 - 6.66 (m, 1H), 6.47 - 6.55 (m, 1H), 5.68 - 5.75 (m, 1H), 4.16 (s, 3H), 3.04 - 3.19 (m, 1H), 2.89 - 3.03 (m, 1H), 2.48 - 2.53 (m, 1H), 2.19 - 2.36 (m, 1H).
166	MS (ESI) calcd. for $C_{29}H_{24}F_2N_{10}O$, 566.21 m/z, found 567.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.25 - 8.40 (m, 2H), 7.90 - 8.10 (m, 2H), 7.55 - 7.85 (m, 2H), 7.20 - 7.40 (m, 4H), 6.72 - 6.78 (m, 1H), 6.40 - 6.60 (m, 2H), 5.50 - 5.65 (m, 1H), 3.03 - 3.15 (m, 1H), 2.82 - 2.95 (m, 1H), 2.46 (s, 4H), 2.02 - 2.25 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -95.13. (formic acid salt)
170	MS (ESI) calcd. for $C_{28}H_{22}F_2N_{10}O$, 552.19 m/z, found 553.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.15 - 8.60 (m, 3H), 8.00 - 8.10 (m, 1H), 7.92 - 8.00 (m, 1H), 7.85 - 7.90 (m, 1H), 7.70 - 7.85 (m, 1H), 7.35 - 7.49 (m, 2H), 7.20 - 7.32 (m, 2H), 7.02 - 7.20 (m, 1H), 6.50 - 6.60 (m, 1H), 6.30 - 6.50 (m, 1H), 5.50 - 5.65 (m, 1H), 2.80 - 3.10 (m, 2H), 2.52 - 2.60 (m, 1H), 2.00 - 2.18 (m, 1H). (formic acid salt)

Cpd ID	Characterization Data
172	MS (ESI) calcd. for $C_{29}H_{26}N_{10}O$, 530.23 m/z, found 531.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.32 - 8.41 (m, 2H), 8.02 - 8.10 (m, 1H), 7.93 - 8.01 (m, 1H), 7.75 - 7.87 (m, 1H), 7.53 - 7.62 (m, 1H), 7.26 - 7.42 (m, 4H), 6.59 - 6.63 (m, 1H), 6.51 - 6.58 (m, 1H), 5.53 - 5.62 (m, 1H), 3.84 (s, 3H), 2.99 - 3.13 (m, 1H), 2.72 - 2.98 (m, 1H), 2.48 - 2.54 (m, 1H), 2.23 (s, 3H), 2.06 - 2.17 (m, 1H). (formic acid salt)
173	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found 543.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.32 - 8.42 (m, 2H), 8.01 - 8.08 (m, 1H), 7.93 - 7.99 (m, 1H), 7.81 - 7.86 (m, 1H), 7.31 - 7.42 (m, 1H), 7.19 - 7.30 (m, 3H), 6.52 - 6.63 (m, 1H), 6.41 - 6.51 (m, 2H), 5.50 - 5.64 (m, 1H), 4.03 - 4.21 (m, 2H), 2.99 - 3.12 (m, 1H), 2.79 - 2.98 (m, 3H), 2.54 - 2.62 (m, 2H), 2.41 - 2.49 (m, 1H), 2.02 - 2.24 (m, 1H).
174	MS (ESI) calcd. for $C_{28}H_{22}F_2N_{10}O$, 552.19 m/z, found 553.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.93 - 8.99 (m, 1H), 8.39 - 8.47 (m, 2H), 8.31 - 8.38 (m, 1H), 7.68 - 8.01 (m, 4H), 7.41 - 7.49 (m, 1H), 7.34 - 7.40 (m, 1H), 7.28 - 7.33 (m, 2H), 6.95 - 7.07 (m, 1H), 6.55 - 6.62 (m, 1H), 6.48 - 6.54 (m, 1H), 5.58 - 5.60 (m, 1H), 2.99 - 3.15 (m, 1H), 2.78 - 2.98 (m, 1H), 2.47 - 2.53 (m, 1H), 2.02 - 2.23 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -94.52.
175	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found, 553.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.63 - 8.70 (m, 1H), 8.30 - 8.38 (m, 2H), 7.99 - 8.03 (m, 1H), 7.92 - 7.98 (m, 1H), 7.74 - 7.80 (m, 2H), 7.21 - 7.40 (m, 5H), 7.05 - 7.11 (m, 1H), 6.98 - 7.04 (m, 1H), 6.50 - 6.57 (m, 1H), 6.41 - 6.50 (m, 1H), 5.57 - 5.69 (m, 1H), 3.00 - 3.13 (m, 1H), 2.80 - 3.97 (m, 1H), 2.55 - 2.63 (m, 1H), 2.08 - 2.25 (m, 1H).
176	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found, 554.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.98 - 9.12 (m, 1H), 8.59 - 8.67 (m, 1H), 8.30 - 8.38 (m, 2H), 7.99 - 8.03 (m, 1H), 7.88 - 7.96 (m, 1H), 7.76 - 7.84 (m, 1H), 7.30 - 7.41 (m, 2H), 7.21 - 7.31 (m, 2H), 7.11 - 7.20 (m, 2H), 6.49 - 6.57 (m, 1H), 6.40 - 6.48 (m, 1H), 5.57 - 5.68 (m, 1H), 3.00 - 3.13 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.63 (m, 1H), 2.15 - 2.25 (m, 1H).
183	MS(ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found 543.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.55 - 8.64 (m, 1H), 8.23 - 8.54 (m, 2H), 7.95 - 8.22 (m, 2H), 7.68 - 8.21 (m, 2H), 7.23 - 7.67 (m, 3H), 6.78 - 7.00 (m, 1H), 6.44 - 6.77 (m, 1H), 5.44 - 5.76 (m, 1H), 2.88 - 3.14 (m, 2H), 2.73 - 2.87 (m, 3H), 2.57 - 2.62 (m, 1H), 2.49- 2.51 (m, 3H), 2.07 - 2.26 (m, 1H). (TFA salt)
184	MS (ESI) calcd. for $C_{30}H_{25}N_9O$, 527.22 m/z, found, 528.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.27 - 8.59 (m, 3H), 7.93 - 8.22 (m, 2H), 7.64 - 7.92 (m, 3H), 7.21 - 7.63 (m, 4H), 6.71 - 6.99 (m, 1H), 6.41 - 6.66 (m, 1H), 5.41 - 5.73 (m, 1H), 2.82 - 3.14 (m, 2H), 2.58 - 2.61 (m, 3H), 2.48 - 2.51 (m, 1H), 2.02 - 2.24 (m, 1H). (TFA salt)
185	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found 529.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.09 - 9.18 (m, 1H), 8.61 - 8.70 (m, 1H), 8.37 - 8.46 (m, 2H), 7.93 - 8.08 (m, 2H), 7.82 - 7.89 (m, 1H), 7.24 - 7.49 (m, 4H), 6.49 - 6.60 (m, 2H), 5.58 - 5.60 (m, 1H), 3.07 - 3.19 (m, 1H), 2.89 - 3.05 (m, 1H), 2.61 (s, 3H), 2.51 - 2.58 (m, 1H), 2.12 - 2.26 (m, 1H). (formic acid salt)
186	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found, 529.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.04 (s, 1H), 8.77 (s, 1H), 8.32 - 8.38 (m, 2H), 7.94 - 8.05 (m, 2H), 7.81 - 7.82 (m, 1H), 7.25 - 7.41 (m, 4H), 6.41 - 6.56 (m, 2H), 5.66 (s, 1H), 3.20 - 3.30 (m, 2H), 2.51-2.59 (m, 3H), 2.45-2.50 (m, 1H), 2.25 - 2.28 (m, 1H). (formic acid salt)

Cpd ID	Characterization Data
187	MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O$: 563.20 m/z, found: 564.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.51 - 8.54 (m, 1H), 8.36 - 8.39 (m, 2H), 8.01 - 8.03 (m, 1H), 7.95 -7.98 (m, 1H), 7.81 - 7.84 (m, 2H), 7.50 - 7.53 (m, 2H), 7.41 - 7.44 (m, 1H), 7.25 - 7.33 (m, 2H), 6.85 (s, 1H), 6.55 - 6.56 (m, 1 H), 6.42 - 6.46 (m, 1H), 5.96 - 5.99 (m, 1H), 3.58 - 3.72 (m, 2H), 2.59 - 2.65 (m, 3H).
189	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O_2$, 568.21 m/z, found 569.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.51 - 8.56 (m, 1H), 8.42 - 8.50 (m, 2H), 8.37 - 8.41 (m, 1H), 8.03 - 8.10 (m, 1H), 7.96 - 8.02 (m, 1H), 7.90 - 7.95 (m, 1H), 7.82 - 7.90 (m, 1H), 7.39 - 7.50 (m, 3H), 7.29 - 7.38 (m, 2H), 6.60 - 6.67 (m, 1H), 6.51 - 6.58 (m, 1H), 5.63 - 5.72 (m, 1H), 2.92 - 3.11 (m, 2H), 2.58 - 2.64 (m, 1H), 2.08 - 2.22 (m, 1H). (formic acid salt)
190	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found 554.15 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.69 - 8.72 (m, 1H), 8.30 - 8.37 (m, 2H), 7.85 - 8.12 (m, 4H), 7.80 - 7.85 (m, 1H), 7.28 - 7.60 (m, 4H), 6.60 - 6.70 (m, 1H), 6.40 - 6.55 (m, 1H), 5.58 - 5.72 (m, 1H), 3.04 - 3.15 (m, 1H), 2.82 - 2.99 (m, 1H), 2.51 - 2.53 (m, 1H), 2.10 - 2.20 (m, 1H).
191	MS (ESI) calcd. for $C_{31}H_{23}N_9O_3$ 569.19 m/z, found, 570.10 $[M+H]^+$. ^{1} H-NMR (400 MHz, DMSO-d_6) δ (ppm); 11.95 (s, 1H), 8.85 - 8.89 (m, 1H), 8.39 - 8.43 (m, 2H), 8.05 - 8.09 (m, 1H), 8.00 - 8.03 (m, 1H), 7.53 - 7.90 (m, 6H), 7.41 - 7.43 (m, 1H), 7.30 - 7.38 (m, 2H), 7.19 - 7.21 (m, 1H), 6.69 - 6.74 (m, 1H), 6.57 - 6.59 (m, 1H), 5.60 - 5.66 (m, 1H), 3.01 - 3.10 (m, 1H), 2.89 - 2.98 (m, 1H), 2.54 - 2.57 (m, 1H), 2.05 - 2.13 (m, 1H). (TFA salt)
192	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found, 554.25 $[M+H]+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 9.06 - 9.07 (m, 1H), 8.80 - 8.81 (m, 1H), 8.37 - 8.38 (m, 2H), 8.35 - 8.36 (m, 1H), 7.94 - 8.03 (m, 2H), 7.81 - 7.82 (m, 1H), 7.41 - 7.45 (m, 2H), 7.27 - 7.33 (m, 2H), 6.53 - 6.56 (m, 1H), 6.44 - 6.49 (m, 1H), 5.65 - 5.70 (m, 1H), 2.91 - 3.10 (m, 2H), 2.56 - 2.58 (m, 1H), 2.11 - 2.16 (m, 1H).
193	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found 553.20 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6) δ (ppm); 8.90 - 9.00 (m, 1H), 8.40 - 8.48 (m, 1H), 8.32 - 8.40 (m, 2H), 8.22 - 8.28 (m, 1H), 8.00 - 8.05 (m, 1H), 7.90 - 8.00 (m, 2H), 7.80 - 7.88 (m, 1H), 7.60 - 7.70 (m, 1H), 7.35 - 7.45 (m, 2H), 7.25 - 7.34 (m, 2H), 6.55 - 6.60 (m, 1H), 6.40 - 6.55 (m, 1H), 5.60 - 5.78 (m, 1H), 2.85 - 3.15 (m, 2H), 2.58 - 2.65 (m, 1H), 2.05 - 2.20 (m, 1H). (formic acid salt)
194	MS (ESI) calcd. for $C_{32}H_{25}N_9O_2$, 567.21 m/z, found 568.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.41 - 8.44 (m, 1H), 8.39 - 8.40 (m, 1H), 8.05 - 8.09 (m, 1H), 8.01 - 8.04 (m, 1H), 7.81 - 7.87 (m, 3H), 7.65 - 7.76 (m, 1H), 7.45 - 7.48 (m, 1H), 7.26 - 7.44 (m, 2H), 6.87 - 6.95 (m, 1H), 6.72 - 6.84 (m, 1H), 6.52 - 6.59 (m, 1H), 5.54 - 5.69 (m, 1H), 3.55 - 3.56 (m, 2H), 3.01- 3.15 (m, 1H), 2.82 - 2.99 (m, 1H), 2.42 - 2.44 (m, 1H), 2.04-2.22 (m, 1H). (TFA salt)
195	MS (ESI) calcd. for $C_{31}H_{27}N_9O_3S$, 605.20 m/z, found 606.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.35 - 8.44 (m, 2H), 8.02 - 8.09 (m, 1H), 7.96 - 8.02 (m, 1H), 7.87 - 7.95 (m, 2H), 7.79 - 7.85 (m, 1H), 7.41 - 7.48 (m, 1H), 7.36 - 7.40 (m, 1H), 7.24 - 7.35 (m, 4H), 6.56 - 6.64 (m, 1H), 6.44 - 6.54 (m, 1H), 5.65 - 5.72 (m, 1H), 3.02 - 3.19 (m, 4H), 2.90 - 3.01 (m, 1H), 2.50 - 2.58 (m, 1H), 2.05 - 2.18 (m, 1H).
196	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$, 569.23 m/z, found 570.15 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6) δ (ppm); 8.75 - 8.85 (m, 1H), 8.30 - 8.40 (m, 2H), 8.00 - 8.05 (m, 1H), 7.95 - 8.00 (m, 1H), 7.85 - 7.95 (m, 2H), 7.81 (s, 1H), 7.60 - 7.72 (m, 2H), 7.30 - 7.40 (m, 2H), 7.25 - 7.30 (m, 2H), 6.52 - 6.60 (m, 1H), 6.40 - 6.52 (m, 1H), 5.55 - 5.70 (m, 1H), 2.85 - 3.15 (m, 2H), 2.45 - 2.50 (m, 1H), 2.00 - 2.20 (m, 4H). (formic acid salt)

Cpd ID	Characterization Data
201	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$ 569.23 m/z, found, 570.15 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.38 (m, 3H), 8.00 - 8.02 (m, 1H), 7.94 - 7.97 (m, 1H), 7.81 - 7.82 (m, 1H), 7.46 - 7.48 (m, 1H), 7.36 - 7.40 (m, 2H), 7.25 - 7.31 (m, 3H), 6.55 - 6.56 (m, 1H), 6.44 - 6.48 (m, 1H), 5.58 - 5.63 (m, 1H), 4.23 - 4.25 (m, 1H), 2.91 - 3.08 (m, 2H), 2.50 - 2.52 (m, 1H), 2.03 - 2.12 (m, 1H), 0.78 - 0.81 (m, 2H), 0.66 - 0.69 (m, 2H).
202	MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O_2$, 579.19 m/z, found 580.25 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.31 - 8.45 (m, 3H), 7.93 - 8.06 (m, 2H), 7.74 - 7.85 (m, 2H), 7.63 - 7.71 (m, 2H), 7.41 - 7.49 (m, 3H), 7.29 - 7.38 (m, 1H), 6.75 - 6.91 (m, 1H), 6.54 - 6.62 (m, 1H), 5.52- 5.69 (m, 1H), 2.85 - 3.15 (m, 2H), 2.43 - 2.52 (m, 1H), 2.01- 2.21 (m, 1H). (TFA salt)
203	MS (ESI) calcd. for $C_{32}H_{29}N_9O_3$ 587.24 m/z, found, 588.15 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.39 (m, 2H), 8.29 - 8.32 (m, 1H), 8.01 - 8.05 (m, 1H), 7.96 - 8.00 (m, 1H), 7.82 - 7.85 (m, 1H), 7.39 - 7.44 (m, 3H), 7.27 - 7.33 (m, 3H), 6.59 - 6.61 (m, 1H), 6.47 - 6.52 (m, 1H), 5.57 - 5.63 (m, 1H), 4.40 - 4.43 (m, 2H), 3.69 - 3.72 (m, 2H), 2.29 (s, 3H), 3.01 - 3.10 (m, 1H), 2.89 - 2.98 (m, 1H), 2.54 - 2.57 (m, 1H), 2.01 - 2.12 (m, 1H).
204	MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found 542.15 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.49 - 8.60 (m, 1H), 8.23 - 8.37 (m, 2H), 7.85 - 8.02 (m, 2H), 7.72 - 7.80 (m, 1H), 7.62 - 7.70 (m, 1H), 7.52 - 7.61 (m, 1H), 7.28 - 7.38 (m, 2H), 7.16 - 7.27 (m, 2H), 6.48 - 6.55 (m, 1H), 6.37 - 6.47 (m, 1H), 5.48 - 5.62 (m, 1H), 2.94 - 3.11 (m, 1H), 2.72 - 2.92 (m, 3H), 2.51 - 2.53 (m, 1H), 1.92 - 2.13 (m, 1H), 1.12 - 1.28 (m, 3H).
205	MS (ESI) calcd. for $C_{32}H_{30}N_{10}O$, 570.26 m/z, found 571.15 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.55 - 8.68 (m, 1H), 8.21 - 8.40 (m, 2H), 7.87 - 8.03 (m, 2H), 7.72 - 7.86 (m, 2H), 7.61 - 7.70 (m, 1H), 7.29 - 7.40 (m, 2H), 7.18 - 7.28 (m, 2H), 6.48 - 6.58 (m, 1H), 6.38 - 6.47 (m, 1H), 5.50 - 5.65 (m, 1H), 3.57 (s, 2H), 2.95 - 3.12 (m, 1H), 2.80 - 2.94 (m, 1H), 2.51 - 2.55 (m, 1H), 2.17 (s, 6H), 1.95 - 2.12 (m, 1H).
207	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found 543.30 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.41 - 8.47 (m, 3H), 8.00 - 8.01 (m, 2H), 7.82 - 7.89 (m, 1H), 7.73 - 7.82 (m, 1H), 7.45 - 7.51 (m, 1H), 7.41 - 7.44 (m, 1H), 7.28 - 7.40 (m, 1H), 6.79 - 6.89 (m, 1H), 6.58 - 6.61 (m, 1H), 5.56 - 5.68 (m, 1H), 2.97 - 3.15 (m, 2H), 2.72 - 2.76 (m, 3H), 2.57 - 2.68 (m, 1H), 2.47 - 2.52 (m, 3H), 2.02 - 2.29 (m, 1H). (TFA salt)
210	MS (ESI) calcd. for $C_{37}H_{27}N_9O$, 613.23 m/z, found 614.15 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm); 9.06 - 9.20 (m, 1H), 8.60 - 8.80 (m, 1H), 8.30 - 8.45 (m, 1H), 8.16 - 8.30 (m, 1H), 7.90 - 8.10 (m, 3H), 7.75 - 7.83 (m, 1H), 7.45 - 7.60 (m, 4H), 7.35 - 7.45 (m, 4H), 7.15 - 7.25 (m, 1H), 7.05 - 7.15 (m, 1H), 6.92 (s, 2H), 6.50 - 6.60 (m, 1H), 6.30 - 6.45 (m, 1H), 5.50 - 5.70 (m, 1H), 2.80 - 3.10 (m, 2H), 2.52 - 2.60 (m, 1H), 1.90 - 2.15 (m, 1H). (formic acid salt)
211	MS (ESI) calcd. for $C_{32}H_{25}N_9O$, 551.22 m/z, found 552.15 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.90 - 9.02 (m, 1H), 8.50 - 8.65 (m, 1H), 8.25 - 8.45 (m, 2H), 7.90 - 8.08 (m, 2H), 7.85 - 7.90 (m, 1H), 7.70 - 7.85 (m, 1H), 7.45 - 7.60 (m, 1H), 7.35 - 7.45 (m, 2H), 7.30 - 7.35 (m, 1H), 7.15 - 7.30 (m, 1H), 6.91 (s, 2H), 6.50 - 6.58 (m, 1H), 6.30 - 6.48 (m, 1H), 5.50 - 5.70 (m, 1H), 2.80 - 3.15 (m, 2H), 2.50 - 2.60 (m, 1H), 1.85 - 2.20 (m, 4H). (formic acid salt)

Cpd ID	Characterization Data
214	MS (ESI) calcd. for $C_{29}H_{23}N_{11}O$, 541.21 m/z, found 542.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.91 - 9.01 (m, 1H), 8.36 - 8.44 (m, 2H), 7.97 - 8.10 (m, 2H), 7.80 - 7.88 (m, 1H), 7.54 - 7.60 (m, 1H), 7.23 - 7.40 (m, 4H), 6.57 - 6.65 (m, 1H), 6.46 - 6.52 (m, 1H), 5.58 - 5.67 (m, 1H), 4.11 (s, 3H), 3.02 - 3.15 (m, 1H), 2.88 - 2.99 (m, 1H), 2.47 - 2.55 (m, 1H), 2.10 - 2.22 (m, 1H). (formic acid salt)
215	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found, 543.15 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.26 - 8.45 (m, 2H), 7.99 - 8.05 (m, 1H), 7.90 - 7.98 (m, 1H), 7.75 - 7.88 (m, 2H), 7.33 - 7.40 (m, 1H), 7.18 - 7.32 (m, 3H), 6.66 - 6.78 (m, 1H), 6.52 - 6.60 (m, 1H), 6.38 - 6.51 (m, 1H), 5.46 - 5.65 (m, 1H), 3.71 - 3.78 (m, 1H), 2.98 - 3.12 (m, 1H), 2.78 - 2.97 (m, 1H), 2.40 - 2.50 (m, 1H), 2.01 - 2.25 (m, 1H), 1.05 - 1.19 (m, 2H), 0.92 - 1.04 (m, 2H).
216	MS (ESI) calcd. for $C_{29}H_{26}N_{10}O_2$ 546.22 m/z, found, 547.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.27 - 8.46 (m, 2H), 7.99 - 8.05 (m, 1H), 7.89 - 7.98 (m, 1H), 7.80 - 7.81 (m, 1H), 7.35 - 7.41 (m, 1H), 7.18 - 7.33 (m, 3H), 6.52 - 6.61 (m, 1H), 6.41 - 6.51 (m, 1H), 6.16 (s, 1H), 5.47 - 5.64 (m, 1H), 3.81 - 4.01 (m, 3H), 3.59 - 3.69 (m, 3H), 2.96 - 3.12 (m, 1H), 2.78 - 2.95 (m,1H), 2.36 - 2.49 (m, 1H), 2.03 - 2.23 (m, 1H). (formic acid salt)
223	MS (ESI) calcd. for $C_{30}H_{24}N_8O_2$ 528.20 m/z, found, 529.15 $[M+H]^+$. ^1HNMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.33 - 8.73 (m, 1H), 8.32 - 8.45 (m, 1H), 8.16 - 8.31 (m, 2H), 8.03 - 8.15 (m, 1H), 7.83 - 8.02 (m, 1H), 7.66 - 7.82 (m, 1H), 7.25 - 7.59 (m, 5H), 6.53 - 6.86 (m, 1H), 5.42 - 5.74 (m, 1H), 2.83 - 3.11 (m, 2H), 2.58 - 2.67 (m, 3H), 2.53 -2.57 (m, 1H), 1.92 - 2.27 (m, 1H). (TFA salt)
224	MS (ESI) calcd. for $C_{32}H_{26}N_{10}O_2$ 568.20 m/z, found, 569.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.80 (d, J = 8.4 Hz, 1H), 8.34 - 8.37 (m, 2H), 7.99 - 8.02 (m, 1H), 7.93 - 7.96 (m, 1H), 7.80 - 7.82 (m, 1H), 7.67 - 7.71 (m, 2H), 7.33 - 7.39 (m, 1H), 7.26 - 7.30 (m, 1H), 7.20 - 7.26 (m, 2H), 7.04 - 7.07 (m, 1H), 6.52 - 6.54 (m, 1H), 6.40 - 6.44 (m, 1H), 5.60 - 5.64 (m, 1H), 3.32 (s, 3H), 3.00 - 3.02 (m, 1H), 2.90 - 2.98 (m, 1H), 2.50 - 2.55 (m, 1H), 2.00 - 2.14 (m, 1H). (formic acid salt)
225	MS (ESI) calcd. for $C_{31}H_{25}N_9O_2$, 555.21 m/z, found 556.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.36 - 8.44 (m, 2H), 7.97 - 8.10 (m, 3H), 7.80 - 7.88 (m, 1H), 7.27-7.48 (m, 4H), 7.14 - 7.20 (m, 1H), 6.42 - 6.59 (m, 2H), 5.59 - 5.68 (m, 1H), 4.59 - 4.63 (m, 2H), 3.46 - 3.55 (m, 2H), 3.02 - 3.13 (m, 1H), 2.88 - 2.99 (m, 1H), 2.57 - 2.63 (m, 1H), 2.01-2.16 (m, 1H).
229	MS (ESI) calcd. for $C_{30}H_{24}N_8O_2$ 528.20 m/z, found, 529.15 $[M+H]^+$. ^1HNMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.33 - 8.73 (m, 1H), 8.32 - 8.45 (m, 1H), 8.16 - 8.31 (m, 2H), 8.03 - 8.15 (m, 1H), 7.83 - 8.02 (m, 1H), 7.66 - 7.82 (m, 1H), 7.25 - 7.59 (m, 5H), 6.53 - 6.86 (m, 1H), 5.42 - 5.74 (m, 1H), 2.83 - 3.11 (m, 2H), 2.58 - 2.67 (m, 3H), 2.53 -2.57 (m, 1H), 1.92 - 2.27 (m, 1H). (TFA salt)
230	MS (ESI) calcd. for $C_{32}H_{26}N_{10}O_2$ 582.22 m/z, found, 583.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.80 (d, J = 8.4 Hz, 1H), 8.34 - 8.37 (m, 2H), 7.99 - 8.02 (m, 1H), 7.93 - 7.96 (m, 1H), 7.80 - 7.82 (m, 1H), 7.67 - 7.71 (m, 2H), 7.33 - 7.39 (m, 1H), 7.26 - 7.30 (m, 1H), 7.20 - 7.26 (m, 2H), 7.04 - 7.07 (m, 1H), 6.52 - 6.54 (m, 1H), 6.40 - 6.44 (m, 1H), 5.60 - 5.64 (m, 1H), 3.32 (s, 3H), 3.00 - 3.02 (m, 1H), 2.90 - 2.98 (m, 1H), 2.50 - 2.55 (m, 1H), 2.00 - 2.14 (m, 1H).

Cpd ID	Characterization Data
231	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O_3S$, 606.19 m/z, found 607.10 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.69 - 8.72 (m, 1H), 8.30 - 8.37 (m, 2H), 8.10 - 8.22 (m, 1H), 7.85 - 8.02 (m, 2H), 7.80 - 7.85 (m, 1H), 7.28 - 7.60 (m, 4H), 6.88 - 7.02 (m, 1H), 6.60 - 6.70 (m, 1H), 6.42 - 6.50 (m, 1H), 5.48 - 5.62 (m, 1H), 3.06 (s, 3H), 2.94 - 3.05 (m, 1H), 2.72 - 2.92 (m, 1H), 2.51 - 2.53 (m, 1H), 1.92 - 2.13 (m, 1H).
232	MS (ESI) calcd. for $C_{31}H_{26}N_{10}O_2$ 570.22 m/z, found, 571.30 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.80 (s, 1H), 8.30 - 8.34 (m, 2H), 8.21 - 8.25 (m, 1H), 8.05 - 8.07 (m, 1H), 7.95 - 7.97 (m, 1H), 7.90 - 7.91 (m, 1H), 7.78 - 7.80 (m, 1H), 7.29 - 7.37 (m, 2H), 7.20 - 7.24 (m, 2H), 6.50 - 6.53 (m, 1H), 6.40 - 6.44 (m, 1H), 5.52 - 5.55 (m, 1H), 2.88 - 3.00 (m, 2H), 2.50 - 2.52 (m, 1H), 2.11 (s, 3H), 2.00 - 2.05 (m, 1H). (formic acid salt)
233	MS (ESI) calcd. for $C_{31}H_{23}N_9O_2S$ 585.17 m/z, found, 586.25 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.38 - 8.45 (m, 1H), 8.34 - 8.36 (m, 1H), 8.09 - 8.13 (m, 1H), 7.95 - 7.99 (m, 2H), 7.87 - 7.91 (m, 1H), 7.83 - 7.86 (m, 1H), 7.76 - 7.82 (m, 1H), 7.42 -7.46 (m, 1H), 7.36 - 7.41 (m, 1H), 7.29 - 7.35 (m, 1H), 7.25 - 7.28 (m, 1H), 6.81 - 6.86 (m, 1H), 6.56 - 6.62 (m, 1H), 5.54 - 5.62 (m, 1H), 3.01 - 3.18 (m, 1H), 2.86 - 3.00 (m, 1H), 2.52 - 2.65 (m, 1H), 2.03 -2.22 (m, 1H). (TFA salt)
235	MS (ESI) calcd. for $C_{32}H_{27}N_9O$, 553.23 m/z, found 554.15 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.36 - 8.48 (m, 3H), 8.02 - 8.10 (m, 1H), 7.94 - 8.01 (m, 1H), 7.79 - 7.86 (m, 1H), 7.40 - 7.49 (m, 2H), 7.27 - 7.38 (m, 3H), 6.54 - 7.62 (m, 1H), 6.42 - 6.49 (m, 1H), 5.56 - 5.63 (m, 1H), 3.11 - 3.20 (m, 2H), 2.92 - 3.10 (m, 4H), 2.54 - 2.63 (m, 1H), 2.01 - 2.19 (m, 3H).
236	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found 554.30 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.40 - 8.52 (m, 1H), 8.34 - 8.39 (m, 2H), 8.25 - 8.33 (m, 1H), 7.96 - 8.13 (m, 3H), 7.66 - 7.95 (m, 3H), 7.54 - 7.65 (m, 1H), 7.36 - 7.53 (m, 1H), 7.29 - 7.35 (m, 1H), 6.73 - 6.99 (m, 1H), 6.45 - 6.72 (m, 1H), 5.52 - 5.81 (m, 1H), 3.06 - 3.27 (m, 1H), 2.87 - 3.05 (m, 1H), 2.55 -2.69 (m, 1H), 2.15 - 2.37 (m, 1H). (TFA salt)
237	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found, 554.15 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.50 (s, 1H), 8.63 (s, 1H), 8.32 - 8.41 (m, 2H), 8.09 - 8.21 (m, 1H), 7.98 - 8.05 (m, 1H), 7.89 - 7.97 (m, 2H), 7.76 - 7.83 (m, 1H), 7.43 - 7.48 (m, 1H), 7.38 - 7.42 (m, 1H), 7.23 - 7.34 (m, 2H), 6.53 - 6.58 (m, 1H), 6.42 - 6.51 (m, 1H), 5.58 - 5.71 (m, 1H), 3.00 - 3.12 (m,1H), 2.85 - 2.99 (m, 1H), 2.53 - 2.65 (m, 1H), 2.02 - 2.18 (m, 1H).
238	MS(ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.21 m/z, found 554.30 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.52 - 9.63 (m, 1H), 8.95 - 9.05 (m, 1H), 8.43 - 8.49 (m, 1H), 8.31 - 8.42 (m, 2H), 7.99 - 8.12 (m, 2H), 7.81 - 7.89 (m, 1H), 7.65 - 7.79 (m, 1H), 7.41 - 7.55 (m, 2H), 7.31 - 7.39 (m, 1H), 6.84 - 6.89 (m, 1H), 6.72 - 6.83 (m, 1H), 6.55 - 6.62 (m, 1H), 5.62 – 5.68 (m, 1H), 2.88 - 3.15 (m, 2H), 2.53 - 2.67 (m, 1H), 2.15 - 2.29 (m, 1H). (TFA salt)
239	MS (ESI) calcd. for $C_{31}H_{27}N_9O_3S$ 605.20 m/z, found, 606.15 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.32 - 8.41 (m, 3H), 8.20 - 8.25 (m, 1H), 8.05 - 8.10 (m, 1H), 7.98 - 8.01 (m, 1H), 7.92 - 7.95 (m, 1H), 7.80 - 7.83 (m, 1H), 7.72 - 7.78 (m, 1H), 7.60 - 7.65 (m, 1H), 7.47 - 7.49 (m, 1H), 7.39 - 7.45 (m, 1H), 7.30 - 7.34 (m, 1H), 6.60 - 6.65 (m, 1H), 6.53 - 6.57 (m, 1H), 5.62 - 5.67 (m, 1H), 2.84 - 3.11 (m, 2H), 2.48 - 2.53 (m, 1H), 2.40 - 2.43 (m, 3H), 2.05 - 2.20 (m, 1H). (TFA salt)

Cpd ID	Characterization Data
240	MS (ESI) calcd. for $C_{31}H_{26}N_8O_2$, 542.22 m/z, found 543.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.90 - 9.00 (m, 1H), 8.30 - 8.45 (m, 2H), 7.90 - 8.10 (m, 3H), 7.82 (s, 2H), 7.30 - 7.60 (m, 6H), 6.57 (s, 1H), 6.42 - 6.50 (m, 1H), 5.60 - 5.78 (m, 1H), 4.56 (s, 2H), 2.85 - 3.15 (m, 2H), 2.55 - 2.60 (m, 1H), 2.05 - 2.25 (m, 1H). (formic acid salt)
241	MS (ESI) calcd. for $C_{31}H_{25}FN_8O_2$, 560.21 m/z, found 561.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.85 - 8.95 (m, 1H), 8.30 - 8.40 (m, 2H), 8.00 - 8.06 (m, 1H), 7.90 - 8.00 (m, 1H), 7.75 - 7.85 (m, 3H), 7.22 - 7.40 (m, 5H), 6.55 - 6.60 (m, 1H), 6.45 - 6.52 (m, 1H), 5.55 - 5.68 (m, 1H), 3.90 (s, 3H), 2.85 - 3.10 (m, 2H), 2.55 - 2.60 (m, 1H), 2.00 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -135.24. (formic acid salt)
242	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$, 544.21 m/z, found, 545.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.43 (m, 2H), 7.86 - 8.10 (m, 2H), 7.71 - 7.84 (m, 1H), 7.17 - 7.50 (m, 4H), 6.33 - 6.62 (m, 2H), 5.88 (s, 1H), 5.42 - 5.63 (m, 1H), 4.98 - 5.20 (m, 2H), 4.20 - 4.46 (m, 2H), 2.95 - 3.15 (m, 1H), 2.78 - 2.94 (m, 1H), 2.37 - 2.48 (m, 1H), 2.00 - 2.22 (m, 1H).
244	MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$: 543.21 m/z, found: 544.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.62 - 8.75 (m, 1H), 8.47 - 8.61 (m, 1H), 8.23 - 8.39 (m, 1H), 8.06 - 8.19 (m, 1H), 7.96 - 8.05 (m, 1H), 7.87 - 7.95 (m, 1H), 7.36 - 7.48 (m, 2H), 7.19 - 7.34 (m, 2H), 6.37 - 6.53 (m, 1H), 5.53 - 5.73 (m, 1H), 2.82 - 3.16 (m, 2H), 2.68 - 2.81 (m, 3H), 2.55 - 2.64 (m, 1H), 2.06 - 2.35 (m, 4H).
255	MS (ESI) calcd for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found, 553.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.59 - 8.66 (m, 1H), 8.33 - 8.41 (m, 2H), 8.19 - 8.26 (m, 1H), 8.05 - 8.10 (m, 1H), 7.99 - 8.05 (m, 1H), 7.93 - 7.99 (m, 1H), 7.80 - 7.84 (m, 1H), 7.70 - 7.77 (m, 1H), 7.38 - 7.46 (m, 3H), 7.27 - 7.34 (m, 2H), 6.55 - 6.60 (m, 1H), 6.46 - 6.53 (m, 1H), 5.62 - 5.70 (m, 1H), 3.01 - 3.12 (m, 1H), 2.87 - 3.00 (m, 1H), 2.55 - 2.62 (m, 1H), 2.06 - 2.20 (m, 1H).
256	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$ 569.23 m/z, found, 570.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.43 - 8.52 (m, 1H), 8.37 - 8.42 (m, 1H), 8.07- 8.13 (m, 1H), 7.98 - 8.06 (m, 3H), 7.86 - 7.97 (m, 2H), 7.82 - 7.86 (m, 1H), 7.76 - 7.81 (m, 1H), 7.47 - 7.51 (m, 1H), 7.40 - 7.46 (m, 1H), 7.32 - 7.39 (m, 1H), 6.79 - 6.88 (m, 1H), 6.56 - 6.62 (m, 1H), 5.60 - 5.70 (m, 1H), 3.01 - 3.18 (m, 1H), 2.84 - 2.99 (m, 1H), 2.84 (s, 3H), 2.45 - 2.51 (m, 1H), 2.09 - 2.19 (m, 1H). (TFA salt)
257	MS (ESI) calcd. for $C_{31}H_{23}F_3N_8O_2$, 596.19 m/z, found 597.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 11.20 - 11.30 (m, 1H), 8.83 - 9.05 (m, 1H), 8.35 - 8.45 (m, 2H), 8.14 - 8.20 (m, 1H), 8.04 - 8.11 (m, 2H), 7.98 - 8.04 (m, 1H), 7.68 - 7.98 (m, 2H), 7.60 - 7.67 (m, 1H), 7.40 - 7.51 (m, 1H), 7.30 - 7.40 (m, 2H), 7.05 - 7.16 (m, 1H), 6.68 - 6.76 (m, 1H), 6.51 - 6.65 (m, 1H), 5.58 - 5.70 (m, 1H), 3.00 - 3.10 (m, 1H), 2.89 - 2.98 (m, 1H), 2.50 - 2.58 (m, 1H), 2.02 - 2.16 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); - 61.09, - 74.07. (TFA salt)
258	MS (ESI) calcd for $C_{30}H_{23}ClN_8O_2$ 562.16 m/z, found, 563.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.70 - 8.81 (m, 1H), 8.32 - 8.43 (m, 2H), 7.91 - 8.07 (m, 3H), 7.78 - 7.84 (m, 1H), 7.68 - 7.77 (m, 1H), 7.24 - 7.43 (m, 4H), 6.91 - 7.03 (m, 1H), 6.53 - 6.63 (m, 1H), 6.42 - 6.53 (m, 1H), 5.53 - 5.66 (m, 1H), 2.81 - 3.21 (m, 2H), 2.44 - 2.50 (m, 1H), 1.99 - 2.16 (m, 1H). (TFA salt)

Cpd ID	Characterization Data
259	MS (ESI) calcd. for $C_{31}H_{23}N_9O_2$, 553.20 m/z, found 554.15 $[M+H]^+$. ^1H NMR (500 MHz, DMSO-d_6) δ (ppm); 11.57 - 12.66 (s, 1H), 8.72 (s, 1H), 8.32 - 8.41 (m, 2H), 8.16 (s, 1H), 8.01 - 8.06 (m, 1H), 7.95 - 8.00 (m, 2H), 7.78 - 7.86 (m, 1H), 7.34 - 7.42 (m, 2H), 7.28 - 7.31 (m, 1H), 7.23 - 7.29 (m, 1H), 6.91 (s, 3H), 6.54 - 6.58 (m, 1H), 6.40 - 6.51 (m, 1H), 5.48 - 5.66 (m, 1H), 2.98 - 3.06 (m, 1H), 2.85 - 2.95 (m, 1H), 2.45 - 2.51 (m, 1H), 1.98 - 2.15 (m, 1H).
260	MS (ESI) calcd. for $C_{31}H_{26}N_8O_3$, 558.21 m/z, found 559.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.57 (brs, 1H), 8.65 - 8.74 (m, 1H), 8.32 - 8.41 (m, 2H), 7.98 - 8.06 (m, 1H), 7.94 - 7.98 (m, 1H), 7.78 - 7.85 (m, 1H), 7.51 - 7.58 (m, 1H), 7.44 - 7.51 (m, 1H), 7.38 - 7.42 (m, 1H), 7.24 - 7.38 (m, 3H), 6.90 - 6.95 (m, 2H), 6.80 - 6.86 (m, 1H), 6.50 - 6.60 (m, 1H), 6.41 - 6.49 (m, 1H), 5.50 - 5.60 (m, 1H), 3.83 (s, 3H), 2.82 - 3.11 (m, 2H), 2.51 - 2.61 (m, 1H), 2.01 - 2.20 (m, 1H).
261	MS (ESI) calcd. for $C_{31}H_{23}FN_{10}O$, 570.20 m/z, found 571.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.46 - 8.51 (m, 1H), 8.35 - 8.45 (m, 2H), 8.31 - 8.35 (m, 1H), 8.01 - 8.09 (m, 2H), 7.72 - 7.89 (m, 3H), 7.42 - 7.51 (m, 2H), 7.32 - 7.41 (m, 1H), 6.82 - 6.89 (m, 1H), 6.55 - 6.62 (m, 1H), 5.52 - 5.81 (m, 1H), 3.02 - 3.37 (m, 1H), 2.83 - 3.01 (m, 1H), 2.55 - 2.63 (m, 1H), 2.08 - 2.22 (m, 1H). (TFA salt)
262	MS (ESI) calcd. for $C_{30}H_{22}F_2N_8O$, 548.19 m/z, found, 549.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.42 (m, 2H), 8.00 - 8.06 (m, 1H), 7.93 - 8.00 (m, 2H), 7.79 - 7.88 (m, 2H), 7.52 - 7.63 (m, 1H), 7.35 - 7.44 (m, 2H), 7.25 - 7.33 (m, 2H), 6.54 - 7.60 (m, 1H), 6.43 - 6.51 (m, 1H), 5.55 - 5.66 (m, 1H), 2.99 - 3.10 (m, 1H), 2.85 - 2.99 (m, 1H), 2.54 - 2.61 (m, 1H), 2.01 - 2.16 (m, 1H). (TFA salt)
263	MS (ESI) calcd. for $C_{30}H_{23}ClN_8O$, 546.17 m/z, found, 547.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.29 - 8.43 (m, 2H), 7.99 - 8.07 (m, 1H), 7.89 - 7.98 (m, 3H), 7.77 (s, 1H), 7.52 - 7.61 (m, 2H), 7.33 - 7.43 (m, 2H), 7.22 - 7.32 (m, 2H), 6.51 - 6.59 (m, 1H), 6.42 - 6.48 (m, 1H), 5.57 - 5.69 (m, 1H), 2.97 - 3.09 (m, 1H), 2.83 - 2.96 (m, 1H), 2.53 - 2.58 (m, 1H), 2.01 - 2.17 (m, 1H).
264	MS (ESI) calcd. for $C_{29}H_{22}FN_9O$, 531.19 m/z, found, 532.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.76 - 8.80 (m, 1H), 8.43 - 8.51 (m, 1H), 8.34 - 8.40 (m, 2H), 8.00 - 8.34 (m, 1H), 7.93 - 7.99 (m, 1H), 7.79 - 7.84 (m, 1H), 7.39 - 7.45 (m, 2H), 7.27 - 7.35 (m, 3H), 6.54 - 6.59 (m, 1H), 6.44 - 6.50 (m, 1H), 5.60 - 5.68 (m, 1H), 3.00 - 3.10 (m, 1H), 2.87 - 2.99 (m, 1H), 2.54 - 2.62 (m, 1H), 2.03 - 2.15 (m, 1H).
266	MS (ESI) calcd. for $C_{29}H_{24}F_2N_{10}O$, 566.21 m/z, found 567.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ(ppm); 8.32 - 8.41 (m, 2H), 8.02 - 8.10 (m, 1H), 7.94 - 8.01 (m, 1H), 7.78 - 7.84 (m, 1H), 7.28 - 7.49 (m, 5H), 7.03 - 7.12 (m, 1H), 6.57 - 6.62 (m, 1H), 6.47 - 6.53 (m, 1H), 5.59 - 5.67 (m, 1H), 3.98 (s, 3H), 3.03- 3.17 (m, 1H), 2.84 - 2.99 (m, 1H), 2.45 - 2.51 (m, 1H), 2.11 - 2.27 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -113.93.
267	MS (ESI) calcd. for $C_{31}H_{26}N_8O_2$, 542.22 m/z, found, 543.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.05 (s, 1H), 8.42 - 8.46 (m, 2H), 8.10 - 8.17 (m, 1H), 8.03 - 8.09 (m, 1H), 7.94 - 7.98 (m, 1H), 7.74 - 7.85 (m, 1H), 7.64 - 7.72 (m, 1H), 7.40 - 7.59 (m, 3H), 6.78 - 6.81 (m, 1H), 5.63 - 5.68 (m, 1H), 2.99 - 3.12 (m, 1H), 2.83 - 2.98 (m, 1H), 2.51 - 2.59 (m, 4H), 2.22 - 2.30 (m, 3H), 2.03 - 2.11 (m, 1H).

Cpd ID	Characterization Data
268	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found, 543.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.91 - 8.94 (m, 1H), 8.22 - 8.31 (m, 1H), 8.12 - 8.21 (m, 1H), 8.06 (s, 1H), 7.97 - 8.03 (m, 1H), 7.89 - 7.95 (m, 1H), 7.33 - 7.43 (m, 3H), 7.21 - 7.31 (m, 2H), 6.39 - 6.51 (m, 1H), 5.58 - 5.69 (m, 1H), 4.21 (s, 3H), 2.99 - 3.11 (m, 1H), 2.84 - 2.98 (m, 1H), 2.56 - 2.61 (m, 1H), 2.49 - 2.55 (m, 3H), 1.99 - 2.17 (m, 1H).
269	MS (ESI) calcd. for $C_{37}H_{36}N_{10}O$, 636.31 m/z, found 637.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.63 - 8.71 (m, 1H), 8.48 - 8.54 (m, 1H), 8.17 - 8.23 (m, 1H), 7.94 - 8.10 (m, 2H), 7.60 - 7.69 (m, 1H), 7.23 - 7.50 (m, 6H), 6.95 - 7.02 (m, 1H), 6.46 - 6.53 (m, 1H), 5.58 - 5.67 (m, 1H), 3.12 - 3.24 (m, 4H), 2.84 - 3.05 (m, 2H), 2.74 (s, 3H), 2.57- 2.63 (m, 2H), 2.45- 2.51 (m, 3H), 2.21 (s, 3H), 2.07 - 2.18 (m, 1H). (formic acid salt)
270	MS (ESI) calcd. for $C_{29}H_{23}N_9O_2$: 529.20 m/z, found, 530.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.66 - 8.73 (m, 1H), 8.49 - 8.56 (m, 1H), 8.28 - 8.39 (m, 1H), 8.20 - 8.28 (m, 1H), 8.11 - 8.19 (m, 1H), 7.98 - 8.07 (m, 1H), 7.38 - 7.49 (m, 3H), 7.23 - 7.37 (m, 2H), 6.46 - 6.52 (m, 1H), 5.60 - 5.71 (m, 1H), 2.86 - 3.15 (m, 2H), 2.78 (s, 3H), 2.53 - 2.60 (m, 1H), 2.09 - 2.20 (m, 1H).
271	MS (ESI) calcd. for $C_{29}H_{25}N_{11}O$, 543.22 m/z, found, 544.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.60 - 8.70 (m, 1H), 8.46 - 8.58 (m, 1H), 8.18 - 8.30 (m, 1H), 8.08 (s, 1H), 7.85 - 8.05 (m, 2H), 7.32 - 7.48 (m, 2H), 7.18 - 7.31 (m, 2H), 6.40 - 6.58 (m, 1H), 5.48 - 5.68 (m, 1H), 4.20 (s, 3H), 2.99 - 3.12 (m, 1H), 2.83 - 2.99 (m, 1H), 2.75 (s, 3H), 2.55 - 2.61 (m, 1H), 2.00 - 2.21 (m, 1H).
275	MS (ESI) calcd for $C_{35}H_{33}N_9O$, 595.28. found, 596.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ8.38 -8.36 (m, 2H), 8.33 - 8.01 (m, 1H), 7.88 – 7.82 (m, 1H), 7.81 – 7.75 (m, 1H), 7.65 - 7.62 (m, 1H), 7.45 (m, 3H), 7.42 – 7.32 (m, 3H), 7.31 – 7.29 (m, 2H), 6.63 (m, 1H), 6.58 – 6.57 (m, 1H), 4.69 (m, 1H), 4.61 – 4.42 (m, 1H), 3.95 -3.93 (m, 1H), 3.65 - 3.59 (m, 1H), 3.39 -3.25 (m, 1H),3.23 - 3.09 (m, 2H), 2.92 – 2.80 (m, 2H), 2.43 -2.02 (m, 3H), 1.46 (m, 2H).
278	MS (ESI) calcd. for $C_{31}H_{33}N_9O$, 547.28 m/z, found, 548.35 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.34 - 8.35 (m, 2H), 8.00 - 8.01 (m, 1H), 7.94 - 7.96 (m, 1H), 7.80 - 7.81 (m, 1H), 7.48 - 7.50 (m, 1H), 7.31 - 7.33 (m, 1H), 7.23 - 7.25 (m, 2H), 6.54 - 6.56 (m, 1H), 6.42 - 6.45 (m, 1H), 4.31 - 4.35 (m, 1H), 4.23 - 4.30 (m, 1H), 3.81 - 3.86 (m, 1H), 3.01 - 3.08 (m, 1H), 2.93 - 2.98 (m, 2H), 2.71 - 2.77 (m, 2H), 2.41 - 2.46 (m, 1H), 2.28 - 2.32 (m, 2H), 1.71 - 1.96 (m, 3H), 1.14 - 1.32 (m, 2H), 0.95 - 1.03 (m, 3H).
280	MS (ESI) calcd. for $C_{31}H_{27}N_9O_2$, 557.23 m/z, found 558.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.06 (d, J = 8.0 Hz, 1H), 8.33 - 8.40 (m, 2H), 8.00 - 8.03 (m, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.39 -7.42 (m, 1H), 7.35 - 7.37 (m, 1H), 7.30 - 7.32 (m, 2H), 7.25 - 7.29 (m, 1H), 7.07 (s, 1H), 6.90 (s, 2H), 6.54 - 6.56 (m, 1H), 6.43 - 6.46 (m, 1H), 5.62 (q, J = 8.0 Hz, 1H), 3.87 (s, 3H), 3.00 - 3.09 (m, 1H), 2.87 - 2.98 (m, 1H), 2.52 - 2.58 (m, 1H), 2.45 (s, 3H), 2.01 - 2.15 (m, 1H).

Cpd ID	Characterization Data
281	MS(ESI) calcd. for $C_{30}H_{24}ClN_9O_2$ 577.17 m/z, found 578.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.12 (d, J = 8.4 Hz, 1H), 8.34 - 8.39 (m, 2H), 8.19 (d, J = 4.8 Hz, 1H), 8.00 - 8.03 (m, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.80 - 7.82 (m, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 2.0 Hz, 1H), 7.30 - 7.34 (m, 1H), 7.22 - 7.27 (m, 1H), 7.14 (d, J = 5.2 Hz, 1H), 6.93 (s, 2H), 6.54 (t, J = 2.0 Hz, 1H), 6.40 - 6.46 (m, 1H), 5.57 (q, J = 8.1 Hz, 1H), 3.97 (s, 3H), 2.98 - 3.05 (m, 1H), 2.87 - 2.95 (m, 1H), 2.52 - 2.58 (m, 1H), 1.95 -2.05 (m, 1H).
282	MS(ESI) calcd. for $C_{31}H_{23}N_9O_2$, 553.20 m/z, found 554.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.28 (d, J = 8.3 Hz, 1H), 8.45 (d, J = 5.1 Hz, 1H), 8.35 - 8.38 (m, 2H), 8.24 (d, J = 2.5 Hz, 1H), 8.02 - 8.03 (m, 1H), 7.96 (d, J = 8.6 Hz, 1H), 7.78 - 7.82 (m, 2H), 7.43 - 7.46 (m, 2H), 7.33 - 7.35 (m, 2H), 7.27 - 7.32 (m, 1H), 6.91 (s, 2H), 6.56 (t, J = 2.1 Hz, 1H), 6.44 - 6.47 (m, 1H), 5.71 (q, J = 8.2 Hz, 1H), 3.04 - 3.10 (m, 1H), 2.91 - 2.99 (m, 1H), 2.55 - 2.62 (m, 1H), 2.11 - 2.19 (m, 1H).
283	MS(ESI) calcd. for $C_{31}H_{27}N_9O_3$, 573.22 m/z, found 574.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.05 (d, J = 8.2 Hz, 1H), 8.36 - 8.38 (m, 2H), 8.01 - 8.03 (m, 1H), 7.96 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 1.7 Hz, 1H), 7.35 - 7.41 (m, 2H), 7.26 - 7.32 (m, 2H), 6.90 (s, 2H), 6.85 (s, 2H), 6.55 - 6.56 (m, 1H), 6.44 - 6.47 (m, 1H), 5.62 (q, J = 8.2 Hz, 1H), 3.90 (s, 6H), 3.01 - 3.08 (m, 1H), 2.87 - 2.96 (m, 1H), 2.52 - 2.56 (m, 1H), 2.04 - 2.14 (m, 1H).
284	MS (ESI) calcd. for $C_{31}H_{27}N_9O_2$, 557.23 m/z, found 558.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.93 (d, J = 8.4 Hz,1H), 8.34 - 8.39 (m, 2H), 8.06 (d, J = 5.2 Hz, 1H), 8.00 - 8.02 (m, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.41 (s, 1H), 7.30 - 7.34 (m, 1H), 7.23 - 7.26 (m, 1H), 6.97 (d, J = 5.2 Hz, 1H), 6.93 (s, 2H), 6.54 (t, J = 2.0 Hz, 1H), 6.41 - 6.44 (m, 1H), 5.58 (q, J = 8.0 Hz, 1H), 3.90 (s, 3H), 2.98 - 3.05 (m, 1H), 2.86 - 2.94 (m, 1H), 2.53 - 2.58 (m, 1H), 2.18 (s, 3H), 1.95 - 2.07 (m, 1H).
286	MS(ESI) calcd. for $C_{30}H_{24}N_{10}O_2$, 556.21 m/z, found 557.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ(ppm); 9.03 - 9.05 (m, 1H), 8.43 -8.45 (m, 1H), 8.14 (s, 2H), 8.01 - 8.04 (m, 3H), 7.34 -7.43 (m, 2H), 7.28 - 7.32 (m, 2H), 7.18 - 7.20 (m, 1H), 6.93 (s, 2H), 6.43 - 6.46 (m, 1H), 5.62 - 5.65 (m, 1H), 4.58 - 4.62 (m, 2H), 3.47 - 3.52 (m, 2H), 3.00 - 3.03 (m, 1H), 2.90 -2.96 (m, 1H), 2.50 – 2.57 (m, 1H), 2.07 - 2.10 (m, 1H).
288	MS (ESI) calcd. for $C_{28}H_{21}F_2N_{11}O$, 565.19 m/z, found 566.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.48 (d, J = 8.4 Hz, 1H), 9.36 (s, 1H), 9.03 (s, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.14 (s, 2H), 7.99 - 8.06 (m, 2H), 7.37 - 7.44 (m, 2H), 7.21 - 7.35 (m, 2H), 7.23 (t, J = 52.0 Hz, 1H) 6.94 (s, 2H), 6.45 (dd, J = 7.6, 4.8 Hz, 1H), 5.70 (q, J = 8.0 Hz, 1H), 3.01 - 3.11 (m, 1H), 2.85 - 2.98 (m, 1H), 2.52 - 2.56 (m, 1H), 2.19 - 2.31 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -117.98.
290	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found, 553.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.31 (s, 1H), 9.02 - 9.11 (m, 1H), 8.31 - 8.42 (m, 2H), 8.11 - 8.22 (m, 1H), 7.92 - 8.07 (m, 2H), 7.64 - 7.88 (m, 3H), 7.37 - 7.51 (m, 2H), 7.21 - 7.36 (m, 2H), 6.65 - 6.79 (m, 1H), 6.52 - 6.61 (m, 1H), 6.41 - 6.51 (m, 1H), 5.58 - 5.74 (m, 1H), 3.00 - 3.13 (m, 1H), 2.86 - 2.99 (m, 1H), 2.54 - 2.65 (m, 1H), 2.02 - 2.37 (m, 1H). (formic acid salt)
291	MS (ESI) calcd for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found, 553.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.18 - 9.28 (m, 1H), 8.49 - 8.57 (m, 1H), 8.34 - 8.45 (m, 2H), 7.96 - 8.07 (m, 2H), 7.80 - 7.87 (m, 1H), 7.59 - 7.66 (m, 1H), 7.49 - 7.57 (m, 1H), 7.39 - 7.49 (m, 2H), 7.29 - 7.38 (m, 1H), 7.07 - 7.15 (m, 1H), 6.54 - 6.71 (m, 3H), 5.59 - 5.70 (m, 1H), 3.01 - 3.14 (m, 1H), 2.87 - 2.99 (m, 1H), 2.58 - 2.65 (m, 1H), 2.03 - 2.16 (m, 1H). (formic acid salt)

Cpd ID	Characterization Data
292	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$, 569.23 m/z, found 570.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.00 - 9.12 (m, 1H), 8.50 - 8.63 (m, 1H), 8.29 - 8.44 (m, 4H), 8.02 - 8.13 (m, 3H), 7.91 - 8.01 (m, 1H),7.75 - 7.91 (m, 1H), 7.55 - 7.65 (m, 1H), 7.22 - 7.46 (m, 4H), 6.40 - 6.64 (m, 2H), 5.60 - 5.72 (m, 1H), 2.90 - 3.01 (m, 2H), 2.76 - 2.87 (m, 3H), 2.66 - 2.70 (m, 1H), 2.03 - 2.23 (m, 1H). (formic acid salt)
293	MS (ESI) calcd. for $C_{30}H_{23}FN_8O_2$, 546.19 m/z, found 547.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.43 (m, 2H), 7.89 - 8.11 (m, 2H), 7.73 - 7.85 (m, 1H), 7.50 - 7.61 (m, 1H), 7.36 - 7.45 (m, 2H), 7.10 - 7.35 (m, 4H), 6.52 - 6.65 (m, 1H), 6.38 - 6.50 (m, 1H), 5.58 - 5.66 (m, 1H), 2.78 - 3.18 (m, 2H), 2.40 - 2.50 (m, 1H), 1.96 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -132.49.
294	MS (ESI) calcd. for $C_{33}H_{27}F_2N_9O_4$, 605.21 m/z, found 606.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.05 - 9.20 (m, 1H), 8.30 - 8.45 (m, 2H), 7.90 - 8.15 (m, 2H), 7.78 - 7.85 (m, 1H), 7.60 - 7.78 (m, 2H), 7.35 - 7.50 (m, 2H), 7.25 - 7.35 (m, 2H), 6.40 - 6.60 (m, 2H), 5.50 - 5.70 (m, 1H), 2.82 - 3.15 (m, 2H), 2.55 - 2.65 (m, 1H), 2.00 - 2.25 (m, 4H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.21. (formic acid salt)
295	MS (ESI) calcd. for C29H22FN9O, 531.19 m/z, found 532.10 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 9.24 - 9.35 (m, 1H), 8.30 - 8.49 (m, 3H), 7.91 - 8.07 (m, 2H), 7.73 - 7.88 (m, 2H), 7.56 - 7.67 (m, 1H), 7.37 - 7.46 (m, 2H), 7.24 - 7.35 (m, 2H), 6.50 - 6.61 (m, 1H), 6.40 - 6.50 (m, 1H), 5.59 - 5.69 (m, 1H), 2.80 - 3.20 (m, 2H), 2.53 - 2.63 (m, 1H), 1.98 - 2.24 (m, 1H). 19F NMR (282 MHz, DMSO-d6) δ (ppm): -67.90. (formic acid salt)
296	MS (ESI) calcd. for $C_{29}H_{22}FN_9O_2$ 547.18 m/z, found, 548.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.29 - 8.49 (m, 2H), 7.92 - 8.09 (m, 3H), 7.77 - 7.91 (m, 2H), 7.21 - 7.47 (m, 4H), 6.53 - 6.64 (m, 1H), 6.42 - 6.52 (m, 1H), 5.49 - 5.68 (m, 1H), 2.79 - 3.14 (m, 2H), 2.43 - 2.51 (m, 1H), 1.94 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -134.20.
297	MS (ESI) calcd. for $C_{29}H_{23}N_9O_2$ 529.20 m/z, found, 530.10 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.40 (m, 2H), 8.05 - 8.15 (m, 1H), 7.90 - 8.00 (m, 3H), 7.79 - 7.83 (m, 1H), 7.20 - 7.40 (m, 4H), 6.53 - 6.59 (m, 1H), 6.32 - 6.50 (m, 2H), 5.50 - 5.65 (m, 1H), 2.80 - 3.15 (m, 2H), 2.55 - 2.60 (m, 1H), 1.90 - 2.15 (m, 1H).
298	MS (ESI) calcd. for $C_{29}H_{23}FN_{10}O$, 546.20 m/z, found 547.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.47 - 8.51 (m, 1H), 8.39 - 8.46 (m, 2H), 8.10 - 8.14 (m, 1H), 8.01 - 8.09 (m, 1H), 7.79 - 7.91 (m, 3H), 7.44 - 7.51 (m, 1H), 7.34 - 7.41 (m, 2H), 6.81 - 6.91 (m, 1H), 6.55 - 6.63 (m, 1H), 5.54 - 5.63 (m, 1H), 2.83 - 3.12 (m, 2H), 2.57 - 2.59 (m, 1H), 2.02 - 2.19 (m, 1H). (TFA salt)
299	MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O$, 563.20 m/z, found 564.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.93 - 8.99 (m, 1H), 8.39 - 8.43 (m, 2H), 8.13 - 8.24 (m, 1H), 8.02 - 8.09 (m, 1H), 7.93 - 8.02 (m, 1H), 7.83 (s, 1H), 7.71 - 7.79 (m, 2H), 7.58 - 7.67 (m, 1H), 7.33 - 7.47 (m, 2H), 6.49 - 6.63 (m, 2H), 5.70 - 5.81 (m, 1H), 3.12 - 3.31 (m, 1H), 2.66 - 2.86 (m, 1H), 2.51 (s, 3H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -84.70. (formic acid salt)
301	MS (ESI) calcd. for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found, 579.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.13 - 9.21 (m, 1H), 8.70 - 8.73 (m, 1H), 8.53 - 8.59 (m, 1H), 8.25 - 8.32 (m, 2H), 7.65 - 8.11 (m, 3H), 7.39 - 7.43 (m, 2H), 7.29 - 7.34 (m, 2H), 6.91 - 6.97 (m, 1H), 6.49 - 6.54 (m, 1H), 5.59 - 5.67 (m, 1H), 2.98 - 3.09 (m, 1H), 2.88 - 2.97 (m, 1H), 2.75 (s, 3H), 2.59 - 2.62 (m, 1H), 2.08 - 2.19 (m, 1H). ^{19}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); -94.18. (formic acid salt)

Cpd ID	Characterization Data
306	MS (ESI) calcd. for $C_{30}H_{23}N_{11}O$, 553.20 m/z, found 554.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.21 - 9.49 (m, 1H), 8.35 - 8.51 (m, 3H), 8.01 - 8.19 (m, 2H), 7.84 - 7.93 (m, 1H), 7.61 - 7.83 (m, 2H), 7.31 - 7.59 (m, 3H), 6.87 - 6.99 (m, 1H), 6.77 - 6.87 (m, 1H), 6.52 - 6.69 (m, 1H), 5.55 - 5.78 (m, 1H), 3.10 - 3.21 (m, 1H), 2.82 - 3.09 (m, 1H), 2.59 - 2.60 (m, 1H), 2.12 - 2.37 (m, 1H). (TFA salt)
307	MS (ESI) calcd. for $C_{30}H_{24}N_8O_2$ 528.20 m/z, found, 529.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.40 - 8.49 (m, 2H), 8.01 - 8.09 (m, 2H), 7.77 - 7.83 (m, 2H), 7.25 - 7.49 (m, 6H), 6.91 - 6.99 (m, 1H), 6.79 - 6.89 (m, 1H), 6.57 - 6.63 (m, 1H), 5.59 - 5.64 (m, 1H), 3.02 - 3.19 (m, 1H), 2.82 - 3.01 (m, 1H), 2.45 - 2.52 (m, 1H), 2.01 - 2.21 (m, 1H). (TFA salt)
308	MS (ESI) calcd. for $C_{31}H_{27}N_9O_3S$ 605.20 m/z, found, 606.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.41 (m, 2H), 7.80 - 8.11 (m, 7H), 7.25 - 7.45 (m, 4H), 6.47 - 6.60 (m, 2H), 5.60 - 5.70 (m, 1H), 2.82 - 3.11 (m, 2H), 2.48 - 2.53 (m, 1H), 2.40 - 2.43 (m, 3H), 2.02 - 2.20 (m, 1H).
309	MS (ESI) calcd. for $C_{32}H_{26}FN_9O_2$, 587.22 m/z, found 588.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.92 (s, 1H), 8.30 - 8.40 (m, 2H), 8.05 - 8.20 (m, 1H), 7.88 - 8.05 (m, 2H), 7.70 - 7.85 (m, 3H), 7.35 - 7.45 (m, 2H), 7.28 - 7.35 (m, 2H), 6.56 (s, 1H), 6.42 - 6.50 (m, 1H), 5.55 - 5.70 (m, 1H), 3.00 - 3.15 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.60 (m, 1H), 2.00 - 2.20 (m, 4H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -124.96. (formic acid salt)
310	MS (ESI) calcd. for $C_{30}H_{23}FN_8O$, 530.20 m/z, found, 531.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.90 - 9.02 (m, 1H), 8.35 - 8.41 (m, 2H), 7.98 - 8.05 (m, 4H), 7.81 - 7.87 (m, 1H), 7.27 - 7.41 (m, 6H), 6.57 - 6.60 (m, 1H), 6.49 - 6.53 (m, 1H), 5.60 - 5.69 (m, 1H), 2.84 - 3.11 (m, 2H), 2.58 - 2.63 (m, 1H), 2.03 - 2.15 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm); -109.47.
311	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$, 528.21 m/z, found, 529.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.48 - 8.60 (m, 1H), 8.30 - 8.41 (m, 2H), 7.86 - 8.06 (m, 3H), 7.77 - 7.86 (m, 1H), 7.21 - 7.42 (m, 4H), 6.51 - 6.60 (m, 1H), 6.39 - 6.50 (m, 2H), 5.52 - 5.65 (m, 1H), 2.96 - 3.10 (m, 1H), 2.79 - 2.96 (m, 1H), 2.41 - 2.49 (m, 1H), 1.98 - 2.14 (m, 1H).
312	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$, 545.58 m/z, found 546.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.92 - 9.03 (m, 1H), 8.30 - 8.40 (m, 2H), 8.15 - 8.25 (m, 1H), 7.90 - 8.10 (m, 2H), 7.82 (s, 1H), 7.65 (s, 1H), 7.45 - 7.60 (m, 2H), 7.38 - 7.42 (m, 1H), 7.30 - 7.38 (m, 1H), 6.55 - 6.62 (m, 1H), 6.46 - 6.55 (m, 1H), 6.00 - 6.25 (m, 1H), 5.50 - 5.65 (m, 1H), 3.00 - 3.25 (m, 1H), 2.53 (s, 3H), 2.15 - 2.40 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -163.04.
313	MS (ESI) calcd for $C_{30}H_{24}FN_9O$, 545.21 m/z, found, 546.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.90 - 8.98 (m, 1H), 8.34 - 8.43 (m, 2H), 8.13 - 8.22 (m, 1H), 7.94 - 8.06 (m, 2H), 7.67 - 7.85 (m, 2H), 7.50 - 7.63 (m, 2H), 7.38 - 7.45 (m, 1H), 7.27 - 7.33 (m, 1H), 6.54 - 6.60 (m, 1H), 6.46 - 6.52 (m, 1H), 6.11 - 6.32 (m, 1H), 5.80 - 5.90 (m, 1H), 2.73 - 2.83 (m, 1H), 2.61 - 2.83 (m, 3H), 2.39 - 2.50 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -161.21.

Cpd ID	Characterization Data
317	MS (ESI) calcd. for $C_{30}H_{21}F_2N_9O_3$, 593.17 m/z, found, 594.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.40 (m, 2H), 8.10 - 8.15 (m, 1H), 8.00 - 8.07 (m, 1H), 7.93 - 8.00 (m, 1H), 7.90 - 7.93 (m, 1H), 7.80 - 7.83 (m, 1H), 7.55 - 7.62 (m, 1H), 7.40 - 7.50 (m, 2H), 7.25 - 7.40 (m, 2H), 6.55 - 6.60 (m, 1H), 6.45 - 6.55 (m, 1H), 5.50 - 5.70 (m, 1H), 2.85 - 3.15 (m, 2H), 2.55 - 2.65 (m, 1H), 2.00 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -48.10. (formic acid salt)
318	MS (ESI) calcd. for $C_{29}H_{23}N_9O_2$, 529.20 m/z, found 530.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 11.81 (s, 1H), 9.03 (d, J = 8.0 Hz, 1H), 8.33 - 8.39 (m, 2H), 7.99 - 8.03 (m, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.47 (d, J = 6.8 Hz, 1H), 7.33 - 7.42 (m, 2H), 7.23 - 7.33 (m, 2H), 6.91 (s, 2H), 6.82 (d, J = 1.6 Hz, 1H), 6.53 - 6.58 (m, 2H), 6.45 (dd, J = 7.6, 4.8 Hz, 1H), 5.57 (q, J = 8.4 Hz, 1H), 2.97 - 3.08 (m, 1H), 2.83 - 2.96 (m, 1H), 2.51 - 2.56 (m, 1H), 2.00 - 2.13 (m, 1H).
319	MS(ESI) calcd. for $C_{30}H_{24}FN_9O_2$, 561.20 m/z, found 562.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.15 (d, J = 8.2 Hz, 1H), 8.36 - 8.38 (m, 2H), 8.01 - 8.06 (m, 2H), 7.96 (d, J = 8.5 Hz, 1H), 7.82 (s, 1H), 7.41 - 7.44 (m, 2H), 7.33 - 7.36 (m, 1H), 7.25 - 7.27 (m, 1H), 7.18 (t, J = 4.6 Hz, 1H), 6.92 (s, 2H), 6.55 (t, J = 2.1 Hz, 1H), 6.43 - 6.46 (m, 1H), 5.58 (q, J = 8.1 Hz, 1H), 3.98 (s, 3H), 3.00 - 3.02 (m, 1H), 2.88 - 2.96 (m, 1H), 2.53- 2.58 (m, 1H), 1.96 - 2.06 (m, 1H).
321	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$ 544.21 m/z, found 545.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.17 (d, J = 8.4 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.30 (d, J = 5.2 Hz, 1H), 8.14 (s, 2H), 7.99 - 8.05 (m, 2H), 7.43 - 7.46 (m, 1H), 7.36 - 7.43 (m, 2H), 7.26 - 7.35 (m, 3H), 6.92 (s, 2H), 6.42 - 6.47 (m, 1H), 5.65 (q, J= 8.0 Hz,1H), 3.90 (s, 3H), 2.98 - 3.07 (m, 1H), 2.85 - 2.97 (m, 1H), 2.52 - 2.59 (m, 1H), 2.02 - 2.14 (m, 1H). (formic acid salt)
322	MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$, 564.19 m/z, found 565.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.46 (d, J = 8.8 Hz, 1H), 9.36 (s, 1H), 9.04 (s, 1H), 8.33 - 8.40 (m, 2H), 7.99 - 8.04 (m, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.42 (s, 1H), 7.37 (s, 1H), 7.25 - 7.31 (m, 2H), 7.24 (t, J = 54.0 Hz, 1H), 6.93 (s, 2H), 6.55 (t, J = 4.0 Hz, 1H), 6.45 (dd, J = 4.8, 7.6 Hz, 1H), 5.69 (q, J = 8.4, 1H), 2.99 - 3.05 (m, 1H), 2.87 - 2.97 (m, 1H), 2.50 - 2.57 (m, 1H), 2.20 - 2.35 (m, 1H).
323	MS (ESI) calcd. for $C_{30}H_{24}N_8O_3$ 544.20 m/z, found, 545.30 $[M+H]^+$. ^{1} H-NMR (400 MHz, DMSO-d_6) δ (ppm); 9.47 (brs, 1H), 9.13 (brs, 1H), 8.57 (d, J = 8.3 Hz, 1H), 8.36 - 8.38 (m, 2H), 8.01 - 8.03 (m, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.81 (d, J = 1.7 Hz, 1H), 7.37 - 7.41 (m, 2H), 7.25 - 7.34 (m, 4H), 6.92 (s, 2H), 6.77 (d, J = 8.3 Hz, 1H), 6.55 - 6.56 (m, 1H), 6.44 - 6.47 (m, 1H), 5.61 (q, J = 8.4 Hz, 1H), 3.00 - 3.06 (m, 1H), 2.85 - 2.93 (m, 1H), 2.44 - 2.49 (m, 1H), 2. 07 - 2.15 (m, 1H).
324	MS (ESI) calcd. for $C_{29}H_{24}F_2N_{10}O_2$ 582.20 m/z, found, 583.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.35 - 8.41 (m, 2H), 7.95 - 8.09 (m, 2H), 7.54 - 7.86 (m, 2H), 7.39 - 7.42 (m, 1H), 7.22 - 7.34 (m, 3H), 6.57 - 6.59 (m, 1H), 6.46 - 6.51 (m, 1H), 6.31 - 6.33 (m, 1H), 5.55 - 5.64 (m, 1H), 3.98 (s, 3H), 3.01 - 3.11 (m, 1H), 2.83 - 2.93 (m, 1H), 2.42 - 2.51 (m, 1H), 2.11 - 2.22 (m, 1H).
328	MS (ESI) calcd. for $C_{32}H_{25}N_9O$, 551.22 m/z, found, 552.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.92 (s, 1H), 8.26 - 8.48 (m, 2H), 7.90 - 8.20 (m, 2H), 7.78 - 7.85 (m, 1H), 7.55 - 7.70 (m, 1H), 7.44 - 7.55 (m, 1H), 7.35 - 7.43 (m, 3H), 7.25 - 7.34 (m, 1H), 7.10 - 7.24 (m, 1H), 6.83 - 6.88 (m, 1H), 6.51 - 6.60 (m, 2H), 6.38 - 6.50 (m, 1H), 5.53 - 5.72 (m, 1H), 2.98 - 3.15 (m, 1H), 2.80 - 2.97 (m, 1H), 2.49 - 2.51 (m, 1H), 2.00 - 2.20 (m, 1H). (formic acid salt)

Cpd ID	Characterization Data
331	MS (ESI) calcd. for $C_{30}H_{22}F_2N_8O$, 548.19 m/z, found, 549.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.43 - 8.49 (m, 1H), 8.39 - 8.42 (m, 1H), 8.01 - 8.09 (m, 2H), 7.81 - 7.89 (m, 1H), 7.73 - 7.81 (m, 1H), 7.55 - 7.66 (m, 2H), 7.39 - 7.49 (m, 3H), 7.31 - 7.39 (m, 1H), 6.81 - 6.91 (m, 1H), 6.55 - 6.61 (m, 1H), 5.54 - 5.61 (m, 1H), 2.83 - 3.12 (m, 2H), 2.57 - 2.59 (m, 1H), 2.02 - 2.19 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -112.67. (TFA salt)
332	MS (ESI) calcd for $C_{30}H_{23}FN_8O$, 530.20 m/z, found, 531.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.29 - 8.44 (m, 2H), 7.90 - 8.06 (m, 2H), 7.68 - 7.85 (m, 3H), 7.49 - 7.61 (m, 1H), 7.34 - 7.47 (m, 3H), 7.22 - 7.34 (m, 2H), 6.53 - 6.58 (m, 1H), 6.42 - 6.54 (m, 1H), 5.55 - 5.69 (m, 1H), 2.99 - 3.10 (m, 1H), 2.84 - 2.99 (m, 1H), 2.56 - 2.63 (m, 1H), 2.00 - 2.19 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -112.67.
333	MS (ESI) calcd. for $C_{30}H_{23}FN_8O$, 530.20 m/z, found, 531.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.41 (m, 2H), 7.93 - 8.04 (m, 2H), 7.81 (s, 1H), 7.60 - 7.71 (m, 1H), 7.37 - 7.59 (m, 3H), 7.21 - 7.36 (m, 4H), 6.52 - 6.61 (m, 1H), 6.41 - 6.49 (m, 1H), 5.54 - 5.64 (m, 1H), 2.83 - 3.09 (m, 2H), 2.49 - 2.52 (m, 1H), 1.94 - 2.14 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -114.53.
334	MS (ESI) calcd for $C_{31}H_{25}FN_8O_2$ 560.21 m/z, found, 561.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.40 (m, 2H), 7.92 - 8.05 (m, 2H), 7.78 - 7.87 (m, 1H), 7.24 - 7.44 (m, 6H), 6.98 - 7.07 (m, 1H), 6.46 - 6.61 (m, 2H), 5.56 - 5.67 (m, 1H), 3.80 (s, 3H), 2.99 - 3.12 (m, 1H), 2.85 - 2.98 (m, 1H), 2.56 - 2.62 (m, 1H), 2.03 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -110.83.
335	MS (ESI) calcd. for $C_{31}H_{26}N_8O_2$, 542.22 m/z, found 543.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 8.30 - 8.45 (m, 2H), 7.90 - 8.10 (m, 2H), 7.81 (s, 1H), 7.50 - 7.60 (m, 1H), 7.45 - 7.50 (m, 1H), 7.30 - 7.45 (m, 3H), 7.20 - 7.30 (m, 2H), 7.00 - 7.20 (m, 1H), 6.40 - 6.60 (m, 2H), 5.60 - 5.70 (m, 1H), 3.81 (s, 3H), 2.85 - 3.15 (m, 2H), 2.55 - 2.58 (m, 1H), 2.00 - 2.20 (m,1H).
336	MS (ESI) calcd. for $C_{31}H_{25}FN_8O_2$ 560.21 m/z, found, 561.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.33 - 8.41 (m, 2H), 7.98 - 8.09 (m, 2H), 7.81 - 7.83 (m, 1H), 7.67 - 7.72 (m, 1H), 7.57 - 7.61 (m, 1H), 7.35 - 7.45 (m, 1H), 7.32 - 7.34 (m, 1H), 7.26 - 7.31 (m, 3H), 6.43 - 6.61 (m, 2H), 5.57 - 5.69 (m, 1H), 3.94 (s, 3H), 2.83 - 3.12 (m, 2H), 2.57 - 2.59 (m, 1H), 2.02 - 2.19 (m, 1H).
337	MS (ESI) calcd. for $C_{30}H_{22}ClFN_8O$, 564.01 m/z, found 565.30 $[M+H]^+$ ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.45 (m, 2H), 8.10 - 8.25 (m, 1H), 7.90 - 8.10 (m, 3H), 7.81 (s, 1H), 7.50 - 7.65 (m, 1H), 7.35 - 7.50 (m, 2H), 7.15 - 7.35 (m, 2H), 6.40 - 6.60 (m, 2H), 5.50 - 5.70 (m, 1H), 2.85 - 3.15 (m, 2H), 2.55 - 2.58 (m, 1H), 1.90 - 2.20 (m,1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -112.20.
338	MS (ESI) calcd. for $C_{30}H_{24}ClN_9O_2$ 577.17 m/z, found, 578.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.21 - 9.29 (m, 1H), 8.38 - 8.49 (m, 2H), 8.01 - 8.16 (m, 2H), 7.83 - 7.89 (m, 1H), 7.74 - 7.81 (m, 1H), 7.53 - 7.57 (m, 1H), 7.46 - 7.52 (m, 1H), 7.34 - 7.45 (m, 2H), 7.25 - 7.33 (m, 1H), 6.74 - 6.89 (m, 1H), 6.57 - 6.59 (m, 1H), 5.55 - 5.63 (m, 1H), 3.86 (s, 3H), 2.81 - 3.13 (m, 2H), 2.63 - 2.64 (m, 1H), 2.02 - 2.19 (m, 1H). (TFA salt)

Cpd ID	Characterization Data
343	MS (ESI) calcd for $C_{30}H_{21}F_3N_8O$, 566.18 m/z, found, 567.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.41 (m, 2H), 7.90 - 8.05 (m, 2H), 7.75 - 7.90 (m, 3H), 7.23 - 7.40 (m, 4H), 6.53 - 6.61 (m, 1H), 6.43 - 6.52 (m, 1H), 5.51 - 5.67 (m, 1H), 2.99 - 3.12 (m, 1H), 2.85 - 2.99 (m, 1H), 2.56 - 2.63 (m, 1H), 2.00 - 2.16 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -133.75, -156.61.
344	MS (ESI) calcd. for $C_{30}H_{24}FN_9O_2$ 561.21 m/z, found, 562.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.45 (m, 2H), 7.89 - 8.09 (m, 2H), 7.75 - 7.87 (m, 1H), 7.19 - 7.49 (m, 5H), 7.09 - 7.18 (m, 1H), 6.52 - 6.63 (m, 1H), 6.37 - 6.62 (m, 1H), 5.54 - 5.69 (m, 1H), 3.89 (s, 3H), 2.81 - 3.20 (m, 2H), 2.55 - 2.63 (m, 1H), 1.98 - 2.21 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); 69.79.
347	MS (ESI) calcd. for $C_{30}H_{21}F_3N_8O$, 566.18 m/z, found 567.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ(ppm); 8.37 - 8.39 (m, 1H), 8.30 - 8.33 (m, 1H), 7.94 - 8.05 (m, 2H), 7.84 (s, 1H), 7.77 - 7.82 (m, 1H), 7.57 - 7.62 (m, 1H), 7.34 - 7.42 (m, 2H), 7.29 - 7.32 (m, 2H), 6.47 - 6.54 (m, 1H), 6.36 - 6.42 (m, 1H), 5.56 - 5.63 (m, 1H), 3.04 - 3.12 (m, 1H), 2.91 - 2.95 (m, 1H), 2.59 - 2.63 (m, 1H), 2.02 - 2.16 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -127.23, -134.40, -137.92.
348	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$ 544.57 m/z, found, 545.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.82 - 8.83 (m, 1H), 8.56 - 8.59 (m, 1H), 8.39 - 8.47 (m, 2H), 8.01 - 8.11 (m, 2H), 7.82 - 7.85 (m, 1H), 7.75 - 7.77 (m, 1H), 7.49 - 7.51 (m, 1H), 7.31 - 7.39 (m, 2H), 6.79 - 6.83 (m, 1H), 6.59 - 6.61 (m, 1H), 5.62 - 5.72 (m, 1H), 4.07 (s, 3H), 3.03 - 3.13 (m, 1H), 2.82 - 3.01 (m, 1H), 2.59 - 2.62 (m, 1H), 2.15 - 2.33 (m, 1H). (TFA salt)
349	MS (ESI) calcd. for $C_{29}H_{21}F_3N_{10}O$, 582.19 m/z, found, 583.30 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d6) δ (ppm); 9.44 - 9.46 (m, 1H), 9.24 - 9.25 (m, 1H), 8.51 - 8.56 (m, 2H), 8.15 - 8.17 (m, 2H), 8.09 - 8.11 (m, 2H), 7.80 - 7.86 (m, 2H), 7.50 - 7.58 (m, 3H), 6.93 - 7.20 (m, 1H), 6.77 - 6.80 (m, 1H), 5.80 - 5.89 (m, 1H), 5.43 - 5.58 (m, 1H), 3.17 - 3.47 (m, 2H), 2.50 - 2.52 (m, 2H). ^{19}F-NMR (400 MHz, DMSO-d6) δ (ppm); -73.31, -116.16, -192.19. (TFA salt)
350	**MS (ESI)** calcd. for $C_{29}H_{21}F_3N_{10}O$, 582.19 m/z, found, 583.25 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d6) δ (ppm); 9.45 - 9.47 (m, 1H), 9.16 - 9.17 (m, 1H), 8.46 - 8.52 (m, 2H), 8.16 - 8.17 (m, 2H), 8.09 - 8.11 (m, 2H), 7.85 - 7.93 (m, 1H), 7.72 - 7.74 (m, 1H), 7.52 - 7.54 (m, 2H), 7.45 - 7.47 (m, 1H), 6.92 - 7.20 (m, 1H), 6.75 - 6.79 (m, 1H), 5.66 - 5.74 (m, 1H), 5.39 - 5.56 (m, 1H), 3.49 - 3.60 (m, 1H), 3.12 - 3.23 (m, 1H), 2.50 - 2.51 (m, 2H). ^{19}F-NMR (400 MHz, DMSO-d6) δ (ppm); -74.29, -116.19, -179.20. (TFA salt)
355	MS (ESI) calcd. for $C_{31}H_{27}N_9O_3$, 573.22 m/z, found 574.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.84 (d, J = 8.3 Hz, 1H), 8.34 - 8.38 (m, 2H), 8.01 (dd, J = 4.8, 1.8 Hz, 1H), 7.93 - 7.97 (m, 2H), 7.80 - 7.82 (m, 1H), 7.44 - 7.47 (m, 1H), 7.41 - 7.43 (m, 1H), 7.30 - 7.34 (m, 1H), 7.25 (dd, J = 7.6, 1.9 Hz, 1H), 7.06 (d, J = 5.1 Hz, 1H), 6.93 (s, 2H), 6.55 (dd, J = 2.6, 1.6 Hz, 1H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 5.58 (q, J = 8.1 Hz, 1H), 3.94 (s, 3H), 3.80 (s, 3H), 2.98 - 3.06 (m, 1H), 2.86 - 2.96 (m, 1H), 2.52 - 2.58 (m, 1H), 1.96 - 2.08 (m, 1H).
356	MS(ESI) calcd. for $C_{31}H_{25}N_9O_3$ 571.21 m/z, found 572.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.73 (d, J = 8.2 Hz, 1H), 8.34 - 8.39 (m, 2H), 8.02 (dd, J = 4.8, 1.9 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.78 - 7.83 (m, 2H), 7.40 - 7.44 (m, 2H), 7.29 - 7.33 (m, 1H), 7.24 - 7.28 (m, 1H), 7.15 (d, J = 5.2 Hz, 1H), 6.92 (s, 2H), 6.55 - 6.57 (m, 1H), 6.45 (dd, J = 7.6, 4.8 Hz, 1H), 5.59 (q, J = 8.4 Hz, 1H), 4.23 - 4.47 (m, 2H), 4.31 - 4.35 (m, 2H), 2.86 - 3.07 (m, 2H), 2.52 - 2.60 (m, 1H), 1.97 - 2.10 (m, 1H).

Cpd ID	Characterization Data
357	MS(ESI) calcd. for $C_{31}H_{27}N_9O_2$, 557.23 m/z, found 558.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.95 (d, J = 8.2 Hz, 1H), 8.34 - 8.39 (m, 2H), 8.06 (s, 1H), 8.01 (dd, J = 4.9, 1.9 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 1.9 Hz, 1H), 7.30 - 7.33 (m, 1H), 7.25 (dd, J = 7.7, 1.9 Hz, 1H), 6.93 (s, 2H), 6.81 (s, 1H), 6.55 (dd, J = 2.6, 1.7 Hz, 1H), 6.43 (dd, J = 7.6, 4.8 Hz, 1H), 5.56 (q, J = 8.1 Hz, 1H), 3.85 (s, 3H), 2.98 - 3.05 (m, 1H), 2.86 - 2.95 (m, 1H), 2.53 - 2.58 (m, 1H), 2.26 (s, 3H), 1.97 - 2.06 (m, 1H).
358	MS (ESI) calcd. for $C_{34}H_{32}N_{10}O$, 596.28 m/z, found, 597.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.64 – 8.55 (m, 1H), 8.42 – 8.33 (m, 2H), 8.05 – 7.90 (m, 3H), 7.85 – 7.79 (m, 1H), 7.70 (s, 1H), 7.62 – 7.54 (m, 1H), 7.54 – 7.45 (m, 1H), 7.42 (s, 1H), 7.36 – 7.23 (m, 3H), 6.91 (s, 2H), 6.59 – 6.52 (m, 1H), 6.48 – 6.39 (m, 1H), 4.82 –4.42 (m, 2H), 3.73 (s, 1H), 3.21 – 2.92 (m, 4H), 2.92 – 2.69 (m, 1H), 2.24 – 1.80 (m, 3H), 1.56 (s, 2H), 1.24 (s, 1H).
359	MS (ESI) calcd. for $C_{34}H_{32}N_{10}O$, 596.28 m/z, found 597.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.71 – 8.53 (m, 2H), 8.40 – 8.32 (m, 2H), 8.10 – 7.93 (m, 2H), 7.87 – 7.76 (m, 2H), 7.57 – 7.19 (m, 5H), 6.93 (s, 2H), 6.63 – 6.36 (m, 2H), 4.35 (s, 2H), 3.57 (s, 1H), 3.17 (s, 1H), 3.04 (s, 3H), 2.81 (s, 1H), 2.11 – 1.74 (m, 4H), 1.53 – 1.18 (m, 3H).
360	MS (ESI) calcd. for $C_{34}H_{32}N_{10}O$, 596.28 m/z, found, 597.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.72 - 8.66 (m, 2H), 8.40 - 8.32 (m, 2H), 8.04 - 7.98 (m, 1H), 7.98 - 7.92 (m, 1H), 7.84 - 7.79 (m, 1H), 7.60 - 7.56 (m, 1H), 7.42 - 7.36 (m, 3H), 7.30 - 7.22 (m, 2H), 6.93 (s, 2H), 6.58 - 6.52 (m, 1H), 6.46 - 6.39 (m, 1H), 4.39 - 4.35 (m, 2H), 3.51 - 3.46 (m, 1H), 3.06 - 3.01 (m, 4H), 2.85 - 2.78 (m, 1H), 1.99 - 1.94 (m, 2H), 1.89 - 1.84 (m, 1H), 1.47 - 1.42 (m, 2H), 1.26 - 1.22 (m, 1H).
361	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$, 569.23 m/z, found 570.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.95 (d, J = 8.2 Hz, 1H), 8.36 - 8.37 (m, 1H), 8.35 (s, 1H), 8.06 (d, J = 4.9 Hz, 1H), 8.01 - 8.02 (m, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.81 (dd, J = 1.7, 0.7 Hz, 1H), 7.44 - 7.46 (m, 1H), 7.41 (s, 1H), 7.30 - 7.32 (m, 1H), 7.23 - 7.26 (m, 1H), 6.98 (d, J = 4.9 Hz, 1H), 6.93 (s, 2H), 6.54 - 6.55 (m, 1H), 6.43 - 6.44 (m, 1H), 5.56 - 5.58 (m, 1H), 4.26 - 4.29 (m, 2H), 2.98 - 3.07 (m, 1H), 2.86 - 2.93 (m, 1H), 2.84 - 2.86 (m, 2H), 2.52- 2.58 (m, 1H), 1.93 - 2.02 (m, 1H), 1.90 - 1.93 (m, 2H).
363	MS (ESI) calcd. for $C_{31}H_{23}N_9OS$ 569.17 m/z, found, 570.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.29 (d, J = 8.2 Hz, 1H), 8.70 (d, J = 4.8 Hz, 1H), 8.33 - 8.40 (m, 2H), 8.00 - 8.05 (m, 2H), 7.96 (d, J = 8.6 Hz, 1H), 7.80 - 7.83 (m, 2H), 7.71 (d, J = 4.8 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.41 - 7.45 (m, 1H), 7.32 - 7.36 (m, 1H), 7.24 - 7.30 (m, 1H), 6.92 (s, 2H), 6.53 - 6.58 (m, 1H), 6.41 - 6.49 (m, 1H), 5.66 - 5.74 (m, 1H), 3.02 - 3.11 (m, 1H), 2.88 - 3.00 (m, 1H), 2.54 - 2.65 (m, 1H), 2.05 - 2.19 (m, 1H).
364	MS(ESI) calcd. for $C_{30}H_{24}F_2N_{10}O_2$, 594.21 m/z, found 595.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.27 (d, J = 8.0 Hz, 1H), 8.74 (s, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.14 (s, 2H), 8.08 (s, 1H), 8.00 - 8.05 (m, 2H), 7.40 - 7.48 (m, 2H), 7.27 - 7.38 (m, 2H), 7.10 (t, J = 53.6 Hz, 1H), 6.90 (s, 2H), 6.42 - 6.48 (m, 1H), 5.66 - 5.74 (m, 1H), 3.97 (s, 3H), 3.00 - 3.10 (m, 1H), 2.88 - 3.00 (m, 1H), 2.53 - 2.68 (m, 1H), 2.03 - 2.14 (m, 1H). ^{19}F-NMR (376 MHz, DMSO-d_6) δ (ppm); -118.98, -119.02.

Cpd ID	Characterization Data
365	MS (ESI) calcd. for $C_{30}H_{22}ClF_2N_9O$, 597.16 m/z, found 598.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.32 (d, J = 8.0 Hz, 1H), 9.10 (s, 1H), 8.56 (s, 1H), 8.33 - 8.40 (m, 2H), 7.99 - 8.05 (m, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.81 (s, 1H), 7.40 - 7.48 (m, 2H), 7.27 - 7.35 (m, 2H), 7.26 (t, J = 53.2 Hz, 1H), 6.89 (s, 2H), 6.53 - 6.58 (m, 1H), 6.43 - 6.48 (m, 1H), 5.65 (q, J = 8.4 Hz, 1H), 3.00 - 3.11(m, 1H), 2.88 - 2.99 (m, 1H), 2.53 - 2.62 (m, 1H), 2.02 - 2.15 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -118.58, -118.63.
369	MS (ESI) calcd. for $C_{33}H_{32}N_{10}O$: 584.27. found:585.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.32 (m, 3H), 8.27 – 8.28 (m, 1H), 7.95 - 7.96 (m, 1H), 7.86 - 7.88 (m, 1H), 7.75 (s, 1H), 7.59 - 7.61 (m, 1H), 7.42 (s, 1H), 7.26 - 7.28 (m, 2H), 6.48 - 6.52 (m, 2H), 4.85 (s. 1H), 4.21 - 4.32 (m, 2H), 3.26 - 3.49 (m, 1H), 3.10 - 3.12 (m, 1H), 3.01 - 3.08 (m, 1H), 2.89 - 2.93 (m, 1H), 2.78 (m, 1H), 2.65 - 2.68 (m, 1H), 1.94 - 2.38 (m, 3H), 1.46 - 1.58 (m, 6H). (formic acid salt)
370	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27. found,578.35 $[M+ H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.24 – 8.30 (m, 2H), 7.74 - 8.00 (m, 2H), 7.56 - 7.57 (m, 2H), 7.32 - 7.38 (m, 1H), 7.23 - 7.26 (m, 2H), 6.47 - 6.51 (m, 2H), 4.78 (m, 1H), 4.09 - 4.15 (m, 3H), 3.25 - 3.42 (m, 1H), 2.78 - 3.15 (m, 4H), 1.79 - 2.27 (m, 3H), 1.65 - 1.67 (m, 2H), 1.23 - 1.28 (m, 2H), 1.10 - 1.67 (m, 2H). F NMR δ (ppm) -185.38. (TFA salt)
371	544.21 m/z, found, 545.15 $[M+H]^+$.^1H NMR (400 MHz, DMSO-d6) δ(ppm); 8.95 – 8.84 (m, 1H), 8.74 – 8.65 (m, 1H), 8.40 – 8.34 (m, 1H), 8.21 – 8.11 (m, 1H), 8.07 (s, 2H), 8.00 – 7.86 (m, 2H), 7.41 – 7.29 (m, 2H), 7.29 – 7.16 (m, 2H), 6.94 – 6.71 (m, 3H), 6.44 – 6.29 (m, 1H), 5.68 – 5.50 (m, 1H), 3.84 (s, 3H), 3.04 – 2.91 (m, 1H), 2.91 – 2.77 (m, 1H), 2.53 – 2.45 (m, 1H), 2.07 – 1.92 (m, 1H).
372	MS (ESI) calcd. for $C_{27}H_{24}N_8O_2$: 492.20 m/z, found: 493.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.29 - 8.43 (m, 2H), 8.00 - 8.08 (m, 1H), 7.91 - 7.98 (m, 1H), 7.75 - 7.88 (m, 1H), 7.33 - 7.43 (m, 2H), 7.22 - 7.32 (m, 2H), 6.55 - 6.61 (m, 1H), 6.44 - 6.53 (m, 1H), 5.36 - 5.49 (m, 1H), 4.97 - 5.09 (m, 1H), 4.52 - 4.69 (m, 2H), 2.80 - 3.08 (m, 3H), 2.58 - 2.69 (m, 1H), 2.35 - 2.50 (m, 1H), 1.96 - 2.13 (m, 1H).
373	MS (ESI) calcd. for $C_{27}H_{24}N_8O_2$, 492.20 m/z, found 493.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.33 - 8.40 (m, 2H), 8.00 - 8.01 (m, 1H), 7.92 - 7.94 (m, 1H), 7.83 - 7.84 (m, 1H), 7.26 - 7.36 (m, 3H), 7.24 - 7.25 (m, 1H), 6.55 - 6.59 (m, 2H), 5.42 - 5.44 (m, 1H), 5.07 - 5.11 (m, 1H), 4.61 - 4.69 (m, 2H), 3.01 - 3.09 (m, 2H), 2.99 - 3.00 (m, 1H), 2.59 - 2.60 (m, 1H), 2.54 - 2.55 (m, 1H), 2.04 - 2.05 (m, 1H).
375	MS (ESI) calcd for $C_{28}H_{23}N_9OS$ 533.17 m/z, found, 534.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.21 - 9.30 (m, 1H), 8.32 - 8.42 (m, 2H), 7.99 - 8.06 (m, 1H), 7.90 - 7.98 (m, 1H), 7.74 - 7.87 (m, 2H), 7.23 - 7.45 (m, 4H), 6.88 (s, 2H), 6.52 - 6.59 (m, 1H), 6.40 - 6.50 (m, 1H), 5.51 - 5.65 (m, 1H), 2.82 - 3.20 (m, 2H), 2.45 - 2.63 (m, 1H), 2.46 (s, 3H), 1.97 - 2.16 (m, 1H).
376	MS (ESI) calcd. for $C_{28}H_{21}F_2N_9OS$ 569.16 m/z, found, 570.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.40 - 9.50 (m, 1H), 8.50 - 8.66 (m, 1H), 8.27 - 8.43 (m, 2H), 8.00 - 8.05 (m, 1H), 7.92 - 7.99 (m, 1H), 7.79 - 7.85 (m, 1H), 7.21 - 7.50 (m, 5H), 6.56 - 6.61 (m, 1H), 6.47 - 6.54 (m, 1H), 5.51 - 5.64 (m, 1H), 3.00 - 3.12 (m, 1H), 2.85 - 2.96 (m, 1H), 2.56 - 2.65 (m, 1H), 2.01 - 2.16 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -110.16. (formic acid salt)

Cpd ID	Characterization Data
377	MS (ESI) calcd for $C_{29}H_{24}N_{10}O_2$ 544.21 m/z, found, 545.45 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.31 - 9.40 (m, 1H), 9.24 - 9.31 (m, 1H), 8.32 - 8.41 (m, 2H), 7.91 - 8.08 (m, 2H), 7.78 - 7.84 (m, 1H), 7.57 - 7.63 (m, 1H), 7.39 - 7.48 (m, 2H), 7.23 - 7.36 (m, 2H), 6.88 (s, 2H), 6.52 - 6.59 (m, 1H), 6.40 - 6.50 (m, 1H), 5.56 - 5.70 (m, 1H), 4.09 (s, 3H), 2.84 - 3.17 (m, 2H), 2.52 - 2.63 (m, 1H), 1.98 - 2.17 (m, 1H).
378	MS (ESI) calcd. for $C_{29}H_{23}N_{10}O_2$, 578.17 m/z, found, 579.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.41 - 8.42 (m, 1H), 8.00 - 8.19 (m, 5H), 7.48 - 7.50 (m, 1H), 7.26 - 7.40 (m, 3H), 7.12 - 7.13 (m, 1H), 6.42 - 6.45 (m, 1H), 5.54 - 5.58 (m, 1H), 3.97 (s, 3H), 2.85 - 3.02 (m, 2H), 2.51 - 2.59 (m, 1H), 1.99 - 2.07 (m, 1H).
379	MS (ESI) calcd for $C_{30}H_{22}N_{10}O_2$ 554.19 m/z, found, 555.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.26 - 9.35 (m, 1H), 8.39 - 8.48 (m, 2H), 8.20 - 8.27 (m, 1H), 8.14 (s, 2H), 7.97 - 8.07 (m, 2H), 7.75 - 7.83 (m, 1H), 7.40 - 7.50 (m, 2H), 7.25 - 7.38 (m, 3H), 6.92 (s, 2H), 6.39 - 6.50 (m, 1H), 5.64 - 5.79 (m, 1H), 2.79 - 3.25 (m, 2H), 2.58 - 2.63 (m, 1H), 2.06 - 2.22 (m, 1H).
380	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O_2$ 558.22 m/z, found, 559.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.41 - 8.44 (m, 1H), 8.12 - 8.15 (m, 2H), 7.99 - 8.09 (m, 3H), 7.41 - 7.49 (m, 2H), 7.26 - 7.36 (m, 2H), 6.93 - 6.96 (m, 1H), 6.41 - 6.47 (m, 1H), 5.54 - 5.61 (m, 1H), 3.90 (s, 3H), 2.99 - 3.04 (m, 1H), 2.81 - 2.93 (m, 1H), 2.52 - 2.59 (m, 1H), 2.17 (s, 3H),1.93 - 2.07 (m, 1H).
381	MS (ESI) calcd. for $C_{30}H_{26}N_{10}O_3$ 574.22 m/z, found, 575.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.47 - 8.52 (m, 1H), 8.03 - 8.19 (m, 4H), 7.74 - 7.79 (m, 1H), 7.31 - 7.51 (m, 3H), 6.77 - 6.84 (m, 3H), 5.55 - 5.62 (m, 1H), 3.81 - 3.95 (m, 6H), 3.01 - 3.09 (m, 1H), 2.80 - 2.94 (m, 1H), 2.57 - 2.59 (m, 1H), 2.02 - 2.17 (m, 1H). (TFA salt)
382	MS (ESI) calcd. for $C_{29}H_{23}FN_{10}O$, 546.20 m/z, found, 547.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.46 - 8.58 (m, 1H), 8.32 - 8.45 (m, 1H), 8.08 - 8.20 (m, 2H), 7.92 - 8.07 (m, 2H), 7.70 - 7.85 (m, 1H), 7.45 - 7.56 (m, 1H), 7.38 - 7.44 (m, 1H), 7.18 - 7.37 (m, 2H), 6.34 - 6.53 (m, 1H), 5.47 - 5.68 (m, 1H), 2.78 - 3.18 (m, 2H), 2.53 - 2.68 (m, 4H), 1.83 - 2.12 (m, 1H). ^{19}F-NMR (282 MHz, DMSO- d_6) δ (ppm); -131.78.
383	MS (ESI) calcd. for $C_{30}H_{22}FN_{11}O$, 571.20 m/z, found, 572.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.40 - 8.48 (m, 1H), 8.27 - 8.39 (m, 2H), 8.13 (m, 2H), 7.98 - 8.09 (m, 2H), 7.67 - 7.89 (m, 1H), 7.37 - 7.47 (m, 2H), 7.24 - 7.36 (m, 2H), 6.42 - 6.52 (m, 1H), 5.59 - 5.74 (m, 1H), 2.99 - 3.12 (m, 1H), 2.81 - 2.98 (m, 1H), 2.55 - 2.64 (m, 1H), 2.03 - 2.33 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -73.63, -130.61. (TFA salt)
389	MS (ESI) calcd. for $C_{31}H_{25}N_9O_2$ 555.21 m/z, found, 556.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.98 (d, J = 8.4 Hz, 1H), 8.47 (s, 1H), 8.34 - 8.39 (m, 2H), 8.22 (s, 1H), 8.00 - 8.04 (m, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.78 - 7.83 (m, 1H), 7.40 - 7.45 (m, 2H), 7.30 - 7.33 (m, 1H), 7.25 - 7.29 (m, 1H), 6.91 (s, 2H), 6.53 - 6.58 (m, 1H), 6.45 (dd, J = 7.6, 4.8 Hz, 1H), 5.64 (q, J = 8.0 Hz, 1H), 4.63 (t, J = 8.8 Hz, 2H), 3.51 (t, J =8.4 Hz, 2H), 2.99 - 3.09 (m, 1H), 2.87 - 2.98 (m, 1H), 2.52 - 2.56 (m, 1H), 2.02 - 2.15 (m, 1H).
390	MS(ESI) calcd. for $C_{30}H_{26}N_{10}O_2$, 558.22 m/z, found 559.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.96 (d, J = 8.4 Hz, 1H), 8.33 - 8.40 (m, 2H), 7.99 - 8.04 (m, 1H), 7.96 (d, J = 9.6 Hz, 1H), 7.77 - 7.84 (m, 1H), 7.36 - 7.41 (m, 1H), 7.21 - 7.33 (m, 3H), 6.89 - 6.98 (m, 2H), 6.53 - 6.58 (m, 1H), 6.44 (dd, J = 7.6, 4.8 Hz, 1H), 5.43 - 5.54 (m, 1H), 3.38 (s, 3H), 3.00 - 3.07 (m, 1H), 2.82 - 2.92 (m, 1H), 2.15 - 2.42 (m, 4H), 1.60 - 1.66 (m, 2H).

Cpd ID	Characterization Data
391	MS (ESI) calcd. for $C_{35}H_{35}N_7O$, 569.29. found, 570.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) 8.20 - 8.22(m. 1H), 7.90 - 7.98 (m, 4H), 7.35 - 7.51 (m, 4H), 7.18 - 7.28 (m, 3H), 6.45 - 6.49 (m, 1H), 4.40 (m, 1H), 2.94 - 3.11 (m, 3H), 2.63 - 2.78 (m, 3H), 2.40 - 2.51 (m, 1H), 1.81 - 1.93 (m, 4H), 1.17 - 1.30 (m, 3H), 0.71 - 0.73 (m, 4H).
392	MS (ESI) calcd. for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found, 579.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d6) δ(ppm); 9.16 – 9.00 (m, 1H), 8.48 – 8.33 (m, 1H), 8.13 (s, 2H), 8.07 – 7.93 (m, 3H), 7.66 – 7.20 (m, 5H), 7.16 – 6.74 (m, 3H), 6.47 – 6.35 (m, 1H), 5.68 – 5.52 (m, 1H), 3.13 – 2.69 (m, 2H), 2.62 (s, 3H), 2.12 – 1.91 (m, 1H), 1.24 (s, 1H).
395	MS (ESI) calcd. for $C_{32}H_{27}N_9O_2$ 569.23 m/z, found, 570.15 $[M+H]^+$. 1H NMR (400 MHz, DMSO-*d6*) δ (ppm); 8.95 (d, J = 8.4 Hz, 1H), 8.41 - 8.33 (m, 2H), 8.01 (dd, J = 4.9, 1.8 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.81 (s, 1H), 7.44 - 7.35 (m, 2H), 7.34 - 7.23 (m, 2H), 7.06 (s, 1H), 6.91 (s, 2H), 6.58 - 6.53 (m, 1H), 6.44 (dd, J = 7.6, 4.8 Hz, 1H), 5.60 (q, J = 8.2 Hz, 1H), 4.57 (t, J = 8.6 Hz, 2H), 3.42 (t, J = 8.7 Hz, 2H), 3.09 - 2.98 (m, 1H), 2.98 - 2.85 (m, 1H), 2.56 - 2.53 (m, 1H), 2.36 (s, 3H), 2.13 - 1.99 (m, 1H).
396	MS (ESI) calcd. for $C_{28}H_{23}FN_{10}O$, 534.20 m/z, found, 535.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.37 - 8.42 (m, 2H), 8.02 - 8.09 (m, 1H), 7.95 - 7.97 (m, 1H), 7.81 - 7.83 (m, 1H), 7.51 - 7.52 (m, 2H), 7.38 - 7.42 (m, 2H), 6.57 - 6.60 (m, 2H), 6.45 - 6.50 (m, 1H), 5.54 - 5.59 (m, 1H), 4.00 (s, 3H), 3.01 - 3.07 (m, 1H), 2.85 - 2.99 (m, 1H), 2.50 - 2.54 (m, 1H), 1.97 - 2.09 (m, 1H).
397	MS (ESI) calcd for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found, 579.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.07 - 9.15 (m, 1H), 8.66 (s, 1H), 8.39 - 8.48 (m, 1H), 7.91 - 8.17 (m, 4H), 7.68 - 7.62 (m, 1H), 7.59 - 7.18 (m, 4H), 6.64 - 7.17 (m, 3H), 6.39 - 6.49 (m, 1H), 5.55 - 5.69 (m, 1H), 2.80 - 3.10 (m, 2H), 2.52 - 2.67 (m, 4H), 1.93 - 2.12 (m, 1H).
398	MS (ESI) calcd. for $C_{31}H_{25}N_{11}O$, 567.22 m/z, found, 568.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.01 - 9.18 (m, 1H), 8.80 - 8.97 (m, 1H), 8.30 - 8.52 (m, 1H), 8.08 - 8.21 (m, 2H), 7.97 - 8.07 (m, 2H), 7.66 - 7.83 (m, 1H), 7.52 - 7.64 (m, 1H), 7.38 - 7.50 (m, 3H), 7.25 - 7.37 (m, 2H), 6.36 - 6.60 (m, 1H), 5.55 - 5.83 (m, 1H), 2.81 - 3.22 (m, 2H), 2.53 - 2.71 (m, 4H), 1.98 - 2.20 (m, 1H).
399	MS (ESI) calcd. for $C_{26}H_{20}N_{10}OS$, 520.15 m/z, found 521.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.40 - 9.45 (m, 1H), 8.35 - 8.42 (m, 2H), 8.00 - 8.05 (m, 1H), 7.90 - 8.00 (m, 1H), 7.81 (s, 1H), 7.40 - 7.50 (m, 2H), 7.25 - 7.35 (m, 2H), 6.56 (s, 1H), 6.43 - 6.50 (m, 1H), 5.53 - 5.65 (m, 1H), 3.00 - 3.10 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.60 (m, 1H), 2.00 - 2.15 (m,1H).
400	MS (ESI) calcd. for $C_{31}H_{25}N_7O$, 511.21 m/z, found 512.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.01 - 9.07 (m, 1H), 8.91 - 8.97 (m, 1H), 8.34 - 8.41 (m, 2H), 8.16 - 8.18 (m, 1H), 7.91 - 7.96 (m, 1H), 7.81 - 7.85 (m, 1H), 7.56 - 7.64 (m, 2H), 7.36 - 7.52 (m, 6H), 7.28 - 7.31 (m, 1H), 6.56 - 6.58 (m, 1H), 5.65 - 5.71 (m, 1H), 3.05 - 3.14 (m, 1H), 2.83 - 2.98 (m, 1H), 2.61 - 2.63 (m, 1H), 2.56 (s, 3H), 2.06 - 2.21 (m, 1H).
401	MS (ESI) calcd. for $C_{31}H_{24}FN_7O$, 529.20 m/z, found, 530.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.85 - 9.12 (m, 1H), 8.30 - 8.50 (m, 2H), 8.08 - 8.21 (m, 1H), 7.90 - 8.07 (m, 1H), 7.80 - 7.89 (m, 1H), 7.70 - 7.79 (m, 1H), 7.51 - 7.68 (m, 1H), 7.12 - 7.45 (m, 6H), 6.45 - 6.61 (m, 1H), 5.50 - 5.72 (m, 1H), 2.72 - 3.20 (m, 2H), 2.52 - 2.61 (m, 4H), 1.90 - 2.20 (m, 1H). ^{19}F-NMR (282 MHz, DMSO- d_6) δ (ppm); -112.56.

Cpd ID	Characterization Data
402	MS (ESI) calcd. for $C_{31}H_{24}FN_7O_2$, 545.20 m/z, found 546.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.39 - 8.41 (m, 2H), 8.29 - 8.30 (m, 1H), 7.98 - 8.01 (m, 1H), 7.82 - 7.83 (m, 1H), 7.73 - 7.75 (m, 1H), 7.62 - 7.71 (m, 1H), 7.22 - 7.60 (m, 7H), 6.57 - 6.58 (m, 1H), 5.55 - 5.61 (m, 1H), 3.89 (s, 3H), 2.87 - 3.02 (m, 2H), 2.52 - 2.53 (m, 1H), 2.03 - 2.10 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -112.60.
403	MS (ESI) calcd for $C_{31}H_{24}F_2N_8OS$: 594.18 m/z, found, 595.35 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 9.03 - 9.10 (m, 1H), 8.95 - 9.00 (m, 1H), 8.31 - 8.38 (m, 1H), 8.10 - 8.25 (m, 3H), 7.99 - 8.06 (m, 1H), 7.41 - 7.44 (m, 1H), 7.35 - 7.40 (m, 2H), 7.27 - 7.35 (m, 2H), 6.97 - 7.20 (m, 1H), 6.89 (s, 2H), 6.43 - 6.51 (m, 1H), 5.61 - 5.72 (m, 1H), 2.98 - 3.04 (m, 1H), 2.87 - 2.98 (m, 1H), 2.51 - 2.63 (m, 4H), 2.05 - 2.15 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -113.20.
413	MS (ESI) calcd. for $C_{26}H_{20}N_{10}OS$, 520.15 m/z, found, 521.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.70 - 8.73 (m, 1H), 8.45 - 8.49 (m, 1H), 8.11 - 8.17 (m, 2H), 8.00 - 8.10 (m, 3H), 7.41 - 7.47 (m, 2H), 7.30 - 7.38 (m, 2H), 6.49 - 6.52 (m, 1H), 5.57 - 5.64 (m, 1H), 2.87 - 3.10 (m, 2H), 2.60 - 2.62 (m, 1H), 2.00 - 2.16 (m, 1H).
414	MS (ESI) calcd. for $C_{33}H_{29}N_9O_3$: 599.24 m/z, found, 600.40 $[M+H]^+$.
415	MS (ESI) calcd. for $C_{34}H_{27}F_3N_8O_2$: 636.22 m/z, found, 637.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.42 (m, 2H), 7.99 - 8.05 (m, 1H), 7.92 - 7.98 (m, 1H), 7.87 - 7.92 (m, 1H), 7.79 - 7.85 (m, 1H), 7.49 - 7.57 (m, 1H), 7.35 - 7.38 (m, 1H), 7.21 - 7.34 (m, 3H), 6.55 - 6.60 (m, 1H), 6.47 - 6.54 (m, 1H), 5.54 - 5.65 (m, 1H), 2.97 - 3.09 (m, 1H), 2.83 - 2.97 (m, 1H), 2.45 - 2.52 (m, 1H), 2.00 - 2.13 (m, 2H), 0.86 - 0.96 (m, 2H), 0.56 - 0.66 (m, 2H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -60.62.
416	MS (ESI) calcd. for $C_{32}H_{25}F_3N_8O_2$: 610.21 m/z, found, 612.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.45 (m, 2H), 7.92 - 8.11 (m, 4H), 7.91 - 7.87 (m, 2H), 7.41 - 7.49 (m, 1H), 7.31 - 7.39 (m, 2H), 6.82 - 6.89 (m, 1H), 6.55 - 6.63 (m, 1H), 5.57 - 5.63 (m, 1H), 3.02 - 3.13 (m, 1H), 2.83 - 3.01 (m, 1H), 2.58 - 2.59 (m, 1H), 2.29 (s, 3H), 2.02 - 2.19 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -60.95, -73.96. (TFA salt)
421	MS (ESI) calcd. for $C_{31}H_{22}F_5N_9O$, 631.18 m/z, found, 632.35 $[M+H]^+$. ^1HNMR (300 MHz, DMSO-d_6) δ (ppm); 9.27 - 9.39 (m, 1H), 8.53 - 8.55 (m, 1H), 8.28 - 8.36 (m, 2H), 8.05 - 8.11 (m, 3H), 7.80 - 7.95 (m, 2H), 7.45 - 7.52 (m, 2H), 7.35 - 7.37 (m, 1H), 6.92 - 6.93 (m, 1H), 6.76 - 6.85 (m, 1H), 5.64 - 5.80 (m, 1H), 2.85 - 3.12 (m, 2H), 2.55 - 2.63 (m, 1H), 2.03 - 2.20 (m, 1H). ^{19}FNMR (282 MHz, DMSO- d_6) δ (ppm); - 66.59, -73.88, -94.27. (TFA salt)
422	MS (ESI) calcd. for $C_{33}H_{35}N_9O$, 573.30. Found, 574.30 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6) δ (ppm);8.35-8.50 (s, 2H), 8.00 - 8.10 (m, 1H), 7.89 - 8.00 (m, 1H), 7.7 - 7.89 (m, 1H), 7.40 - 7.55 (m, 1H), 7.30 - 7.40 (m, 1H),7.10 - 7.30 (m, 2H), 6.82 - 7.10 (m, 2H), 6.55 - 6.75 (m, 1H), 6.40 - 6.52 (m, 1H), 4.15 - 4.30 (m, 1H), 4.30 - 4.45 (m, 1H), 3.65 - 3.75 (m, 1H), 3.10 - 3.20 (m, 1H), 2.90 - 3.10 (m, 3H), 2.70 - 2.80 (m, 2H), 2.40 - 2.50 (m, 1H), 2.10 - 2.20 (m, 4H), 1.70 - 1.95 (m, 5H), 1.10 - 1.30 (m, 2H). (formic acid salt)
423	MS (ESI) calcd. for $C_{32}H_{33}N_9O_2$ 575.28. Found, 576.40 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d6) δ (ppm); 8.20 - 8.50 (m, 2H), 8.00 - 8.10 (m, 1H), 7.89 - 8.00 (m, 1H), 7.80 - 7.89 (m, 1H), 7.60 - 7.80 (m, 1H), 7.35 - 7.60 (m, 2H), 7.20 - 7.35 (m, 1H), 6.80 - 7.00 (m, 2H), 6.55 - 6.75 (m, 1H), 6.30 - 6.52 (m, 1H), 5.35 - 5.55 (m, 1H), 4.70 - 5.10 (m, 1H), 4.50 - 4.70 (m, 1H), 4.25 - 4.45 (m, 2H), 3.60 - 3.80 (m, 1H), 3.10 - 3.20 (m, 2H), 2.70 - 3.00 (m, 4H), 2.50 - 2.60 (m, 1H), 2.00 - 2.25 (m, 3H), 1.40 - 1.60 (m, 2H),1.15 - 1.25 (m, 1H).

Cpd ID	Characterization Data
424	MS (ESI) calcd. for $C_{32}H_{33}N_9O_2$, 575.28 m/z, found 576.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.43 (m, 2H), 8.27 - 8.31 (m, 1H), 8.00 - 8.08 (m, 1H), 7.94 - 7.99 (m, 1H), 7.81 - 7.90 (m, 1H), 7.54 - 7.69 (m, 1H), 7.41 - 7.49 (m, 1H), 7.21 - 7.34 (m, 2H), 6.60 - 6.67 (m, 1H), 6.51 - 6.58 (m, 1H), 5.46 - 5.53 (m, 1H), 4.69 - 4.78 (m, 1H), 4.52 - 4.61 (m, 1H), 4.29 - 4.47 (m, 2H), 3.63 - 3.77 (m, 1H), 3.21 - 3.42 (m, 1H), 2.93 - 3.14 (m, 2H), 2.83 - 2.92 (m, 1H), 2.67 - 2.82 (m, 3H), 2.41 - 2.49 (m, 1H), 1.83 - 2.18 (m, 3H), 1.37 - 1.52 (m, 3H). (formic acid salt)
425	MS (ESI) calcd. for $C_{32}H_{33}N_9O_2$ 575.28, found, 576.30$[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6) δ (ppm);8.20 - 8.50 (m, 2H), 8.00 - 8.10 (m, 1H), 7.89 - 8.00 (m, 1H), 7.80 - 7.89 (m, 1H), 7.60 - 7.80 (m, 1H), 7.35 - 7.60 (m, 2H), 7.20 - 7.35 (m, 1H), 6.80 - 7.00 (m, 2H), 6.55 - 6.75 (m, 1H), 6.30 - 6.52 (m, 1H), 5.35 - 5.55 (m, 1H), 4.70 - 5.10 (m, 1H), 4.50 - 4.70 (m, 1H), 4.25 - 4.45 (m, 2H), 3.60 - 3.80 (m, 1H), 3.10 - 3.20 (m, 2H), 2.70 - 3.00 (m, 4H), 2.50 - 2.60 (m, 1H), 2.00 - 2.25 (m, 3H), 1.40 - 1.60 (m, 2H), 1.15 - 1.25 (m, 1H). (formic acid salt)
426	MS (ESI) calcd. for $C_{28}H_{23}N_{11}O_2$, 545.20 m/z, found, 546.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.25 - 9.26 (m, 1H), 8.41 - 8.44 (m, 1H), 8.12 - 8.15 (m, 2H), 8.00 - 8.06 (m, 2H), 7.59 - 7.60 (m, 1H), 7.41 - 7.46 (m, 2H), 7.30 - 7.35 (m, 2H), 6.45 - 6.49 (m, 1H), 5.60 - 5.65 (m, 1H), 4.05 - 4.12 (m, 3H), 2.95 - 3.12 (m, 2H), 2.55 - 2.62 (m, 1H), 2.03 - 2.20 (m, 1H).
427	MS (ESI) calcd. for $C_{27}H_{20}F_2N_{10}OS$, 570.15 m/z, found 571.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.61 (s, 1H), 8.42 - 8.45 (m, 1H), 8.13 - 8.14 (m, 2H), 8.01 - 8.06 (m, 2H), 7.18 - 7.53 (m, 5H), 6.44 - 6.48 (m, 1H), 5.58 - 5.63 (m, 1H), 2.89 - 3.08 (m, 2H), 2.74 - 2.78 (m, 1H), 2.03 - 2.10 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -110.22.
428	MS (ESI) calcd. for $C_{28}H_{23}FN_{10}O$, 534.20 m/z, found, 535.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.50 - 8.68 (m, 1H), 8.27 - 8.46 (m, 2H), 7.89 - 8.15 (m, 2H), 7.72 - 7.85 (m, 1H), 7.20 - 7.52 (m, 4H), 6.49 - 6.68 (m, 2H), 6.32 - 6.48 (m, 1H), 5.41 - 5.68 (m, 1H), 3.65 - 3.88 (m, 3H), 2.98 - 3.21 (m, 1H), 2.73 - 2.97 (m, 1H), 2.41 - 2.47 (m, 1H), 1.98 - 2.26 (m, 1H). ^{19}F-NMR (282 MHz, DMSO-d_6) δ (ppm); -132.754.
429	MS (ESI) calcd. for $C_{29}H_{23}N_9O_2S$, 549.17 m/z, found 550.20 $[M+H]^+$.^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.40 (m, 2H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H), 7.75 - 7.85 (m, 1H), 7.35 - 7.45 (m, 3H), 7.25 - 7.35 (m, 2H), 6.55 - 6.60 (m, 1H), 6.45 - 6.55 (m, 1H), 5.50 - 5.60 (m, 1H), 3.95 - 4.00 (m, 3H), 2.85 - 3.15 (m, 2H), 2.60 - 2.65 (m, 1H), 1.95 - 2.10 (m, 1H).
433	MS (ESI) calcd. for $C_{32}H_{31}F_2N_9O$, 595.26 m/z, found, 596.15 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d6) δ (ppm); 8.35 - 8.40 (m, 2H), 8.23 - 8.25 (m, 1H), 8.05 - 8.10 (m, 1H), 7.97 - 8.00 (m, 1H), 7.83 - 7.90 (m, 1H), 7.51 - 7.55 (m, 1H), 7.37 - 7.40 (m, 1H), 7.28 - 7.30 (m, 2H), 6.93 (s, 2H), 6.53 - 6.55 (m, 1H), 6.42 - 6.50 (m, 1H), 4.41 - 4.45 (m, 1H), 4.13 - 4.28 (m, 1H), 3.83 - 3.99 (m, 1H), 3.13 - 3.31 (m, 2H), 2.89 - 3.02 (m, 4H), 2.45 - 2.50 (m, 1H), 1.78 - 2.01 (m, 5H), 1.34 - 1.57 (m, 1H), 1.18 - 1.31 (m, 2H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -125.60, -138.21. (formic acid salt)
436	MS (ESI) calcd for $C_{25}H_{19}N_{11}OS$ 521.15 m/z, found, 522.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.59 - 9.68 (m, 1H), 9.43 (s, 1H), 8.39 - 8.48 (m, 1H), 8.11 - 8.17 (m, 2H), 7.97 - 8.08 (m, 2H), 7.41 - 7.52 (m, 2H), 7.26 - 7.40 (m, 2H), 6.89 (s, 2H), 6.40 - 6.50 (m, 1H), 5.54 - 5.68 (m, 1H), 2.84 - 3.20 (m, 2H), 2.55 - 2.64 (m, 1H), 1.99 - 2.15 (m, 1H).
438	MS (ESI) calcd. for $C_{27}H_{22}N_{10}OS$, 534.17 m/z, found, 535.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.39 (m, 1H), 7.95 - 8.13 (m, 2H), 7.81 - 7.83 (m, 1H), 7.41 - 7.48

Cpd ID	Characterization Data
	(m, 2H), 7.30 - 7.35 (m, 2H), 6.50 - 6.59 (m, 2H), 5.54 - 5.58 (m, 1H), 3.02 - 3.10 (m, 1H), 2.90 - 2.99 (m, 1H), 2.81 (s, 3H), 2.55 - 2.60 (m, 1H), 1.99 - 2.15 (m, 1H).
443	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.35 - 8.37 (m, 2H), 8.01 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.22 - 7.28 (m, 2H), 6.95 (s, 2H), 6.55 (s, 1H), 6.41 - 6.44 (m, 1H), 4.85 - 5.01 (m, 1H), 4.48 - 4.64 (m, 1H), 4.25 - 4.42 (m, 2H), 3.43 - 3.51 (m, 1H), 3.16 - 3.22 (m, 1H), 2.94 - 3.05 (m, 2H), 2.79 - 2.81 (m, 1H), 2.42 - 2.43 (m, 1H), 2.14 - 2.16 (m, 1H), 1.97 - 2.00 (m, 1H), 1.43 - 1.83 (m, 3H), 0.70 - 0.72 (m, 4H).
444	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.35 - 8.37 (m, 2H), 8.00 - 8.01 (m, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.23 - 7.29 (m, 2H), 6.96 (s, 2H), 6.54 - 6.55 (m, 1H), 6.41 - 6.44 (m, 1H), 4.30 - 4.41 (m, 2H), 3.93 - 4.12 (m, 2H), 3.63 - 3.79 (m, 1H), 3.48 - 3.49 (m, 2H), 3.11 - 3.12 (m, 1H), 2.94 - 2.99 (m, 1H), 2.75 - 2.83 (m, 1H), 2.33 2.35 (m, 1H), 1.95 - 2.05 (m, 2H), 1.75 - 1.80 (m, 1H), 1.51 - 1.45 (m, 1H), 0.70 - 0.72 (m, 4H).
445	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.35 - 8.37 (m, 2H), 8.00 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.22 - 7.27 (m, 2H), 6.95 (s, 2H), 6.55 (s, 1H), 6.41 - 6.44 (m, 1H), 4.76 - 4.95 (m, 1H), 4.49 - 4.59 (m, 1H), 4.25 - 4.40 (m, 2H), 3.44 - 3.51 (m, 1H), 3.17 - 3.24 (m, 1H), 2.95 - 3.05 (m, 2H), 2.75 - 2.83 (m, 1H), 2.42 - 2.43 (m, 1H), 1.79 - 2.02 (m, 4H), 1.43 - 1.64 (m, 1H), 0.70 - 0.71 (m, 4H).
446	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.35 - 8.37 (m, 2H), 8.00 - 8.02 (m, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 1H), 7.22 - 7.29 (m, 2H), 6.96 (s, 2H), 6.54 - 6.55 (m, 1H), 6.41 - 6.44 (m, 1H), 4.36 - 4.59 (m, 2H), 3.82 - 4.18 (m, 2H), 3.51 3.60 (m, 2H), 3.11 - 3.15 (m, 1H), 2.90 - 2.96 (m, 1H), 2.80 - 2.85 (m, 1H), 2.43 - 2.45 (m, 1H), 1.78 - 2.02 (m, 3H), 1.43 - 1.45 (m, 1H), 1.23 - 1.26 (m, 1H), 0.69 - 0.71 (m, 4H).
451	MS (ESI) calcd. for $C_{28}H_{23}N_9OS$ 533.17 m/z, found, 534.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.41 - 8.50 (m, 1H), 8.31 - 8.41 (m, 2H), 7.98 - 8.06 (m, 1H), 7.92 - 7.98 (m, 1H), 7.77 - 7.86 (m, 1H), 7.36 - 7.46 (m, 2H), 7.25 - 7.35 (m, 2H), 6.55 - 6.65 (m, 1H), 6.43 - 6.55 (m, 1H), 5.51 - 5.60 (m, 1H), 2.99 - 3.11 (m, 1H), 2.86 - 2.98 (m, 1H), 2.43 - 2.51 (m, 1H), 2.42 (s, 3H), 2.02 - 2.15 (m, 1H).
452	MS (ESI) calcd. for $C_{28}H_{21}F_2N_9OS$, 569.16 m/z, found 570.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.45 (m, 3H), 8.27 (s, 1H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H), 7.81 (s, 1H), 7.40 - 7.50 (m, 2H), 7.00 - 7.36 (m, 3H), 6.55 - 6.62 (m, 1H), 6.45 - 6.55 (m, 1H), 5.55 - 5.65 (m, 1H), 3.00 - 3.15 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.60 (m, 1H), 2.00 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -113.98.
466	MS (ESI) calcd. for $C_{29}H_{23}FN_{10}O$: 546.20 *m/z*. found: 547.15 [M+H]+. ^1H NMR (400 MHz, DMSO-*d6*) δ(ppm): 9.00 (d, *J* = 8.4 Hz, 1H), 8.94 (d, *J* = 2.4 Hz, 1H), 8.58 (d, *J* = 10.4 Hz, 1H), 8.18 - 8.20 (m, 2H), 8.10 - 8.15 (m, 1H), 7.92 - 8.09 (m, 1H), 7.40 - 7.53 (m, 1H), 7.18 - 7.39 (m, 4H), 6.91 (s, 2H), 6.36 - 6.59 (m, 1H), 5.50 - 5.72 (m, 1H), 2.93 - 3.12 (m, 1H), 2.73 - 2.91 (m, 1H), 2.50 - 2.55 (m, 4H), 1.89 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-*d6*) δ (ppm): -134.685.
475	MS (ESI) calcd. for $C_{30}H_{29}F_2N_9O$, 569.25 m/z, found, 570.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ(ppm); 8.32 (d, *J* = 3.3 Hz, 2H), 7.92 - 7.95 (m, 1H), 7.91 (d, *J* = 4.8 Hz, 1H), 7.76 (d, *J* = 1.2 Hz,1H), 7.46 - 7.49 (m, 1H), 7.25 - 7.28 (m, 1H), 7.15 - 7.19 (m, 2H), 6.61 - 6.65 (m, 2H), 6.37 - 6.41 (m, 1 H), 4.26 - 4.30 (m, 1H), 4.06 - 4.16 (m,1H), 3.85 - 3.87

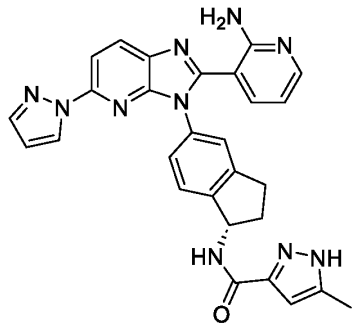
Cpd ID	Characterization Data
	(m,1H), 3.12 - 3.21 (m,1H), 2.81 - 2.95 (m, 3H), 2.61 - 2.67 (m, 1H), 2.32 - 2.37 (m, 1H), 1.77 - 1.92 (m, 3H), 1.11 - 1.26 (m, 2H). ^{19}F NMR (282 MHz, DMSO-d_6) δ(ppm); -124.399, -124.409.
476	MS (ESI) calcd. for $C_{32}H_{31}F_2N_9O$, 595.26. Found, 596.36 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm); 8.40 - 8.50 (m, 2H), 8.02 - 8.05 (m, 1H), 7.90 - 8.00 (m, 1H), 7.80 - 7.90 (m, 1H), 7.50 - 7.60 (m, 1H),7.40 - 7.50 (m, 1H), 7.20 - 7.40 (m, 2H), 6.91 (s, 2H), 6.55 - 6.60 (m, 1H), 6.41 - 6.45 (m, 1H), 4.45 - 4.75 (m, 1H), 4.15 - 4.45 (m, 1H), 3.90 - 4.15 (m, 1H), 3.15 - 3.30 (m, 3H), 3.00 - 3.10 (m, 1H), 2.75 - 2.95 (m, 2H), 2.45 - 2.50 (m, 2H),1.75 - 2.15 (m, 5H),1.20 - 1.60 (m, 2H). (formic acid salt)
477	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.20 $[M+H]^+$. 1H-NMR (400 MHz, DMSO-d6) δ (ppm); 8.37 (m, 2H), 8.15 (m, 1H), 7.97 (m, 2H), 7.79 (m, 1H), 7.50-7.60 (m, 1H), 7.37 (m, 1H), 7.20-7.35 (m, 2H), 6.93 (s, 2H), 6.49 (m, 1H), 6.37 (m, 1H), 4.90-5.10 (m, 1H), 4.50-4.63 (m, 1H), 4.25-4.40 (m, 2H), 3.10-3.30 (m, 2H), 3.02-3.09 (m, 1H), 2.75-2.89 (m, 2H), 2.50-2.60 (m, 1H), 1.85-2.35 (m, 4H), 1.23-1.60 (m, 3H), 0.90-1.10 (m, 1H). (formic acid)
478	MS(ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found 578.15 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm); 8.32 - 8.43 (m, 2H), 8.11 - 8.19 (m, 1H), 7.99 - 8.08 (m, 1H), 7.91 - 7.98 (m, 1H), 7.79 - 7.84 (m, 1H), 7.50 - 7.59 (m, 1H), 7.37 - 7.42 (m, 1H), 7.22 - 7.35 (m, 2H), 6.90 - 7.05 (m, 2H), 6.51 - 6.62 (m, 1H), 6.39 - 6.48 (m, 1H), 4.78 - 5.12 (m, 1H), 4.45 - 4.59 (m, 1H), 4.16 - 4.39 (m, 2H), 2.95 - 3.14 (m, 2H), 2.75 - 2.93 (m, 2H), 2.37 - 2.42 (m, 1H), 2.10 - 2.27 (m, 1H), 1.99 - 2.08 (m, 2H), 1.89 - 1.98 (m, 2H), 1.46 - 1.61 (m, 1H), 1.11 - 1.38 (m, 2H), 0.92 - 1.09 (m, 1H); ^{19}F NMR (282 MHz, DMSO-d_6) δ(ppm); -218.510. (formic acid salt)
479	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27 m/z, found, 578.25 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm);8.37 (m, 2H), 8.15 (m, 2H), 7.81 (m, 1H), 7.60 (m, 1H), 7.42 (m, 1H), 7.33 (m, 1H), 7.25 (m, 1H), 6.90 (s, 2H), 6.55 (m, 1H), 6.43 (m, 1H), 4.89 (m, 1H), 4.50-4.70 (m, 1H), 4.20-4.30 (m, 2H), 3.10-3.30 (m, 2H), 3.02-3.09 (m, 1H), 2.70-2.90 (m, 2H), 2.63 (m, 1H), 2.41-2.45 (m, 1H), 1.87-2.15 (m, 3H), 1.23-1.45 (m, 3H), 1.10-1.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d6) δ (ppm); -69.182, -71.072. (formic acid salt)
484	MS (ESI) calcd. for $C_{31}H_{31}N_9O_2$: 561.26 *m/z*. found,562.20 $[M+H]+$. ^{1}H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.25 - 8.41 (m, 1H), 8.18 (d, J = 2.4 Hz, 1H), 7.90 - 8.08 (m, 1H), 7.68 - 7.87 (m, 1H), 7.40 - 7.60 (m, 1H), 7.33 (s, 1H), 7.10 - 7.26 (m, 2H), 6.91 (s, 1H), 6.31 - 6.58 (m, 1H), 6.05 (d, J = 2.4 Hz, 1H), 4.30 - 4.51 (m, 1H), 4.10 - 4.29 (m, 1H), 3.87 - 4.09 (m, 5H), 3.69 - 3.84 (m, 1H), 3.52 - 3.60 (m, 1H), 2.90 - 3.13 (m, 1H), 2.72 - 2.89 (m, 1H), 2.29 - 2.38 (m, 1H), 1.66 - 1.93 (m, 1H), 1.40 - 1.65 (m, 1H), 0.61 - 0.78 (m, 4H).
489	MS (ESI) clad. for $C_{33}H_{32}N_{10}O_2$ 600.27 m/z, found, 601.30 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm); 8.69 - 8.71 (m, 1H), 8.34 - 8.37 (m, 2H), 8.00 - 8.01 (m, 1H), 7.96 - 7.98(m, 1H), 7.81 - 7.83 (m, 1H), 7.47 - 7.49 (m, 1H), 7.34 – 7.37 (m, 1H), 7.24 - 7.27 (m, 2H), 6.95 (s, 2H), 6.44 - 6.46 (m, 1H), 6.40 - 6.41 (m, 1H), 4.34 - 4.37 (m, 1H), 4.27 - 4.32 (m, 1H), 3.34 - 3.69 (m, 1H), 3.17 - 3.22 (m, 2H), 2.96 - 3.06 (m, 2H), 2.78 - 2.84 (m, 1H), 2.50 - 2.73 (s, 4H), 2.23 - 2.26(m, 1H), 1.75 - 1.96 (m, 3H), 1.23 - 1.32 (m, 2H).
490	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$, 544.21 m/z, found, 545.30 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.90 - 9.15 (m, 1H), 8.42 - 8.62 (m, 1H), 8.31 - 8.41 (m, 1H), 8.15 - 8.25 (m, 2H), 8.02 - 8.14 (m, 2H), 7.77 - 7.92 (m, 1H), 7.55 - 7.73 (m, 1H), 7.27 - 7.52 (m, 3H), 6.72 - 6.92 (m, 1H), 5.52 - 5.80 (m, 1H), 4.67 (s, 2H), 2.80 - 3.21 (m, 2H), 2.55 - 2.62 (m, 1H), 1.93 - 2.23 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -74.08. (TFA salt)

Cpd ID	Characterization Data
491	MS (ESI) calcd. for $C_{31}H_{26}N_{10}O$, 554.23 m/z, found 555.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.90 - 8.94 (m, 1H), 8.41 - 8.44 (m, 1H), 8.12 - 8.14 (m, 3H), 8.00 - 8.06 (m, 2H), 7.38 - 7.40 (m, 3H), 7.29 - 7.32 (m, 2H), 6.45 - 6.49 (m, 1H), 5.61 - 5.66 (m, 1H), 2.88 - 3.07 (m, 2H), 2.75 - 2.76 (m, 1H), 2.04 - 2.19 (m, 2H), 1.04 - 1.23 (m, 4H).
492	MS (ESI) calcd. for $C_{27}H_{22}N_{10}OS$ 534.17 m/z, found, 535.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.05 - 9.18 (m, 1H), 8.39 - 8.49 (m, 1H), 8.29 (s, 1H), 8.14 (s, 2H), 7.97 - 8.09 (m, 2H), 7.26 - 7.46 (m, 4H), 6.43 - 6.51 (m, 1H), 5.53 - 5.64 (m, 1H), 2.97 - 3.09 (m, 1H), 2.82 - 2.96 (m, 1H), 2.69 (s, 3H), 2.53 - 2.61 (m, 1H), 1.98 - 2.12 (m, 1H).
520	Observed mass (ESI): 561.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.43 - 8.46 (m, 1H), 8.24 (s, 1H), 8.13 (s, 2H), 7.97 - 8.09 (m, 2H), 7.26 - 7.44 (m, 4H), 6.35 - 6.67 (m, 1H), 5.47 - 5.69 (m, 1H), 2.82 - 3.19 (m, 2H), 2.39 - 2.41 (m, 2H), 1.91 - 2.03 (m, 1H), 1.12 - 1.24 (m, 2H), 0.88 - 1.31 (m, 2H).
522	Observed mass (ESI): 579.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.29 - 8.41 (m, 2H), 7.98 - 8.02 (m, 1H), 7.93 - 7.97 (m, 1H), 7.80 - 7.83 (m, 1H), 7.51 - 7.55 (m, 1H), 7.38 - 7.40 (m, 1H), 7.29 - 7.33 (m, 1H), 7.19 - 7.25 (m, 1H), 6.88 - 6.95 (m, 2H), 6.52 - 6.54 (m, 1H), 6.38 - 6.42 (m, 1H), 5.34 - 5.52 (m, 1H), 4.50 - 4.58 (m, 1H), 3.67 - 3.95 (m, 3H), 3.10 - 3.25 (m, 2H), 2.97 - 3.02 (m, 1H), 2.62 - 2.85 (m, 4H), 1.91 - 2.01 (m, 1H), 1.68 - 1.73 (m, 1H), 0.65 - 0.76 (m, 4H). 19F-NMR (300 MHz, DMSO-d6) δ (ppm): -195.05. (formic acid salt)
526	Observed mass (ESI): 589.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.74 - 8.76 (m, 1H), 8.43 - 8.46 (m, 1H), 8.12 - 8.15 (m, 2H), 8.02 - 8.09 (m, 2H), 7.42 - 7.47 (m, 2H), 7.31 - 7.38 (m, 2H), 6.46 - 6.53 (m, 1H), 5.56 - 5.63 (m, 1H), 3.01 - 3.19 (m, 1H), 2.86 - 2.99 (m, 1H), 2.56 - 2.65 (m, 1H), 2.02 - 2.13 (m, 1H).
527	Observed mass (ESI): 411.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.25 - 8.46 (m, 2H), 7.91 - 8.04 (m, 1H), 7.76 - 7.89 (m, 1H), 7.62 - 7.75 (m, 1H), 7.52 - 7.62 (m, 1H), 7.18 - 7.48 (m, 5H), 6.44 - 6.63 (m, 1H), 4.18 - 4.32 (m, 1H), 2.82 - 2.93 (m, 1H), 2.69 - 2.81 (m, 1H), 2.33 - 2.42 (m, 1H), 1.58 - 1.73 (m, 1H).
534	Observed mass (ESI): 636.05 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.63 (s, 1H), 8.26 - 8.34 (m, 2H), 7.98 - 8.06 (m, 1H), 7.64 - 7.89 (m, 1H), 7.11 - 7.60 (m, 6H), 6.41 - 6.51 (m, 1H), 6.32 - 6.39 (m, 1H), 5.54 - 5.65 (m, 1H), 2.73 - 3.23 (m, 2H), 2.50 - 2.64 (m, 1H), 2.01 - 2.14 (m, 1H).
535	Observed mass (ESI): 594.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ 8.94 (d, J = 2.4 Hz, 1H), 8.41 – 8.30 (m, 2H), 8.17 (dd, J = 8.1, 2.4 Hz, 1H), 8.02 (dd, J = 4.9, 1.8 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.61 – 7.23 (m, 6H), 6.48 (dd, J = 7.6, 4.8 Hz, 1H), 6.35 (d, J = 2.7 Hz, 1H), 5.63-5.60 (m, 1H), 3.09 – 3.00 (m, 1H), 2.93 (q, J = 8.2 Hz, 1H), 2.55 (s, 3H), 2.18 – 2.01 (m, 2H).
536	Observed mass (ESI): 545.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.43 - 8.45 (m, 1H), 8.11 - 8.14 (m, 2H), 8.01 - 8.09 (m, 2H), 7.65 - 7.69 (m, 1H), 7.29 - 7.41 (m, 4H), 6.45 - 6.49 (m, 1H), 5.52 - 5.57 (m, 1H), 3.01 - 3.07 (m, 1H), 2.82 - 2.98 (m, 1H), 2.49 - 2.52(m, 1H), 2.14 - 2.21 (m, 1H), 2.01 - 2.13 (m, 1H), 1.04 - 1.17 (m, 4H).
537	Observed mass (ESI): 620.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.95 - 9.05 (m, 1H), 8.84 - 8.94 (m, 1H), 8.35 - 8.43 (m, 1H), 8.29 - 8.34 (m, 1H), 8.09 - 8.18 (m, 1H), 7.97 - 8.05 (m, 1H), 7.76 - 7.86 (m, 1H), 7.43 - 7.66 (m, 1H), 7.34 - 7.42 (m, 3H), 7.21 - 7.33 (m, 2H), 6.41 - 6.51 (m, 1H), 6.29 - 6.39 (m, 1H), 5.57 - 5.71 (m, 1H), 2.98 - 3.09 (m, 1H),

Cpd ID	Characterization Data
	2.84 - 2.97 (m, 1H), 2.53 - 2.62 (m, 1H), 2.13 - 2.23 (m, 1H), 2.04 - 2.12 (m, 1H), 0.92 - 1.11(m, 4H).
538	Observed mass (ESI): 555.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.43 - 8.63 (m, 1H), 8.13 (s, 2H), 7.95 - 8.09 (m, 3H), 7.40 - 7.50 (m, 2H), 6.80 - 7.39 (3), 6.29 - 6.58 (m, 1H), 5.45 - 5.81 (m, 1H), 2.81 - 3.15 (m, 2H), 2.62 - 2.67 (m, 1H), 2.01 - 2.22 (m, 1H). 19F NMR (282 MHz, DMSO-d6) δ (ppm): -119.34.
539	Observed mass (ESI): 569.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.41 - 8.46 (m, 1H), 7.99 - 8.17 (m, 4H), 7.61 - 7.71 (m, 1H), 7.36 - 7.51 (m, 2H), 7.25 - 7.35 (m, 2H), 7.09 - 7.17 (m, 1H), 6.42 - 6.52 (m, 1H), 5.53 - 5.62 (m, 1H), 2.96 - 3.07 (m, 1H), 2.82 - 2.95 (m, 1H), 2.55 - 2.61 (m, 1H), 2.45 - 2.51 (m, 3H), 1.93 - 2.16 (m, 2H), 0.95 - 1.05 (m, 2H), 0.87 - 0.94 (m, 2H).
540	Observed mass (ESI): 558.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.65 - 8.70 (m, 1H), 8.43 - 8.50 (m, 1H), 8.13 (s, 2H), 7.98 - 8.07 (m, 1H), 7.40 - 7.52 (m, 1H), 7.33 - 7.42 (m, 1H), 7.19 - 7.48 (m, 4H), 6.36 - 6.67 (m, 1H), 5.40 - 5.70 (m, 1H), 3.93 (s, 3H), 2.95 - 3.06 (m, 1H), 2.73 - 2.88 (m, 1H), 2.49 - 2.50 (m, 1H), 1.85 - 2.13 (m, 2H), 0.96 - 1.09 (m, 2H), 0.84 -0.91 (m, 2H).
541	Observed mass (ESI): 585.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6+D2O) δ (ppm): 8.88 - 9.19 (m, 1H), 8.29 - 8.59 (m, 1H), 8.07 - 8.16 (m, 2H), 7.96 - 8.06 (m, 2H), 7.23 - 7.48 (m, 5H), 6.33 - 6.62 (m, 1H), 5.42 - 5.73 (m, 1H), 2.97 - 3.22 (m, 1H), 2.74 - 2.96 (m, 1H), 2.61 - 2.66 (m, 3H), 2.54 - 2.60 (m, 1H), 1.95 - 2.14 (m, 1H).
558	Observed mass (ESI): 600.62 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 9.35 (d, J = 8.2 Hz, 1H), 8.61 – 8.58 (m, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.10 – 8.01 (m, 1H), 7.73 – 7.64 (m, 2H), 7.59 – 7.16 (m, 4H), 7.03 (d, J = 8.6 Hz, 1H), 6.80 – 6.70 (m, 1H), 6.01 (d, J = 2.3 Hz, 1H), 5.62 – 5.50 (m, 1H), 3.73 (s, 3H), 3.10 – 2.82 (m, 2H), 2.08 – 2.00 (m, 1H), 1.25 (d, J = 10.0 Hz, 1H). (TFA salt)
578	Observed mass (ESI): 568.25 [M+H]+. 1H-NMR (300 MHz, DMSO-d6) δ (ppm): 8.39 - 8.45 (m, 1H), 7.95 - 8.12 (m, 4H), 7.69 (s, 1H), 7.35 - 7.42 (m, 2H), 7.00 - 7.35 (m, 3H), 6.45 - 6.52 (m, 1H), 4.00 (s, 3H), 3.00 - 3.15 (m, 1H), 2.85 - 3.00 (m, 1H), 2.50 - 2.52 (m, 1H), 2.00 - 2.12 (m, 1H).
583	Observed mass (ESI): 589.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 9.30-9.27(m, 1H), 9.16 (m, 1H), 8.48-8.45(m, 1H), 8.16 (s,2H).8.03-8.00(m, 2H), 7.84-7.81(m, 1H), 7.45-7.43(m, 2H), 7.36-7.33(m, 2H),7.22-7.04 (m, 3H). 6.89-6.85(m, 1H), 6.48-6.44(m, 1H), 5.04 (s,1H).2.94-2.91(m, 2H),1.47-1.45(m, 2H).
585	Observed mass (ESI): 609.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.32 - 8.40 (m, 2H), 8.22 (s, 1H), 8.01 (dd, J = 5.0, 1.8 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.78 - 7.84 (m, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.35 (s, 1H), 7.20 - 7.29 (m, 2H), 6.94 (s, 2H), 6.52 - 6.58 (m, 1H), 6.39 - 6.47(m, 1H), 4.35 - 4.40 (m, 1H), 4.01 - 4.14 (m, 2H), 3.09 - 3.20 (m, 2H), 2.91 - 3.04 (m, 2H), 2.73 - 2.86 (m, 1H), 2.43 - 2.48 (m, 1H), 2.29 (s, 3H), 2.02 - 2.07 (m, 1H), 1.92 - 1.99 (m, 1H), 1.78 - 1.83 (m, 1H), 1.36 - 1.49 (m, 2H).
587	Observed mass (ESI): 553.22 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 9.07-9.05(m, 1H), 8.97-8.96 (m, 1H), 8.18-8.16(m, 2H), 8.03-8.01 (m,1H).7.42-7.33 (m, 4H), 7.20 (s, 1H),6.90 (s, 1H),6.66 (s, 1H),6.48-6.45 (m, 1H). 6.67-6.65 (m, 1H), 5.33-5.31(m, 2H),5.04(s, 1H),2.92 (s,1H).2.67 (s,2H),2.09-2.06 (m, 1H).1.47-1.43 (m, 2H).

Cpd ID	Characterization Data
588	Observed mass (ESI): 611.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.61 - 8.75 (m, 1H), 8.39 - 8.59 (m, 1H), 7.92 - 8.05 (m, 2H), 7.87 (s, 1H), 7.11 - 7.65 (m, 5H), 6.46 - 6.54 (m, 1H), 5.45 - 5.65 (m, 1H), 2.85 - 3.15 (m, 2H), 2.61 - 2.72 (m, 1H), 1.83 - 2.22 (m, 2H), 0.98 - 1.10 (m, 2H), 0.77 - 0.88 (m, 2H).
595	Observed mass (ESI): 637.05 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ 9.40 (d, J = 8.3 Hz, 1H), 8.65 – 8.59 (m, 1H), 8.47 – 8.40 (m, 1H), 8.10 (d, J = 2.9 Hz, 1H), 8.03 – 7.99 (m, 1H), 7.98 – 7.92 (m, 1H), 7.64 – 7.41 (m, 3H), 7.39 – 7.22 (m, 3H), 6.88 (s, 1H), 6.47 – 6.40 (m, 1H), 5.67 – 5.56 (m, 1H), 3.07 – 2.99 (m, 1H), 2.97 – 2.87 (m, 1H), 2.61 – 2.55 (m, 1H), 2.12 – 2.01 (m, 1H).

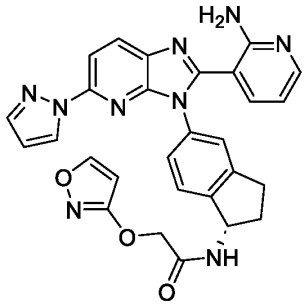
[00267] Example 4: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-5-methyl-1*H*-pyrazole-3-carboxamide (Compound 4)



Compound 4

[00268] **Compound 4** was prepared in a manner analogous to **Compound 3** using 5-methyl-3-pyrazolecarboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calculated for $C_{28}H_{24}N_{10}O$: 516.21 m/z, found 517.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) (ppm) δ 8.45 – 8.40 (m, 2H), 8.39 (d, J = 2.6 Hz, 1H), 8.08 (dd, J = 5.9, 1.7 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H), 7.73 (dd, J = 7.6, 1.7 Hz, 1H), 7.44 (s, 1H), 7.34 (s, 1H), 7.33 (s, 1H), 6.80 (dd, J = 7.6, 5.9 Hz, 1H), 6.56 (dd, J = 2.6, 1.7 Hz, 1H), 6.49 (s, 1H), 5.58 (dd, J = 8.4, 8.4 Hz, 1H), 3.03 (ddd, J = 16.3, 8.9, 2.7 Hz, 1H), 2.88 (ddd, J = 16.4, 8.5, 8.5 Hz, 1H), 2.48 – 2.41 (m, 1H), 2.26 (s, 3H), 2.14 (dddd, J = 12.3, 8.9, 8.9, 8.8 Hz, 1H). (TFA salt)

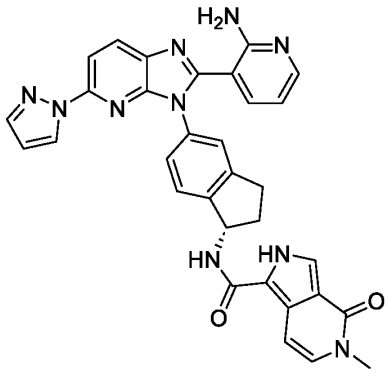
[00269] Example 5: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-2-(isoxazol-3-yloxy)acetamide (Compound 5)



Compound 5

[00270] **Compound 5** was prepared in a manner analogous to **Compound 3** using potassium (3-isoxazolyloxy)acetate in place of 3,4-difluoro-5-anisic acid and excluding the initial addition of N,N-diisopropylethylamine. MS (ESI) calculated for $C_{28}H_{23}N_9O_3$: 533.19 m/z, found 534.25 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm) 8.67 – 8.63 (m, 2H), 8.42 (d, J = 8.6 Hz, 1H), 8.36 (d, J = 2.5 Hz, 1H), 8.07 (dd, J = 6.0, 1.7 Hz, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.82 (d, J = 1.7 Hz, 1H), 7.77 (dd, J = 7.5, 1.7 Hz, 1H), 7.44 (s, 1H), 7.34 (s, 1H), 7.33 (s, 1H), 6.81 (dd, J = 7.6, 6.0 Hz, 1H), 6.56 (dd, J = 2.6, 1.7 Hz, 1H), 6.35 (d, J = 1.8 Hz, 1H), 5.42 (dd, J = 8.3, 8.3 Hz, 1H), 4.75 (s, 2H), 2.99 (ddd, J = 16.4, 8.9, 2.9 Hz, 1H), 2.87 (ddd, J = 16.4, 8.5, 8.5 Hz, 1H), 2.47 – 2.41 (m, 1H), 1.96 (dddd, J = 12.4, 8.9, 8.9, 8.8 Hz, 1H). (TFA salt)

[00271] **Example 6: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-5-methyl-4-oxo-4,5-dihydro-2*H*-pyrrolo[3,4-*c*]pyridine-1-carboxamide (Compound 6)**

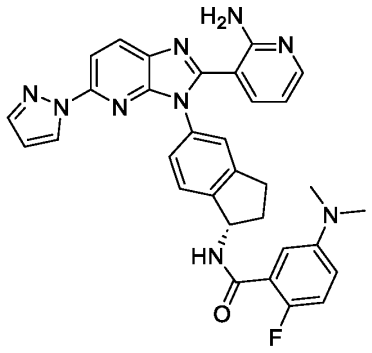


Compound 6

[00272] **Compound 6** was prepared in a manner analogous to **Compound 3** using 5-methyl-4-oxo-2,5-dihydro-2,5-diaza-1-indenecarboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calculated for $C_{32}H_{26}N_{10}O_2$: 582.22 m/z, found 583.30 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm) 12.51 (d, J = 3.4 Hz, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.39 (dd, J = 2.6, 0.7 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.08 (dd, J = 5.8, 1.7 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.83 (dd, J = 1.7, 0.7 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.49 – 7.42 (m, 2H), 7.36 (dd, J = 8.1, 2.0

Hz, 1H), 7.10 (d, J = 7.4 Hz, 1H), 6.88 (dd, J = 7.4, 0.7 Hz, 1H), 6.76 (dd, J = 7.6, 5.8 Hz, 1H), 6.57 (dd, J = 2.6, 1.7 Hz, 1H), 5.61 (q, J = 8.0 Hz, 1H), 3.39 (s, 3H), 3.06 (ddd, J = 16.7, 9.0, 3.3 Hz, 1H), 2.92 (ddd, J = 16.3, 8.4, 8.4 Hz, 1H), 2.57 (dddd, J = 12.4, 7.9, 7.9, 3.1 Hz, 1H), 2.05 (dddd, J = 12.5, 8.7, 8.7, 8.7 Hz, 1H). (TFA salt)

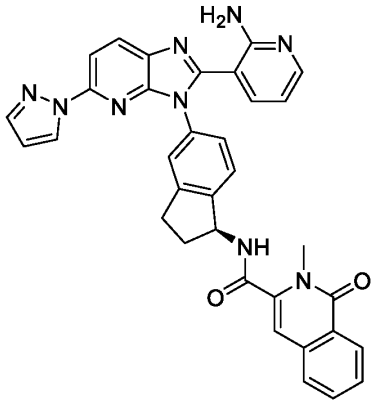
[00273] Example 7: N-{(S)-5-[2-(2-amino-3-pyridyl)-5-(1-pyrazolyl)-3H-1,3,4-triazainden-3-yl]-1-indanyl}5-(dimethylamino)-2-fluorobenzamide (Compound 7)



Compound 7

[00274] **Compound 7** was prepared in a manner analogous to **Compound 3** using 5-(dimethylamino)-2-fluorobenzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calculated for $C_{32}H_{28}FN_9O$: 573.24 m/z, found 574.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.63 (dd, J = 8.2, 1.6 Hz, 1H), 8.37 (d, J = 8.7 Hz, 1H), 8.31 (dd, J = 2.6, 0.7 Hz, 1H), 8.04 (dd, J = 6.1, 1.7 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.76 – 7.75 (m, 1H), 7.73 (d, J = 1.7 Hz, 1H), 7.41 (d, J = 1.9 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.31 (dd, J = 8.0, 1.9 Hz, 1H), 7.09 – 7.02 (m, 1H), 6.89 (dd, J = 5.7, 3.2 Hz, 1H), 6.82 (ddd, J = 9.1, 3.6, 3.6 Hz, 1H), 6.77 (dd, J = 7.5, 6.1 Hz, 1H), 6.49 (dd, J = 2.6, 1.7 Hz, 1H), 5.52 (dd, J = 8.2, 8.2 Hz, 1H), 3.02 – 2.92 (m, 1H), 2.89 – 2.79 (m, 7H), 2.50 – 2.45 (m, 1H), 2.07 – 1.91 (m, 1H). (TFA salt)

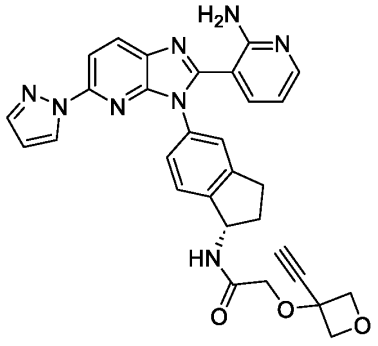
[00275] Example 8: N-{(S)-5-[2-(2-amino-3-pyridyl)-5-(1-pyrazolyl)-3H-1,3,4-triazainden-3-yl]-1-indanyl}-2-methyl-1-oxo-1,2-dihydro-3-isoquinolinecarboxamide (Compound 8)



Compound 8

[00276] **Compound 8** was prepared in a manner analogous to **Compound 3** using 2-methyl-1-oxo-1,2-dihydro-3-isoquinolinecarboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calculated for $C_{34}H_{27}N_9O_2$: 593.23 m/z, found 594.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 9.31 (d, J = 8.1 Hz, 1H), 8.37 (d, J = 8.6 Hz, 1H), 8.32 (dd, J = 2.6, 0.7 Hz, 1H), 8.18 (dd, J = 8.1, 1.1 Hz, 1H), 8.03 (dd, J = 5.9, 1.7 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.76 (dd, J = 1.7, 0.7 Hz, 1H), 7.72 – 7.65 (m, 3H), 7.51 (ddd, J = 8.2, 5.0, 3.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 2.0 Hz, 1H), 7.33 (dd, J = 8.0, 2.0 Hz, 1H), 6.83 (s, 1H), 6.72 (dd, J = 7.6, 5.9 Hz, 1H), 6.49 (dd, J = 2.6, 1.6 Hz, 1H), 5.50 (dd, J = 8.0, 8.0 Hz, 1H), 3.48 (s, 3H), 3.00 (ddd, J = 16.4, 8.9, 3.3 Hz, 1H), 2.87 (ddd, J = 16.3, 8.3, 8.3 Hz, 1H), 2.52 (dddd, J = 12.6, 7.9, 7.9, 3.3 Hz, 1H), 2.07 – 1.96 (m, 1H). (TFA salt)

[00277] **Example 9: N-{(S)-5-[2-(2-amino-3-pyridyl)-5-(1-pyrazolyl)-3H-1,3,4-triazainden-3-yl]-1-indanyl}(3-ethynyl-3-oxetanyloxy)acetamide (Compound 9)**

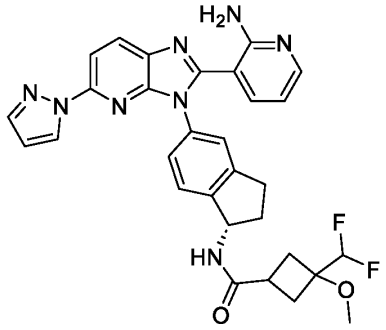


Compound 9

[00278] **Compound 9** was prepared in a manner analogous to **Compound 3** using (3-ethynyl-3-oxetanyloxy)acetic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calculated for $C_{30}H_{26}N_8O_3$: 546.21 m/z, found 547.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.42 (d, J = 8.6 Hz, 1H), 8.40 – 8.36 (m, 2H), 8.08 (dd, J = 5.8, 1.8 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H),

7.83 (dd, J = 1.6, 0.7 Hz, 1H), 7.70 (dd, J = 7.6, 1.7 Hz, 1H), 7.44 (s, 1H), 7.34 (d, J = 1.4 Hz, 2H), 6.76 (dd, J = 7.6, 5.8 Hz, 1H), 6.57 (dd, J = 2.6, 1.7 Hz, 1H), 5.45 (dd, J = 8.4, 8.4 Hz, 1H), 4.69 (dd, J = 7.4, 2.3 Hz, 2H), 4.64 (d, J = 6.8 Hz, 2H), 4.06 (d, J = 1.8 Hz, 2H), 3.99 (s, 1H), 3.01 (ddd, J = 16.3, 8.9, 2.7 Hz, 1H), 2.88 (ddd, J = 16.4, 8.5, 8.5 Hz, 1H), 2.44 (dddd, J = 12.4, 8.0, 7.9, 2.8 Hz, 1H), 2.04 (dddd, J = 12.4, 9.0, 9.0, 9.0 Hz, 1H). (TFA salt)

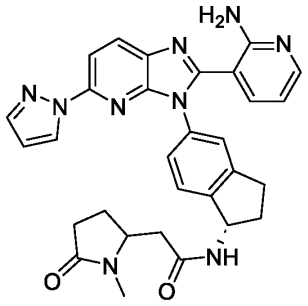
[00279] Example 10: N-{(S)-5-[2-(2-amino-3-pyridyl)-5-(1-pyrazolyl)-3H-1,3,4-triazainden-3-yl]-1-indanyl}3-(difluoromethyl)-3-methoxycyclobutanecarboxamide (Compound 10)



Compound 10

[00280] Compound 10 was prepared in a manner analogous to **Compound 3** using 3-(difluoromethyl)-3-methoxycyclobutanecarboxylic acid in place of 3,4-difluoro-5-anisic acid. Note that racemic acid was used but a single unknown diastereomer was obtained. MS (ESI) calculated for $C_{30}H_{28}F_2N_8O_2$: 570.23 m/z, found 571.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) (ppm) δ 8.42 (d, J = 8.6 Hz, 1H), 8.39 – 8.34 (m, 2H), 8.07 (dd, J = 5.8, 1.7 Hz, 1H), 8.00 (d, J = 8.6 Hz, 1H), 7.83 (dd, J = 1.6, 0.7 Hz, 1H), 7.67 (dd, J = 7.6, 1.7 Hz, 1H), 7.43 (s, 1H), 7.34 – 7.29 (m, 2H), 6.74 (dd, J = 7.6, 5.8 Hz, 1H), 6.56 (dd, J = 2.6, 1.7 Hz, 1H), 6.15 (t, J = 55.4 Hz, 1H), 5.36 (dd, J = 8.1, 8.1 Hz, 1H), 3.27 (s, 3H), 2.97 (ddd, J = 16.3, 8.9, 3.0 Hz, 1H), 2.86 (ddd, J = 16.3, 8.4, 8.4 Hz, 1H), 2.74 (ddd, J = 8.7, 8.7, 8.7 Hz, 1H), 2.47 – 2.39 (m, 3H), 2.35 – 2.25 (m, 2H), 1.87 (dddd, J = 12.4, 8.9, 8.9, 8.9 Hz, 1H). 19F NMR (376 MHz, DMSO) δ (ppm): -132.55. (TFA salt)

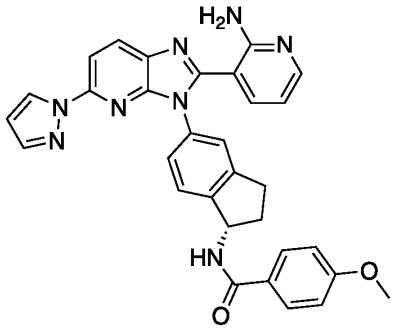
[00281] Example 11: N-{(S)-5-[2-(2-amino-3-pyridyl)-5-(1-pyrazolyl)-3H-1,3,4-triazainden-3-yl]-1-indanyl}(1-methyl-5-oxo-2-pyrrolidinyl)acetamide (Compound 11)



Compound 11

[00282] **Compound 11** was prepared in a manner analogous to **Compound 3** using (1-methyl-5-oxo-2-pyrrolidinyl)acetic acid in place of 3,4-difluoro-5-anisic acid. Note that racemic acid was used and a mixture of diastereomers was obtained. MS (ESI) calculated for $C_{30}H_{29}N_9O_2$: 547.24 m/z, found 548.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.44 (dd, J = 8.1, 3.3 Hz, 1H), 8.37 (d, J = 8.6 Hz, 1H), 8.31 (dd, J = 2.6, 0.7 Hz, 1H), 8.03 (dd, J = 6.0, 1.7 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.76 (dd, J = 1.6, 0.7 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.40 – 7.38 (m, 1H), 7.31 – 7.23 (m, 2H), 6.76 – 6.71 (m, 1H), 6.51 – 6.48 (m, 1H), 5.35 – 5.26 (m, 1H), 3.84 – 3.76 (m, 1H), 2.98 – 2.87 (m, 1H), 2.85 – 2.72 (m, 1H), 2.63 (s, 3H), 2.58 – 2.51 (m, 1H), 2.42 – 2.34 (m, 1H), 2.24 – 1.98 (m, 4H), 1.88 – 1.60 (m, 2H). (TFA salt)

[00283] **Example 12: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-methoxybenzamide (Compound 12)**

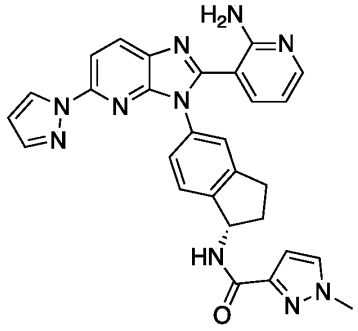


Compound 12

[00284] **Compound 12** was prepared in a manner analogous to **Compound 3** using 4-methoxybenzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{26}N_8O_2$: 542.22 m/z, found 543.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.40 - 8.50 (m, 2H), 8.02 - 8.10 (m, 2H), 7.90 - 7.95 (m, 2H), 7.83 - 7.85 (m, 1H), 7.74 - 7.78 (m, 1H), 7.45 - 7.49 (m, 1H), 7.30 - 7.40 (m, 2H), 7.01 - 7.09 (m, 2H), 6.78 - 6.90 (m, 1H), 6.60 - 6.62 (m, 1H),

5.60 - 5.69 (m, 1H), 3.80 (s, 3H), 3.05 - 3.13 (m, 1H), 2.88 - 3.00 (m, 1H), 2.50 - 2.54 (m, 1H), 2.03 - 2.18 (m, 1H). (TFA salt)

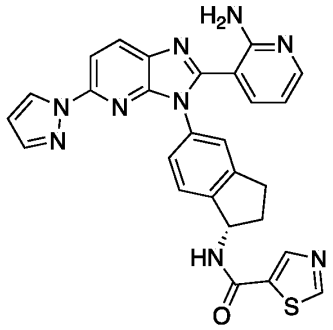
[00285] Example 13: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide (Compound 13)



Compound 13

[00286] **Compound 13** was prepared in a manner analogous to **Compound 3** using 1-methyl-1*H*-pyrazole-3-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$: 516.21 m/z, found 517.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.41 - 8.49 (m, 1H), 8.33 - 8.40 (m, 1H), 8.04 - 8.11 (m, 1H), 7.97 - 8.03 (m, 1H), 7.73 - 7.88 (m, 3H), 7.44 (s, 1H), 7.27 - 7.38 (m, 2H), 6.77 - 6.91 (m, 1H), 6.64 - 6.76 (m, 1H), 6.50 - 6.61 (m, 1H), 5.47 - 5.66 (m, 1H), 3.90 (s, 3H), 2.98 - 3.15 (m, 1H), 2.78 - 2.97 (m, 1H), 2.37 - 2.51 (m, 1H), 2.03 - 2.22 (m, 1H). (TFA salt)

[00287] Example 14: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)thiazole-5-carboxamide (Compound 14)

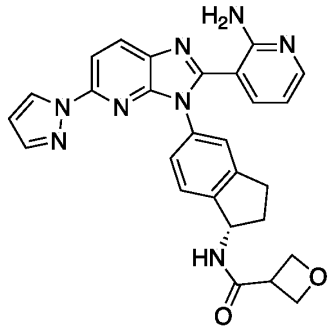


Compound 14

[00288] **Compound 14** was prepared in a manner analogous to **Compound 3** using thiazole-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{27}H_{21}N_9OS$: 519.16 m/z, found 520.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.21

- 9.27 (m, 1H), 8.55 - 8.59 (m, 1H), 8.32 - 8.39 (m, 2H), 8.01 - 8.05 (m, 1H), 7.94 - 7.99 (m, 1H), 7.83 - 7.90 (m, 1H), 7.36 - 7.40 (m, 2H), 7.26 - 7.31 (m, 2H), 6.56 - 6.60 (m, 1H), 6.45 - 6.52 (m, 1H), 5.56 - 5.64 (m, 1H), 2.98 - 3.11 (m, 1H), 2.84 - 2.96 (m, 1H), 2.60 - 2.63 (m, 1H), 2.05 - 2.16 (m, 1H). (formic acid salt)

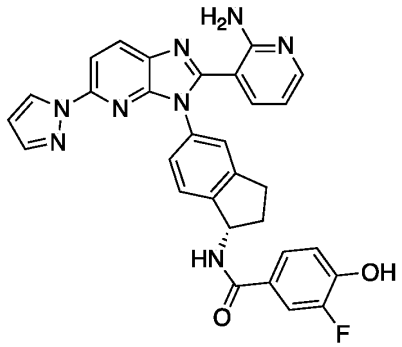
[00289] Example 15: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)oxetane-3-carboxamide (Compound 15)



Compound 15

[00290] **Compound 15** was prepared in a manner analogous to **Compound 3** using oxetane-3-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{27}H_{24}N_8O_2$: 492.20 m/z, found: 493.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.35 - 8.40 (m, 2H), 8.01 - 8.07 (m, 1H), 7.95 - 7.99 (m, 1H), 7.83- 7.86 (m, 1H), 7.29 - 7.40 (m, 4H), 6.57 - 6.60 (m, 1H), 6.44 - 6.49 (m, 1H), 5.37 - 5.48 (m, 1H), 4.65 - 4.71 (m, 4H), 3.79 - 3.90 (m, 1H), 2.85 - 3.03 (m, 2H), 2.55 - 2.62 (m, 1H), 1.85 - 1.93 (m, 1H).

[00291] Example 16: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-fluoro-4-hydroxybenzamide (Compound 16)

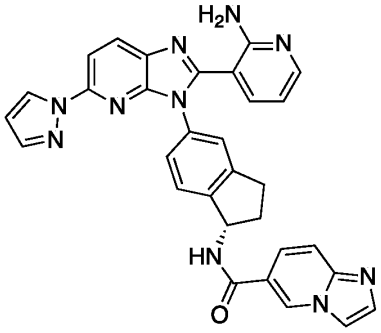


Compound 16

[00292] **Compound 16** was prepared in a manner analogous to **Compound 3** using 3-fluoro-4-hydroxybenzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for

$C_{30}H_{23}FN_8O_2$: 546.19 m/z, found 547.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.35 - 8.40 (m, 2H), 8.01 - 8.07 (m, 1H), 7.92 - 7.97 (m, 1H), 7.80 - 7.82 (m, 1H), 7.72 - 7.78 (m, 1H), 7.65 - 7.69 (m, 1H), 7.37 - 7.40 (m, 1H), 7.31 - 7.35 (m, 1H), 7.25 - 7.30 (m, 2H), 6.97 - 7.05 (m, 1H), 6.55 - 6.58 (m, 1H), 6.43 - 6.48 (m, 1H), 5.58 - 5.65 (m, 1H), 2.99 - 3.07 (m, 1H), 2.82 - 2.94 (m, 1H), 2.54 - 2.57 (m, 1H), 2.01 - 2.10 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm): -136.43.

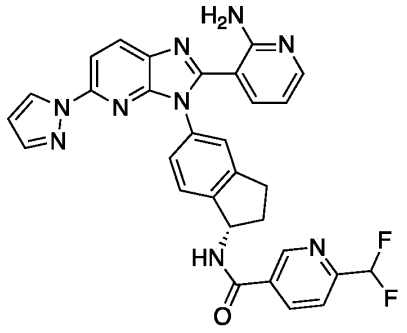
[00293] Example 17: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)imidazo[1,2-a]pyridine-6-carboxamide (Compound 17)



Compound 17

[00294] **Compound 17** was prepared in a manner analogous to **Compound 3** using imidazo[1,2-*a*]pyridine-6-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found: 553.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.12 - 9.22 (m, 1H), 8.29 - 8.41 (m, 2H), 8.06 - 8.11 (m, 1H), 7.98 - 8.05 (m, 1H), 7.89 - 7.97 (m, 1H), 7.79 - 7.86 (m, 1H), 7.70 - 7.78 (m, 1H), 7.58 - 7.69 (m, 2H), 7.36 - 7.48 (m, 2H), 7.22 - 7.35 (m, 2H), 6.51 - 6.60 (m, 1H), 6.39 - 6.50 (m, 1H), 5.57 - 5.70 (m, 1H), 3.01 - 3.17 (m, 1H), 2.85 - 3.00 (m, 1H), 2.53 - 2.69 (m, 1H), 2.01 - 2.21 (m, 1H).

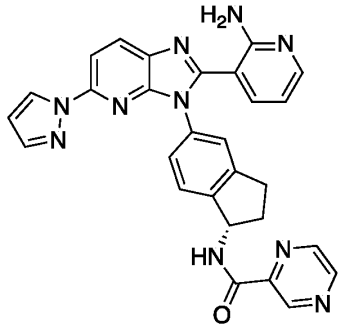
[00295] Example 18: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 18)



Compound 18

[00296] **Compound 18** was prepared in a manner analogous to **Compound 3** using 6-(difluoromethyl)nicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O$: 563.20 m/z, found: 564.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.06 - 8.25 (m, 1H), 8.23 - 8.55 (m, 3H), 7.95 - 8.22 (m, 2H), 7.60 - 7.90 (m, 3H), 7.28 - 7.60 (m, 3H), 6.72 - 7.25 (m, 2H), 6.40 - 6.70 (m, 1H), 5.48 - 5.78 (m, 1H), 2.95 - 3.20 (m, 1H), 2.85 - 2.95 (m, 1H), 2.51 - 2.60 (m, 1H), 1.98 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -116.08.

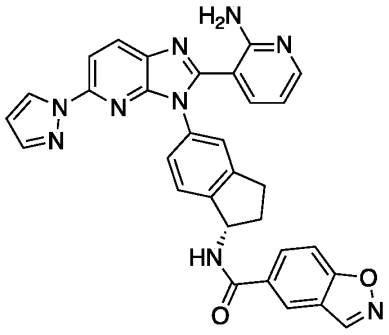
[00297] **Example 19: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyrazine-2-carboxamide (Compound 19)**



Compound 19

[00298] **Compound 19** was prepared in a manner analogous to **Compound 3** using pyrazine-2-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{28}H_{22}N_{10}O$: 514.20 m/z, found 515.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.23 - 9.26 (m, 1H), 8.87 - 8.92 (m, 1H), 8.75 - 8.79 (m, 1H), 8.31 - 8.39 (m, 2H), 8.01 - 8.06 (m, 1H), 7.95 - 7.99 (m, 1H), 7.81- 7.85 (m, 1H), 7.37 - 7.40 (m, 1H), 7.34 - 7.37 (m, 1H), 7.26 - 7.31 (m, 2H), 6.53 - 6.57 (m, 1H), 6.44 - 6.49 (m, 1H), 5.64 - 5.69 (m, 1H), 3.01 - 3.11 (m, 1H), 2.89 - 2.97 (m, 1H), 2.60 - 2.62 (m, 1H), 2.17 - 2.26 (m, 1H). (formic acid salt)

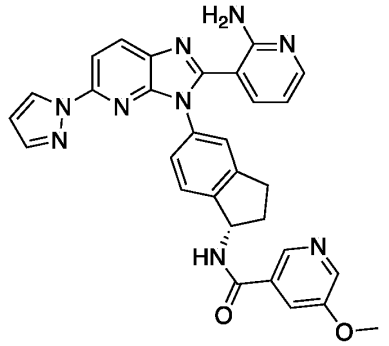
[00299] Example 20: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)benzo[d]isoxazole-5-carboxamide (Compound 20)



Compound 20

[00300] **Compound 20** was prepared in a manner analogous to **Compound 3** using benzo[*d*]isoxazole-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{23}N_9O_2$: 553.20 m/z, found 554.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.83 - 8.91 (m, 1H), 8.31 - 8.39 (m, 2H), 8.21 - 8.28 (m, 1H), 8.06 - 8.11 (m, 1H), 8.01 - 8.05 (m, 1H), 7.94 - 7.99 (m, 1H), 7.80 - 7.89 (m, 1H), 7.33 - 7.43 (m, 2H), 7.26 - 7.31 (m, 2H), 7.06 - 7.15 (m, 1H), 6.57 - 6.61 (m, 1H), 6.43 - 6.51 (m, 1H), 5.51 - 5.64 (m, 1H), 2.98 - 3.11 (m, 1H), 2.84 - 2.96 (m, 1H), 2.56 - 2.61 (m, 1H), 2.05 - 2.18 (m, 1H). (formic acid salt)

[00301] Example 21: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-5-methoxynicotinamide (Compound 21)

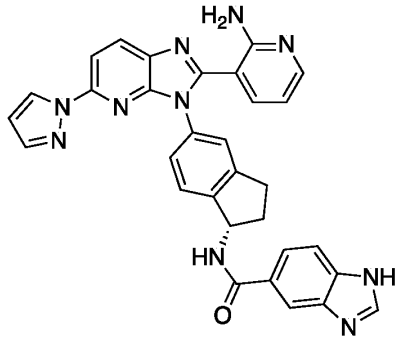


Compound 21

[00302] **Compound 21** was prepared in a manner analogous to **Compound 3** using 5-methoxynicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$: 543.21m/z, found 544.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.70 - 8.80 (m, 1H), 8.45 - 8.59 (m, 2H), 8.29 - 8.35 (m, 1H), 8.09 - 8.19 (m, 1H), 8.01 - 8.08 (m, 1H), 7.76 - 7.91 (m, 3H), 7.31 - 7.52 (m, 3H), 6.81 - 6.99 (m, 1H), 6.51 - 6.75 (m, 1H), 5.64 - 5.79 (m, 1H),

3.89 (s, 3H), 3.01 - 3.18 (m, 1H), 2.82 - 2.99 (m, 1H), 2.59 - 2.61 (m, 1H), 2.01 - 2.26 (m, 1H). (TFA salt)

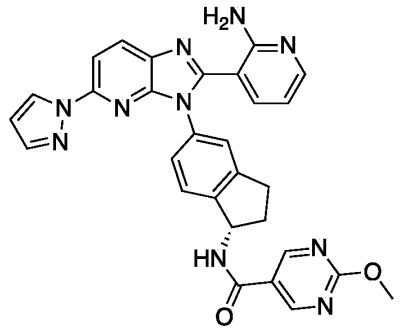
[00303] Example 22: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1H-benzo[d]imidazole-5-carboxamide (Compound 22)



Compound 22

[00304] **Compound 22** was prepared in a manner analogous to **Compound 3** using 1*H*-benzo[*d*]imidazole-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$: 552.21 m/z, found 553.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.26 (s, 1H), 8.25 - 8.46 (m, 3H), 7.95 - 8.12 (m, 3H), 7.69 - 7.88 (m, 3H), 7.30 - 7.51 (m, 3H), 6.79 - 6.83 (m, 1H), 6.51 - 6.60 (m, 1H), 5.55 - 5.68 (m, 1H), 3.09 - 3.21 (m, 1H), 2.88 - 3.02 (m, 1H), 2.58 - 2.68 (m, 1H), 2.03 - 2.23 (m, 1H). (TFA salt)

[00305] Example 23: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-methoxypyrimidine-5-carboxamide (Compound 23)

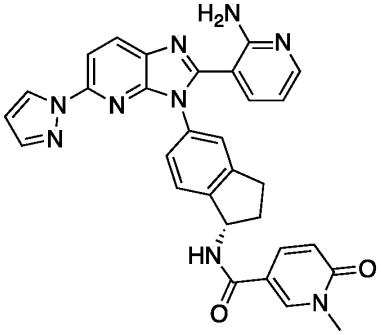


Compound 23

[00306] **Compound 23** was prepared in a manner analogous to **Compound 3** using 2-methoxypyrimidine-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{29}H_{24}N_{10}O_2$: 544.21 m/z, found 545.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.08 (m, 3H), 8.35 - 8.37 (m, 2H), 8.01 - 8.02 (m, 1H), 7.94 - 7.96 (m, 1H), 7.81 - 7.82 (m, 1H), 7.41

- 7.44 (m, 2H), 7.31 - 7.33 (m, 2H), 6.88 - 6.89 (m, 2H), 6.55 - 6.56 (m, 1H), 6.46 - 6.47 (m, 1H), 5.63 - 5.65 (m, 1H), 3.99 (s, 3H), 3.05 - 3.06 (m, 1H), 2.93 - 2.95 (m, 1H), 2.50 - 2.51 (m, 1H), 2.06 - 2.09 (m, 1H).

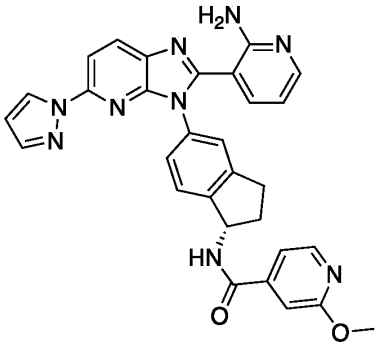
[00307] Example 24: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide (Compound 24)



Compound 24

[00308] **Compound 24** was prepared in a manner analogous to **Compound 3** using 1-methyl-6-oxo-1,6-dihydropyridine-3-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$: 543.21 m/z, found 544.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 8.63 - 8.65 (m, 1H), 8.45 - 8.46 (m, 1H), 8.36 - 8.38 (m, 2H), 8.02 - 8.03 (m, 1H), 7.94 - 7.96 (m, 2H), 7.81 - 7.82 (m, 1H), 7.35 - 7.37 (m, 1H), 7.29 - 7.31 (m, 1H), 7.28 - 7.29 (m, 2H), 6.92 - 6.93 (m, 2H), 6.47 - 6.56 (m, 1H), 6.41 - 6.43 (m, 2H), 5.56 - 5.63 (m, 1H), 3.49 (s, 3H), 3.00 - 3.02 (m, 1H), 2.92 - 2.95 (m, 1H), 2.50 - 2.52 (m, 1H), 2.00 - 2.01 (m, 1H).

[00309] Example 25: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-methoxyisonicotinamide (Compound 25)

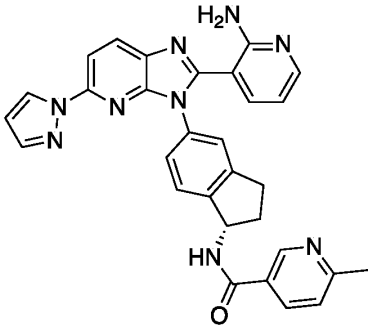


Compound 25

[00310] **Compound 25** was prepared in a manner analogous to **Compound 3** using 2-methoxyisonicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$,

543.21 m/z, found: 544.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.13 - 9.15 (m, 1H), 8.37 - 8.38 (m, 2H), 8.30 - 8.31 (m, 1H), 8.01 - 8.02 (m, 1H), 7.94 - 7.96 (m, 1H), 7.81 - 7.82 (m, 1H), 7.39 - 7.45 (m, 3H), 7.28 - 7.32 (m, 3H), 6.90 (s, 2H), 6.55 - 6.56 (m, 1H), 6.43 - 6.45 (m, 1H), 5.62 - 5.64 (m, 1H), 3.90 (s, 3H), 2.96 - 3.05 (m, 2H), 2.50 - 2.55 (m, 1H), 2.09 - 2.12 (m,1H).

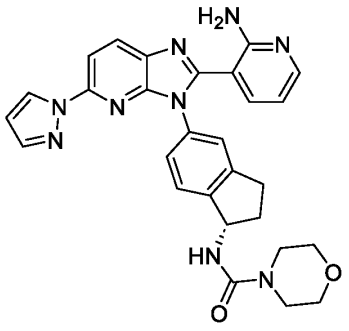
[00311] Example 26: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 26)



Compound 26

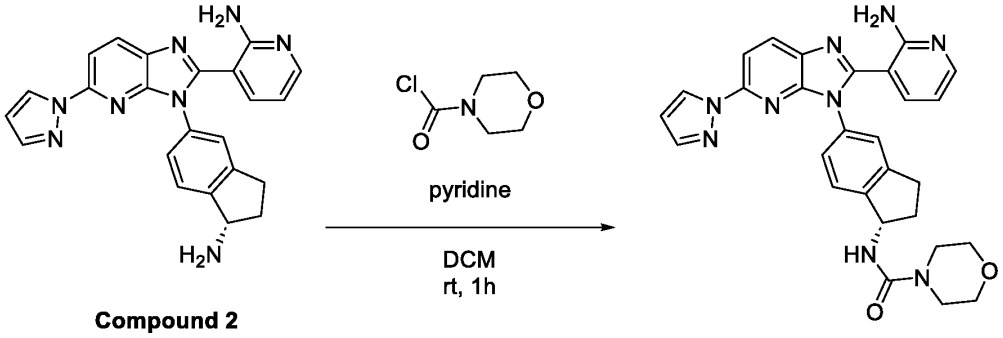
[00312] **Compound 26** was prepared in a manner analogous to **Compound 3** using 6-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found: 528.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.92 - 8.93 (m, 1H), 8.37 - 8.41 (m, 2H), 8.16 - 8.21 (m, 1H), 8.00 - 8.05 (m, 1H), 7.95 - 7.99 (m, 1H), 7.79 - 7.81 (m, 1H), 7.38 - 7.44 (m, 3H), 7.28 - 7.31 (m, 2H), 6.56 - 6.59 (m, 1H), 6.47 - 6.53 (m, 1H), 5.60 - 5.67 (m, 1H), 3.00 - 3.10 (m, 1H), 2.88 - 2.98 (m, 1H), 2.59 - 2.61 (m, 1H), 2.54 (s, 3H), 2.03 - 2.18 (m, 1H). (TFA salt)

[00313] Example 27: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)morpholine-4-carboxamide (Compound 27)



Compound 27

[00314] **Synthetic Route:**



Compound 2 **Compound 27**

[00315] **Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)morpholine-4-carboxamide (Compound 27)**

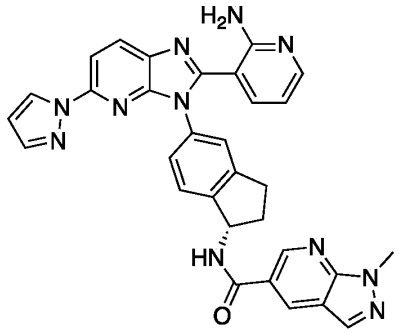
[00316] A suspension of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (200 mg, 0.490 mmol, 1.2 equiv) in dichloromethane was treated with pyridine (484 mg, 6.12 mmol, 15 equiv) and the resulting mixture was stirred for 3 min at room temperature followed by the addition of morpholine-4-carbonyl chloride (61 mg, 0.408 mmol, 1 equiv) dropwise at room temperature. The resulting mixture was stirred for 1 h at room temperature. The reaction mixture was concentrated under reduced pressure then taken up into dichloromethane and concentrated to dryness under reduced pressure. The crude residue was purified by preparative HPLC on a YMC Triart C18 ExRs column using a gradient of acetonitrile in water (+ 10 mmol/L ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)morpholine-4-carboxamide (**Compound 27**) (17.5 mg, 8%) as a white solid. MS (ESI) calcd. for $C_{28}H_{27}N_9O_2$: 521.23 m/z, found 522.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.35 - 8.47 (m, 2H), 7.93 - 8.09 (m, 2H), 7.81 - 7.89 (s, 1H), 7.29 - 7.48 (m, 4H), 6.52 - 6.64 (m, 2H), 5.21 - 5.33 (m, 1H), 2.55 - 2.68 (m, 4H), 3.32 - 3.43 (m, 4H), 2.92 - 3.06 (m, 1H), 2.78 - 2.89 (m, 1H), 2.46 - 2.51 (m, 1H), 1.89 - 2.03 (m, 1H).

[00317] The following compounds were prepared analogous to the synthetic preparation in Example 27 (Compound 27).

[00318] **Table 3A.** Characterization data of compounds prepared analogously to compound 27.

Cpd ID	Characterization Data
82	MS (ESI) calcd. for $C_{29}H_{25}N_9O_2S$: 563.19 m/z, found: 564.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 8.85 - 8.92 (m, 1H), 8.32 - 8.36 (m, 2H), 8.15 - 8.20 (m, 1H), 7.96 - 8.02 (m, 1H), 7.92 - 7.95 (m, 1H), 7.80 - 7.85 (m, 1H), 7.52 -7.61 (m, 1H), 7.18 - 7.32 (m, 4H), 6.52 - 6.56 (m, 1H), 6.44 - 6.50 (m, 1H), 4.80 - 4.88 (m, 1H), 2.83 - 2.93 (m, 1H), 2.69 - 2.76 (m, 1H), 2.53 - 2.56 (m, 3H), 2.10 - 2.21 (m, 1H), 1.60 - 1.79 (m, 1H).
139	MS (ESI) calcd. for $C_{29}H_{25}N_9O_2S$, 563.19 m/z, found 564.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.65 - 8.75 (m, 1H), 8.30 - 8.40 (m, 2H), 8.25 - 8.30 (m, 1H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H), 7.81 (m, 1H), 7.45 - 7.55 (m, 1H), 7.34 (s, 1H), 7.20 - 7.30 (m, 3H), 6.52 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 4.70 - 4.81 (m, 1H), 2.85 - 3.00 (m, 1H), 2.89 (s, 3H), 2.65 - 2.80 (m, 1H), 2.05 - 2.20 (m, 1H), 1.70 - 1.90 (m, 1H).

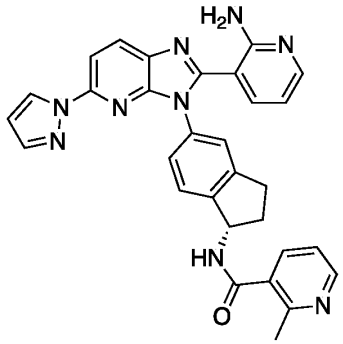
[00319] Example 28: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide (Compound 28)



Compound 28

[00320] **Compound 28** was prepared in a manner analogous to **Compound 3** using 1-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{25}N_{11}O$: 567.22 m/z, found: 568.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.04 - 9.06 (m, 1H), 8.76 - 8.78 (m, 1H), 8.28 - 8.41 (m, 3H), 8.00 - 8.02 (m, 1H), 7.93 - 7.95 (m, 1H), 7.80 - 7.83 (m, 1H), 7.42 - 7.46 (m, 1H), 7.37 - 7.39 (m, 1H), 7.31 - 7.33 (m, 2H), 6.48 - 6.61 (m, 2H), 5.60 - 5.66 (m, 1H), 4.10 (s, 3H), 2.90 - 3.08 (m, 2H), 2.50 - 2.54 (m, 1H), 2.10 - 2.13 (m, 1H).

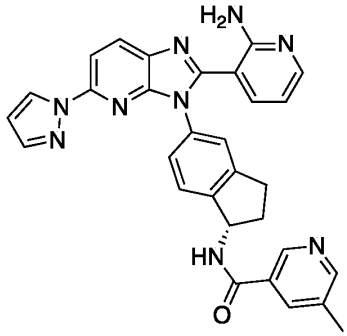
[00321] Example 29: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-methylnicotinamide (Compound 29)



Compound 29

[00322] **Compound 29** was prepared in a manner analogous to **Compound 3** using 2-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.50 - 8.52 (m, 1H), 8.32 - 8.40 (m, 2H), 8.00 - 8.02 (m, 1H), 7.93 - 7.96 (m, 1H), 7.76 - 7.85 (m, 2H), 7.46 - 7.48 (m, 1H), 7.25 - 7.42 (m, 4H), 6.54 - 6.57 (m, 1H), 6.50 - 6.52 (m, 1H), 5.54 - 5.58 (m, 1H), 2.83 - 3.11 (m, 2H), 2.58 - 2.60 (m, 1H), 2.55 - 3.57 (m, 3H),1.98 - 2.02 (m, 1H).

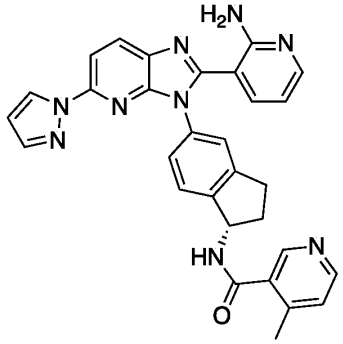
[00323] **Example 30: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-5-methylnicotinamide (Compound 30)**



Compound 30

[00324] **Compound 30** was prepared in a manner analogous to **Compound 3** using 5-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.81 - 8.89 (m, 1H), 8.48 - 8.58 (m, 1H), 8.27 - 8.40 (m, 2H), 8.05 - 8.14 (m, 1H), 7.98 - 8.04 (m, 1H), 7.89 - 7.97 (m, 1H), 7.76 - 7.85 (m, 1H), 7.34 - 7.46 (m, 2H), 7.21 - 7.33 (m, 2H), 6.51 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 5.57 - 5.73 (m, 1H), 2.99 - 3.13 (m, 1H), 2.83 - 2.98 (m, 1H), 2.57 - 2.61 (m, 1H), 2.36 (s, 3H), 1.98 - 2.21 (m, 1H).

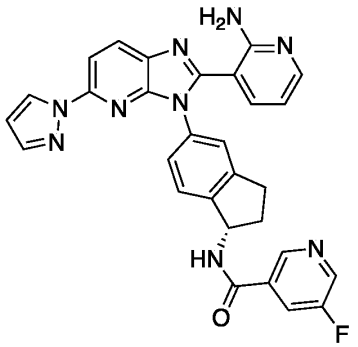
[00325] Example 31: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-methylnicotinamide (Compound 31)



Compound 31

[00326] Compound 31 was prepared in a manner analogous to **Compound 3** using 4-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.54 - 8.55 (m, 1H), 8.48 - 8.49 (m, 1H), 8.35 - 8.36 (m, 2H), 8.00 - 8.01 (m, 1H), 7.94 - 7.96 (m, 1H), 7.80 - 7.81 (m, 1H), 7.46 - 7.48 (m, 1H), 7.39 - 7.40 (m, 1H), 7.31 - 7.32 (m, 2H), 7.26 - 7.27 (m, 1H), 6.55 - 6.56 (m, 1H), 6.45 - 6.46 (m, 1H), 5.58 - 5.62 (m, 1H), 2.92 - 3.93 (m, 2H), 2.50 - 2.51 (m, 1H), 2.41 - 2.42 (m, 3H), 2.02 - 2.03 (m, 1H).

[00327] Example 32: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-5-fluoronicotinamide (Compound 32)

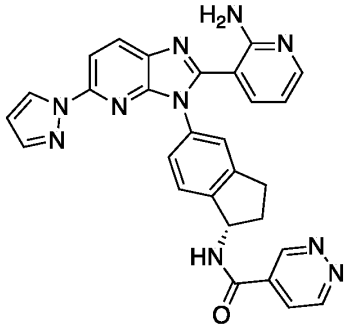


Compound 32

[00328] Compound 32 was prepared in a manner analogous to **Compound 3** using 5-fluoronicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{29}H_{22}FN_9O$: 531.19 m/z, found 532.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.15 - 9.23 (m, 1H), 8.89 - 8.96 (m, 1H), 8.68 - 8.75 (m, 1H), 8.30 - 8.39 (m, 2H), 8.03 - 8.17 (m, 1H), 7.97 - 8.01 (m, 1H), 7.87 - 7.96 (m, 1H), 7.73 - 7.79 (m, 1H), 7.32 - 7.41 (m, 2H), 7.19 - 7.31 (m, 2H),

6.50 - 6.56 (m, 1H), 6.38 - 6.48 (m, 1H), 5.53 - 5.66 (m, 1H), 2.86 - 3.09 (m, 2H), 2.56 - 2.61 (m, 1H), 2.01 - 2.16 (m, 1H). (formic acid salt)

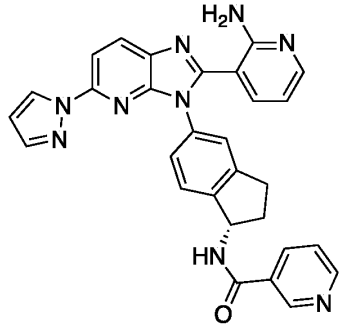
[00329] Example 33: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyridazine-4-carboxamide (Compound 33)



Compound 33

[00330] **Compound 33** was prepared in a manner analogous to **Compound 3** using pyridazine-4-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{28}H_{22}N_{10}O$: 514.20 m/z, found 515.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.58 - 9.64 (m, 1H), 9.41 - 9.48 (m, 1H), 8.33 - 8.41 (m, 2H), 7.92 - 8.14 (m, 3H), 7.78 - 7.83 (m, 1H), 7.40 - 7.47 (m, 2H), 7.28 - 7.39 (m, 2H), 6.48 - 6.58 (m, 2H), 5.59 - 5.68 (m, 1H), 2.93 - 3.05 (m, 2H), 2.50 - 2.51 (m, 1H), 2.11 - 2.06 (m, 1H). (TFA salt)

[00331] Example 34: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]pyridine-3-carboxamide (Compound 34)

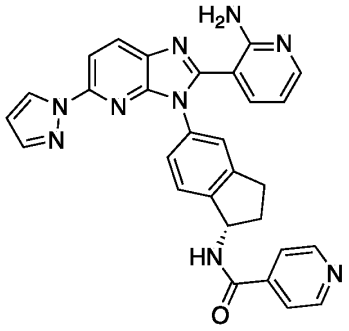


Compound 34

[00332] **Compound 34** was prepared in a manner analogous to **Compound 3** using niacin in place of 3,4-difluoro-5-anisic acid and PyBOP in place of HATU. MS (ESI) calcd. for $C_{29}H_{23}N_9O$: 513.20 m/z, found 514.25 $[M-H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.14 – 9.16 (m, 1H), 9.05 – 9.08 (m, 1H), 8.71 – 8.72 (m, 1H), 8.33 – 8.36 (m, 2H), 8.25 – 8.28 (m, 1H), 8.16 (s, 1H), 7.93 – 8.02 (m, 1H), 7.80 (s, 1H), 7.51 – 7.54 (m, 1H), 7.38 – 7.40 (m, 2H), 7.26 –

7.31 (m, 2H), 6.54 – 6.55 (m, 1H), 6.44 – 6.47 (m, 1H), 5.62 – 5.68 (m, 1H), 2.87 – 3.08 (m, 2H), 2.53 – 2.58 (m, 1H), 2.09 – 2.14 (m, 1H).

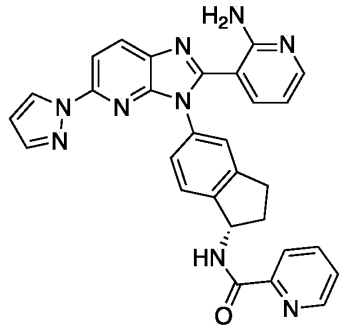
[00333] Example 35: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]pyridine-4-carboxamide (Compound 35)



Compound 35

[00334] **Compound 35** was prepared in a manner analogous to **Compound 3** using isonicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{29}H_{23}N_9O$: 513.57 m/z, found 514.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.70- 8.72 (m, 2H), 8.32 - 8.34 (m, 2H), 7.99 -8.00 (m, 1H), 7.94 - 7.98 (m, 1H), 7.78 - 7.82 (m, 3H), 7.35 - 7.37 (m, 2H), 7.25 - 7.27 (m, 2H), 6.53 - 6.54 (m, 1H), 6.44 - 6.47 (m, 1H), 5.58 - 5.63 (m, 1H), 3.00 - 3.05 (m, 1H), 2.85 - 2.94 (m, 1H), 2.51 - 2.52 (m, 1H), 2.07 - 2.13 (m, 1H).

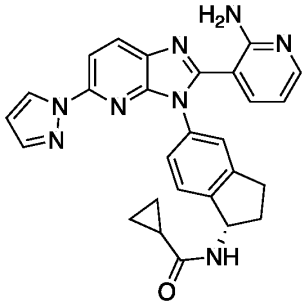
[00335] Example 36: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]pyridine-2-carboxamide (Compound 36)



Compound 36

[00336] **Compound 36** was prepared in a manner analogous to **Compound 3** using picolinic acid in place of 3,4-difluoro-5-anisic acid and PyBOP in place of HATU. MS (ESI) calcd. for $C_{29}H_{23}N_9O$ 513.20 m/z, found: 514.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.64 - 8.66 (m, 1H), 8.35 - 8.37 (m, 2H), 8.02 - 8.13 (m, 1H), 7.96 - 8.05 (m, 2H), 7.94 - 7.96 (m, 1H), 7.80 - 7.81 (m, 1H), 7.61 - 7.64 (m, 1H), 7.38 - 7.39 (m, 1H), 7.32 - 7.34 (m, 1H), 7.24 - 7.28 (m, 2H), 6.54 - 6.55 (m, 1H), 6.44 - 6.47 (m, 1H), 5.63 - 5.65 (m, 1H), 3.45 - 3.52 (m, 1H), 2.91 - 2.94 (m, 1H), 2.50 - 2.51 (m, 1H), 2.23 - 2.33 (m, 1H).

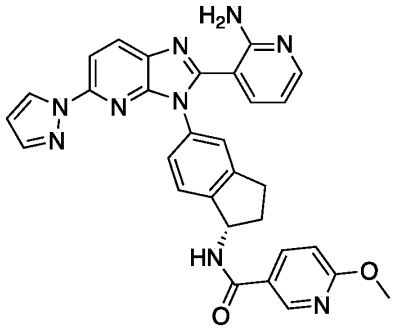
[00337] Example 37: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl) imidazo[4,5-b]pyridin -3-yl]-2,3-dihydro-1H-inden-1-yl]cyclopropanecarboxamide (Compound 37)



Compound 37

[00338] **Compound 37** was prepared in a manner analogous to **Compound 3** using cyclopropanecarboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{27}H_{24}N_8O$: 476.21 m/z, found 477.05 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.52 - 8.79 (m, 1H), 8.27 - 8.51 (m, 2H), 7.95 - 8.04 (m, 1H), 7.90 - 7.99 (m, 1H), 7.78 - 7.90 (m, 1H), 7.32 - 7.48 (m, 1H), 7.24 - 7.31 (m, 3H), 6.45 - 6.49 (m, 1H), 6.41 - 6.41 (m, 1H), 5.30 - 5.48 (m, 1H), 2.95 - 3.08 (m, 1H), 2.81 - 2.95 (m, 1H), 2.42 - 2.55 (m, 1H), 1.97 - 1.99 (m, 1H), 1.48 - 1.67 (m, 1H), 0.70 - 0.82 (m, 4H).

[00339] Example 38: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-methoxypyridine-3-carboxamide (Compound 38)

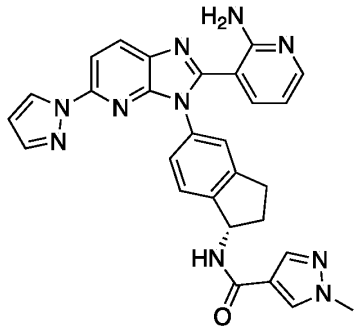


Compound 38

[00340] **Compound 38** was prepared in a manner analogous to **Compound 3** using 6-methoxynicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$: 543.21 m/z, found 544.25 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.85 - 9.09 (m, 1H), 8.61 - 9.85 (m, 1H), 8.42 - 8.49 (m, 2H), 8.09 - 8.27 (m, 1H), 7.98 - 8.10 (m, 1H), 7.89 - 7.95 (m, 1H), 7.56 - 7.89 (m, 1H), 7.14 - 7.44 (m, 4H), 6.85 - 6.92 (m, 1H), 6.55 - 6.70 (s, 1H),

6.35 - 6.55 (m, 1H), 5.55 - 5.70 (m, 1H), 3.85 - 3.99 (m, 3H), 3.08 - 3.14 (m, 1H), 2.81 - 2.99 (m, 1H), 2.52 - 2.61 (m, 1H), 2.01 - 2.15 (m, 1H).

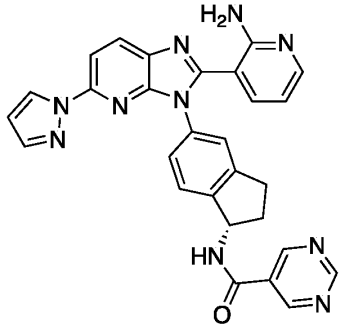
[00341] Example 39: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-1-methyl-1*H*-pyrazole-4-carboxamide (Compound 39)



Compound 39

[00342] **Compound 39** was prepared in a manner analogous to **Compound 3** using 1-methyl-1*H*-pyrazole-4-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$: 516.21 m/z, found 517.15 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.55 - 8.75 (m, 1H), 8.30 - 8.45 (m, 2H), 8.15 - 8.28 (m, 1H), 8.00 - 8.05 (m, 1H), 7.91 - 8.00 (m, 2H), 7.78 - 7.89 (m, 1H), 7.20 -7.45 (m, 4H), 6.55 - 6.65 (m, 1H), 6.35 - 6.55 (m, 1H), 3.89 - 3.91 (m, 3H), 2.90 - 3.15 (m, 1H), 2.80 - 2.90 (m, 1H), 2.50 - 2.51 (m, 1H), 1.90 - 2.14 (m, 1H).

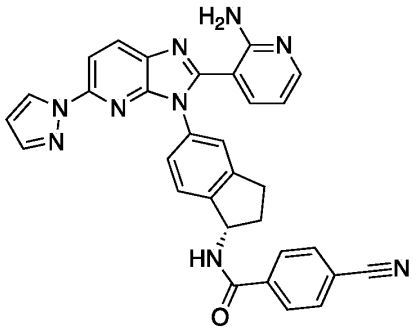
[00343] Example 40: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]pyrimidine-5-carboxamide (Compound 40)



Compound 40

[00344] **Compound 40** was prepared in a manner analogous to **Compound 3** using pyrimidine-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{28}H_{22}N_{10}O$: 514.20 m/z, found 515.15 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 9.25 - 9.30 (m, 1H), 9.35 - 9.40 (m, 2H), 8.45 - 8.61 (m, 2H), 7.98 - 8.10 (m, 2H), 7.80 - 7.82 (s, 1H), 7.50 - 7.60 (m, 2H), 7.30 - 7.44 (m, 2H), 6.55 - 6.66 (m, 1H), 6.45 - 6.50 (m, 1H), 5.55 - 5.80 (m, 1H), 2.80 - 3.20 (m, 2H), 2.45 - 2.52 (m, 1H), 2.01 - 2.15 (m, 1H).

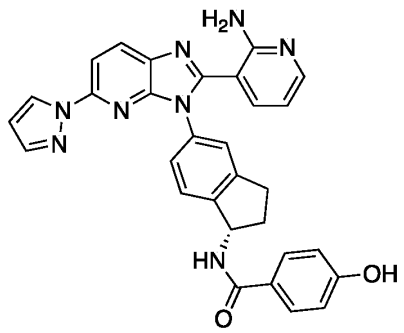
[00345] Example 41: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-4-cyanobenzamide (Compound 41)



Compound 41

[00346] **Compound 41** was prepared in a manner analogous to **Compound 3** using 4-cyanobenzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{23}N_9O$: 537.20 m/z, found 538.20 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.30 - 8.60 (m, 2H), 7.90 - 8.30 (m, 6H), 7.65 - 7.90 (m, 1H), 7.38 - 7.65 (m, 2H), 7.19 - 7.38 (m, 2H), 6.55 - 6.80 (m, 1H), 6.38 - 6.55 (m, 1H), 5.50 - 5.88 (m, 1H), 2.89 - 3.30 (m, 2H), 2.58 - 2.70 (m, 1H), 1.95 - 2.30 (m, 1H).

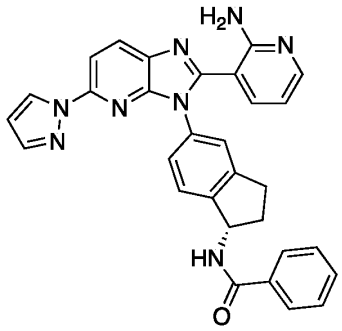
[00347] Example 42: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-4-hydroxybenzamide (Compound 42)



Compound 42

[00348] **Compound 42** was prepared in a manner analogous to **Compound 3** using 4-hydroxybenzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{24}N_8O_2$: 528.20 m/z, found 529.30 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.35 - 8.37 (m, 2H), 8.01 - 8.02 (m, 1H), 7.94 - 8.00 (m, 1H), 7.81 - 7.83 (m, 3H), 7.25 - 7.38 (m, 4H), 6.88 - 7.08 (m, 2H), 6.55 - 6.58 (m, 1H), 6.44 - 6.46 (m, 1H), 5.60 - 5.64 (m, 1H), 2.87 - 3.03 (m, 2H), 2.51 - 2.52 (m, 1H), 2.10 - 2.30 (m, 1H).

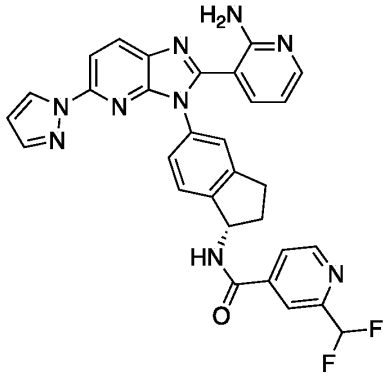
[00349] Example 43: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)benzamide (Compound 43)



Compound 43

[00350] Compound 43 was prepared in a manner analogous to **Compound 3** using benzoic acid in place of 3,4-difluoro-5-anisic acid and PyBOP in place of HATU. MS (ESI) calcd. for $C_{30}H_{24}N_8O$: 512.21 m/z, found 513.15 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm): 8.94 (s, 1H), 8.36 - 8.38 (m, 2H), 8.04 (m, 1H), 7.94 - 7.97 (m, 3H), 7.81 7.82 (m, 1H), 7.48 - 7.51 (m, 3H), 7.41 (m, 2H), 7.40 (m, 2H), 6.56 - 6.60 (m, 1H), 6.45 - 6.54 (m, 1H), 5.60 - 5.70 (m, 1H), 2.96 - 3.12 (m, 1H), 2.85 - 2.95 (m, 1H), 2.50 - 2.52 (m, 1H), 2.01 - 2.22 (m, 1H).

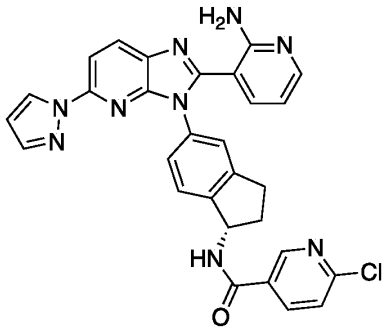
[00351] Example 44: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(difluoromethyl)isonicotinamide (Compound 44)



Compound 44

[00352] Compound 44 was prepared in a manner analogous to **Compound 3** using 2-(difluoromethyl)isonicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{23}F_2N_9O$: 563.20 m/z, found 564.25 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.80 - 8.90 (m, 1H), 8.28 - 8.40 (m, 2H), 8.11 - 8.21 (m, 1H), 8.00 - 8.09 (m, 2H), 7.88 - 7.99 (m, 1H), 7.76 - 7.85 (m, 1H), 7.36 - 7.47 (m, 2H), 7.24 - 7.34 (m, 2H), 6.82 - 7.33 (m, 1H), 6.50 - 6.60 (m, 1H), 6.39 - 6.49 (m, 1H), 5.57 - 5.71 (m, 1H), 2.82 - 3.15 (m, 2H), 2.51 - 2.62 (m, 1H), 1.98 - 2.20 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -115.65.

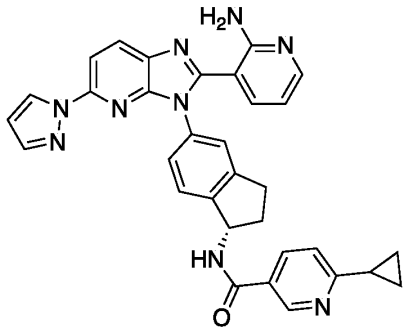
[00353] Example 45: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-chloronicotinamide (Compound 45)



Compound 45

[00354] **Compound 45** was prepared in a manner analogous to **Compound 3** using 6-chloronicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{29}H_{22}ClN_9O$: 547.16 m/z, found 548.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.78 - 8.84 (m, 1H), 8.22 - 8.43 (m, 3H), 7.89 - 8.06 (m, 2H), 7.82 - 7.87 (m, 1H), 7.62 - 7.68 (m, 1H), 7.23 - 7.49 (m, 4H), 6.54 - 6.62 (m, 2H), 5.57 - 5.64 (m, 1H), 2.85 - 3.11 (m, 2H), 2.61 - 2.69 (m, 1H), 2.04 - 2.16 (m, 1H).

[00355] Example 46: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-cyclopropylpyridine-3-carboxamide (Compound 46)

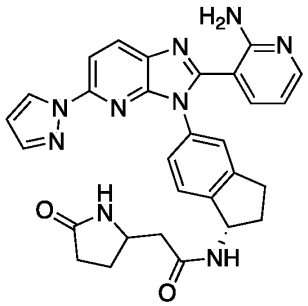


Compound 46

[00356] **Compound 46** was prepared in a manner analogous to **Compound 3** using 6-cyclopropylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{32}H_{27}N_9O$: 553.23 m/z, found 554.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.96 - 9.06 (m, 1H), 8.85 - 8.95 (m, 1H), 8.28 - 8.43 (m, 2H), 8.08 - 8.18 (m, 1H), 7.98 - 8.07 (m, 1H), 7.89 - 7.97 (m, 1H), 7.75 - 7.85 (m, 1H), 7.34 - 7.46 (m, 3H), 7.22 - 7.33 (m, 2H), 6.50 - 6.60 (m, 1H),

6.39 - 6.49 (m, 1H), 5.54 - 5.72 (m, 1H), 2.79 - 3.13 (m, 2H), 2.52 - 2.60 (m, 1H), 1.95 - 2.23 (m, 2H), 0.89 - 1.10 (m, 4H).

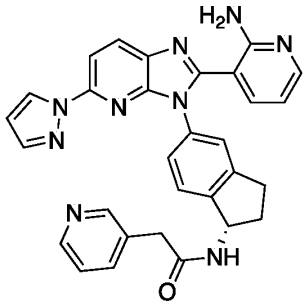
[00357] Example 47: N-((S)-5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(5-oxopyrrolidin-2-yl)acetamide (Compound 47)



Compound 47

[00358] **Compound 47** was prepared in a manner analogous to **Compound 3** using 2-(5-oxopyrrolidin-2-yl)acetic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{29}H_{27}N_9O_2$: 533.23 m/z, found 534.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.31 - 8.40 (m, 2H), 7.95 - 8.03 (m, 2H), 7.98 - 7.82 (m, 1H), 7.25 - 7.50 (m, 4H), 6.50 - 6.60 (m, 2H), 5.33 - 5.41 (m, 1H), 3.88 - 3.93 (m, 1H), 2.79 - 3.02 (m, 2H), 2.45 - 2.65 (m, 2H), 2.29 - 2.35 (m, 1H), 2.09 - 2.25 (m, 3H), 1.80 - 1.92 (m, 1H), 1.65 - 1.78 (m, 1H). (formic acid salt)

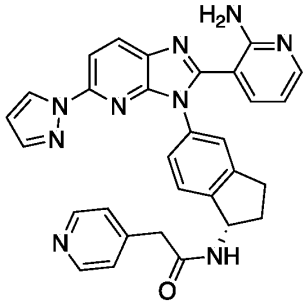
[00359] Example 48: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(pyridin-3-yl)acetamide (Compound 48)



Compound 48

[00360] **Compound 48** was prepared in a manner analogous to **Compound 3** using 2-(pyridin-3-yl)acetic acid (HCl salt) in place of 3,4-difluoro-5-anisic acid and an additional equivalent of N,N-diisopropylethylamine. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.30 - 8.39 (m, 3H), 8.21 - 8.26 (m, 1H), 7.90 - 7.95 (m, 1H), 7.78 - 7.83 (m, 1H), 7.70 - 7.76 (m, 2H), 7.28 - 7.39 (m, 3H), 7.10 - 7.19 (m, 2H), 6.50 - 6.57 (m, 2H), 5.19 - 5.25 (m, 1H), 3.53 (s, 2H), 2.90 - 2.98 (m, 1H), 2.72 - 2.81 (m, 1H), 2.37 - 2.40 (m, 1H), 1.79 - 1.91 (m, 1H).

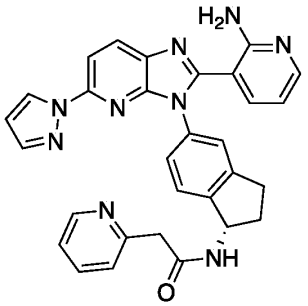
[00361] **Example 49: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-(pyridin-4-yl)acetamide (Compound 49)**



Compound 49

[00362] **Compound 49** was prepared in a manner analogous to **Compound 3** using 2-(pyridin-4-yl)acetic acid (HCl salt) in place of 3,4-difluoro-5-anisic acid and an additional equivalent of N,N-diisopropylethylamine. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.25 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm): 8.73 - 8.75 (m, 1H), 8.48 - 8.50 (m, 2H), 8.34 - 8.36 (m, 2H), 8.00 - 8.01 (m, 1H), 7.93 - 7.96 (m, 1H), 7.80 - 7.81 (m, 1H), 7.32 - 7.37 (m, 3H), 7.24 - 7.28 (m, 3H), 6.55 - 6.56 (m, 1H), 6.43 - 6.46 (m, 1H), 5.32 - 5.34 (m, 1H), 3.55 (s, 2H), 2.94 - 2.96 (m, 1H), 2.85 - 2.87 (m, 1H), 2.50 - 2.51 (m, 1H), 1.88 - 1.90 (m, 1H).

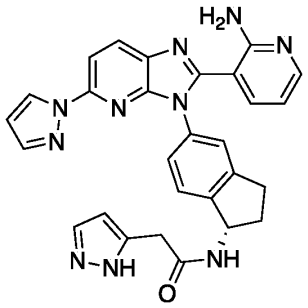
[00363] **Example 50: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(pyridin-2-yl)acetamide (Compound 50)**



Compound 50

[00364] **Compound 50** was prepared in a manner analogous to **Compound 3** using 2-(pyridin-2-yl)acetic acid (HCl salt) in place of 3,4-difluoro-5-anisic acid and an additional equivalent of N,N-diisopropylethylamine. MS (ESI) calcd. for $C_{30}H_{25}N_9O$: 527.22 m/z, found 528.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.42 - 8.56 (m, 1H), 8.32 - 8.41 (m, 2H), 7.88 - 8.06 (m, 2H), 7.72 - 7.88 (m, 2H), 7.19 - 7.43 (m, 6H), 6.53 - 6.59 (m, 1H), 6.45 - 6.51 (m, 1H), 5.31 - 5.42 (m, 1H), 3.81 - 3.96 (m, 1H), 3.69 - 3.76 (m, 1H), 2.81 - 3.04 (m, 2H), 2.46 - 2.51 (m, 1H), 1.83 - 2.01 (m, 1H). (formic acid salt)

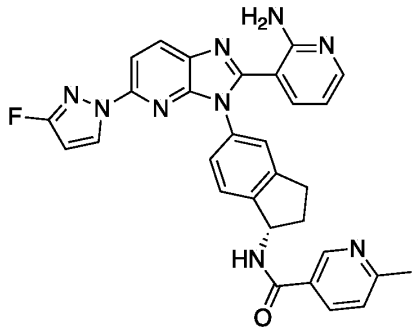
[00365] **Example 51: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(1H-pyrazol-5-yl)acetamide (Compound 51)**



Compound 51

[00366] **Compound 51** was prepared in a manner analogous to **Compound 3** using 2-(1H-pyrazol-5-yl)acetic acid (HCl salt) in place of 3,4-difluoro-5-anisic acid and an additional equivalent of N,N-diisopropylethylamine. MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$: 516.21 m/z, found 517.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32 - 8.41 (m, 2H), 8.00 - 8.02 (m, 1H), 7.92 - 7.96 (m, 1H), 7.81 - 7.83 (m, 1H), 7.60 - 7.62 (m, 1H), 7.21 - 7.35 (m, 4H), 6.52 - 6.56 (m, 1H), 6.42 - 6.46 (m, 1H), 6.18 (s, 1H), 5.33 - 5.35 (m, 1H), 3.57 - 3.59 (m, 1H), 3.55 - 5.57 (m, 1H), 2.78 - 3.05 (m, 2H), 2.44 - 2.47 (m, 1H), 1.90 - 1.92 (m, 1H).

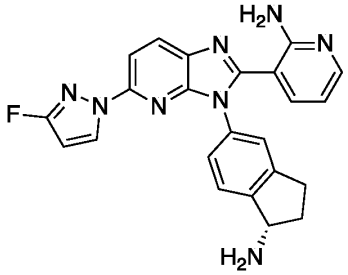
[00367] **Example 52: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-fluoro-1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 52)**



Compound 52

[00368] **Compound 52** was prepared in a manner analogous to **Compound 3** using 6-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid, **Intermediate 52-1** in place of **Compound 2** and PyBOP in place of HATU. MS (ESI) calcd. for $C_{30}H_{24}FON_9$: 545.21, found 546.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.02 - 9.07 (m, 1H), 8.42 - 8.49 (m, 2H), 8.30 - 8.36 (m, 1H), 8.04 - 8.11 (m, 1H), 7.81 - 7.88 (m, 2H), 7.63 - 7.69 (m, 1H), 7.46 - 7.51 (m, 1H), 7.40 - 7.45 (m, 1H), 7.32 - 7.39 (m, 1H), 6.82 - 6.89 (m, 1H), 6.35 - 6.41 (m, 1H), 5. 59 - 5.68 (m, 1H), 3.03 - 3.13 (m, 1H), 2.88 - 3.00 (m, 1H), 2.64 (s, 3H), 2.53 - 2.62 (m, 1H), 2.04 - 2.17 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm): -126.82. (TFA salt)

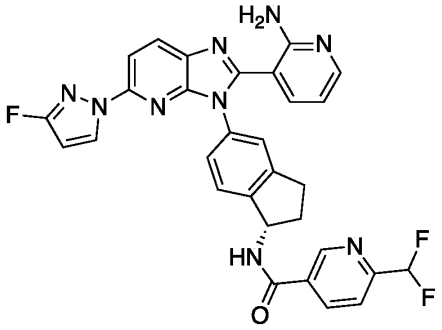
[00369] **Intermediate 52-1: (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-(3-fluoro-1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine**



Intermediate 52-1

[00370] **Intermediate 52-1** was prepared in a manner analogous to **Compound 1** using 3-fluoropyrazole in place of pyrazole. MS (ESI) calculated for $C_{23}H_{19}FN_8$: 426.17 m/z, found 427.10 $[M+H]^+$.

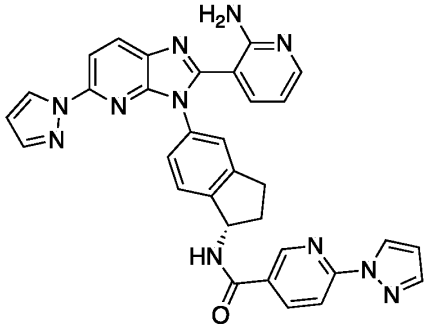
[00371] **Example 53: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-fluoro-1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 53)**



Compound 53

[00372] **Compound 53** was prepared in a manner analogous to **Compound 3** using 6-(difluoromethyl)nicotinic acid in place of 3,4-difluoro-5-anisic acid and **Intermediate 52-1** in place of **Compound 2**. MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O$: 581.19 m/z, found 582.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.13 - 9.14 (m, 1H), 8.40 - 8.46 (m, 1H), 8.30 - 8.36 (m, 1H), 8.28 - 8.29 (m, 1H), 8.01 - 8.03 (m, 1H), 7.84 - 7.86 (m, 1H), 7.76 - 7.79 (m, 1H), 7.38 - 7.44 (m, 2H), 7.19 - 7.31 (m, 2H), 6.83 - 7.20 (m, 1H), 6.45 - 6.55 (m, 1H), 6.30 - 6.35 (m, 1H), 5.83 - 5.88 (m, 1H), 2.80 - 3.15 (m, 2H), 2.51 - 2.53 (m, 1H), 2.15 - 2.18 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm): -116.08, -127.28.

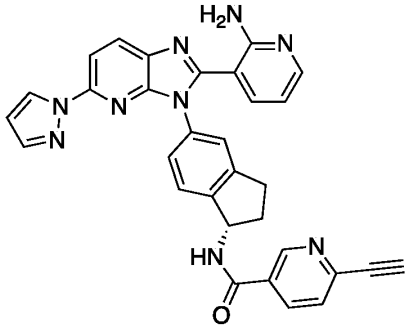
[00373] **Example 54: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(1H-pyrazol-1-yl)nicotinamide (Compound 54)**



Compound 54

[00374] **Compound 54** was prepared in a manner analogous to **Compound 3** using 6-(1H-pyrazol-1-yl)nicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{32}H_{25}N_{11}O$: 579.22 m/z, found 580.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.91 - 8.99 (m, 1H), 8.62 - 8.69 (m, 1H), 8.34 - 8.48 (m, 3H), 7.96 - 8.11 (m, 3H), 7.89 - 7.95 (m, 1H), 7.81 - 7.87 (m, 1H), 7.29 - 7.51 (m, 4H), 6.69 - 6.72 (m, 1H), 6.57 - 6.65 (m, 2H), 5.63 - 5.72 (m, 1H), 3.05 - 3.17 (m, 1H), 2.82 - 3.04 (m, 1H), 2.61 - 2.69 (m, 1H), 2.07 - 2.21 (m, 1H).

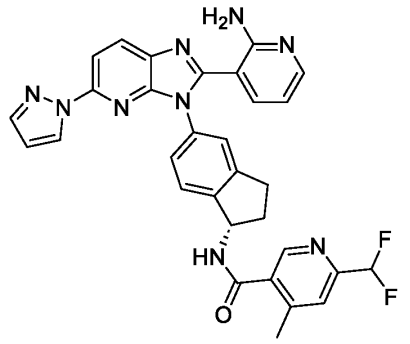
[00375] Example 55: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-ethynylnicotinamide (Compound 55)



Compound 55

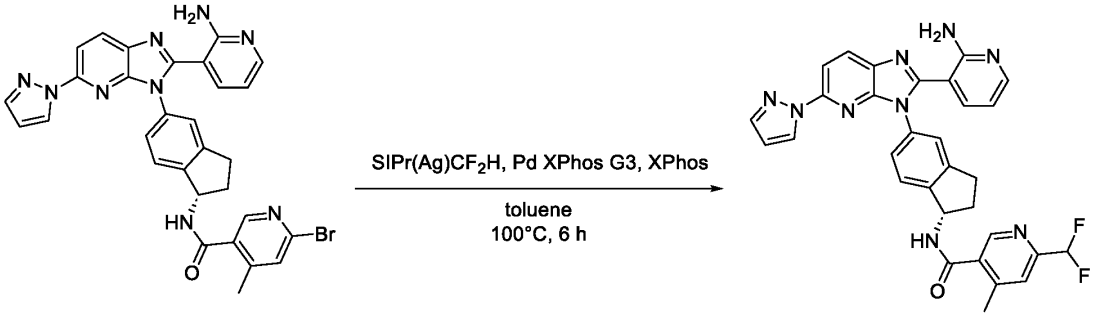
[00376] **Compound 55** was prepared in a manner analogous to **Compound 3** using 6-ethynylpyridine-3-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS(ESI) calcd. for $C_{31}H_{23}N_9O$: 537.20 m/z, found 538.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.93 - 8.99 (m, 1H), 8.40 - 8.48 (m, 1H), 8.31 - 8.39 (m, 1H), 8.23 - 8.29 (m, 1H), 8.01 - 8.08 (m, 1H), 7.89 - 7.96 (m, 1H), 7.81 - 7.88 (m, 1H), 7.72 - 7.78 (m, 1H), 7.39 - 7.47 (m, 3H), 7.24 - 7.31 (m, 1H), 6.56 - 6.67 (m, 2H), 5.52 - 5.64 (m, 1H), 4.16 - 4.21 (m, 1H), 3.07 - 3.18 (m, 1H), 2.83 - 3.06 (m, 1H), 2.61 - 2.69 (m, 1H), 2.05 - 2.21 (m, 1H). (formic acid salt)

[00377] Example 56: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b] pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)-4-methylnicotinamide (Compound 56)



Compound 56

[00378] Synthetic Route:



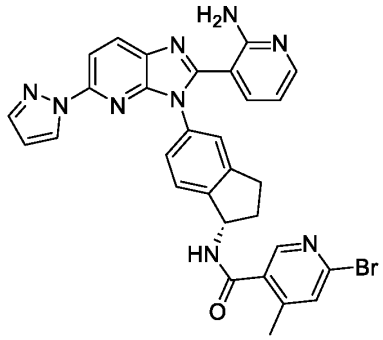
Intermediate 56-1

Compound 56

[00379] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b] pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)-4-methylnicotinamide (Compound 56)

[00380] To a solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-bromo-4-methylnicotinamide (**Intermediate 56-1**) (80 mg, 0.13 mmol, 1 equiv) and [1,3-Bis[2,6-bis(i-propyl) phenyl]-2-imidazolidinylidene] difluoromethylsilver(I) (94 mg, 0.17 mmol, 1.3 equiv) in toluene (6 mL) were added XPhos (6.3 mg, 0.013 mmol, 0.1 equiv) and XPhos Pd G3 (11 mg, 0.013 mmol, 0.1 equiv) and the resulting mixture was stirred for 6 h at 100 °C under nitrogen atmosphere. The reaction was quenched with water at room temperature. The resulting mixture was extracted with ethyl acetate 3 times. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Preparative HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.1% formic acid) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)-4-methylnicotinamide (**Compound 56**) (6.4 mg, 8%) as a white solid. MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$: 577.22 m/z, found 578.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.64 (s, 1H), 8.35 - 8.37 (m, 2H), 7.94 - 8.03 (m, 2H), 7.94 - 7.97 (m, 1H), 7.66 (s, 1H), 7.49 - 7.51 (m, 1H), 7.33 - 7.39 (m, 1H), 7.26 - 7.29 (m, 2H), 6.57 - 7.12 (m, 1H), 6.56 - 7.57 (m, 1H), 6.45 - 6.49 (m, 1H), 5.57 - 5.62 (m, 1H), 2.89 - 3.15 (m, 2H), 2.51 - 2.53 (m, 1H), 2.41 - 2.48 (m, 3H), 1.95 - 2.18 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm): -115.64.

[00381] Intermediate 56-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-bromo-4-methylnicotinamide



Intermediate 56-1

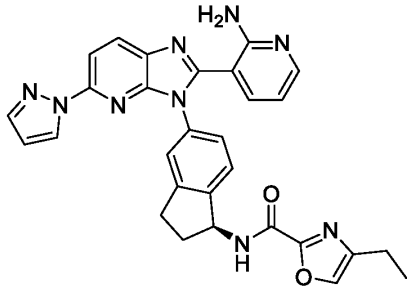
[00382] **Intermediate 56-1** was prepared in a manner analogous to **Compound 3** using 6-bromo-4-methylnicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{30}H_{24}BrN_9O$: 605.13 m/z, found 605.95, 607.95 $[M+H, M+H+2]^+$.

[00383] The following compounds were prepared analogous to the synthetic preparation in Example 56 (Compound 56).

[00384] **Table 4.** Characterization data of compounds prepared analogously to compound 56.

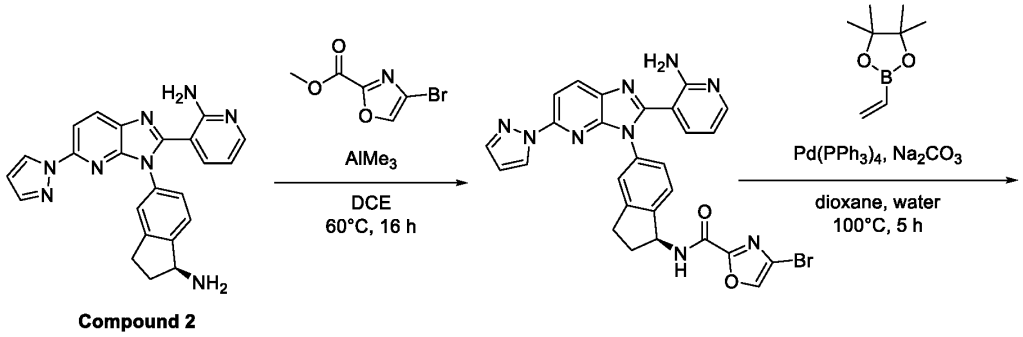
Cpd ID	Characterization Data
97	MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O$, 581.19 m/z, found 582.10 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.78 - 9.01 (m, 1H), 8.22 - 8.50 (m, 2H), 7.88 - 8.13 (m, 2H), 8.68 - 7.87 (m, 2H), 7.23 - 7.55 (m, 4H), 6.80 - 7.22 (m, 1H), 6.37 - 6.79 (m, 2H), 5.45 - 5.70 (m, 1H), 2.80 - 3.18 (m, 2H), 2.60 - 2.68 (m, 1H), 1.83 - 2.14 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -101.82, -116.64.
102	MS (ESI) calcd. for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found 579.10 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.20 - 9.45 (m, 1H), 8.92 (s, 1H), 8.40 - 8.59 (m, 1H), 8.20 - 8.35 (m, 1H), 8.08 - 8.20 (m, 3H), 7.95 - 8.08 (m, 1H), 7.55 - 7.70 (m, 1H), 7.40 - 7.50 (m, 2H), 7.30 - 7.40 (m, 1H), 6.90 - 7.28 (m, 1H), 6.62 - 6.75 (m, 1H), 5.40 - 5.78 (m, 1H), 3.00 - 3.15 (m, 1H), 2.18 - 3.00 (m, 1H), 2.45 - 2.50 (m, 4H), 2.00 - 2.20 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm); -116.12.
121	MS (ESI) calcd. for $C_{29}H_{21}F_3N_{10}O$, 582.55 m/z, found 583.25 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.42 (m, 1H), 9.34 (s, 1H), 8.26 - 8.50 (m, 2H), 8.12 (s, 2H), 8.00 - 8.10 (m, 2H), 7.40 - 7.55 (m, 2H), 7.30 - 7.40 (m, 1H), 7.22 - 7.30 (m, 1H), 6.85 - 7.20 (m, 3H), 6.35 - 6.50 (m, 1H), 5.60 - 5.78 (m, 1H), 3.00 - 3.15 (m, 1H), 2.85 - 3.00 (m, 1H), 2.56 - 2.65 (m, 1H), 2.00 - 2.15 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm); -117.74, -126.65.

[00385] **Example 57: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-ethyloxazole-2-carboxamide (Compound 57)**

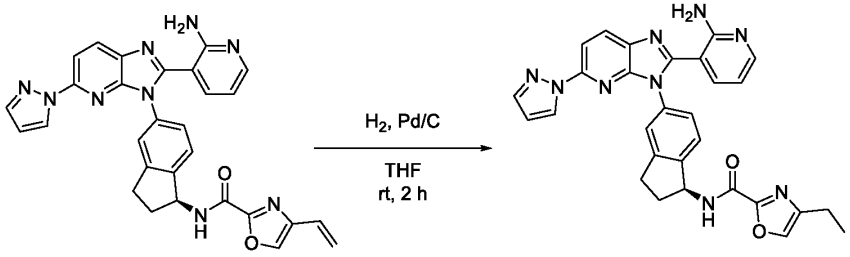


Compound 57

[00386] Synthetic Route:



Compound 2



Compound 57

[00387] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-bromooxazole-2-carboxamide

[00388] To a solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (180 mg, 0.441 mmol, 1 equiv) in DCE (5 mL) was added $AlMe_3$ (1.15 mL, 2.21 mmol, 2M in toluene, 5 equiv) at 0°C. Then methyl 4-bromooxazole-2-carboxylate (107 mg, 0.485 mmol, 1.1 equiv) was added. The resulting mixture was maintained under nitrogen and stirred at 60 °C for 16 h. After cooling to room temperature, the reaction was quenched with water. The resulting mixture was extracted with ethyl acetate 3 times. The organic layers were combined, dried over anhydrous Na_2SO_4,

filtered and concentrated. The crude product was purified by reverse-phase flash column chromataography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-bromooxazole-2-carboxamide (80 mg, 31%) as a yellow solid. MS (ESI) calcd. for $C_{27}H_{20}BrN_9O_2$: 581.09 m/z, found 582.00 $[M+H]^+$.

[00389] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-vinyloxazole-2-carboxamide

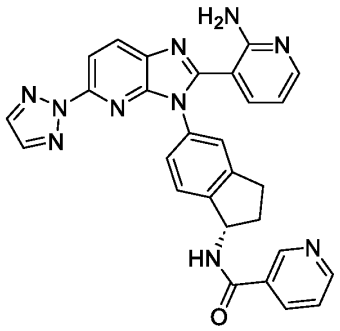
[00390] To a solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-bromooxazole-2-carboxamide (60 mg, 0.103 mmol, 1 equiv) in 1,4-dioxane (1.6 mL) and water (0.4 mL) was added 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (159 mg, 1.03 mmol, 1 equiv), $Pd(PPh_3)_4$ (12 mg, 0.010 mmol, 0.1 equiv) and Na_2CO_3 (55 mg, 0.52 mmol, 5 equiv). The resulting mixture was maintained under nitrogen atmosphere and stirred at 100 °C for 5 h. After cooling to room temperature, the reaction was quenched with water. The resulting mixture was extracted with ethyl acetate 3 times. The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by reverse-phase flash column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-vinyloxazole-2-carboxamide (40 mg, 73%) as a yellow solid. MS (ESI) calcd. for $C_{29}H_{23}N_9O_2$: 529.20 m/z found 530.10 $[M+H]^+$.

[00391] Step 3: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-ethyloxazole-2-carboxamide (Compound 57)

[00392] A mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-vinyloxazole-2-carboxamide (30 mg, 0.057 mmol, 1 equiv) and 10% Pd/C (30 mg, 0.026 mmol, 0.5 equiv) in THF (5 mL) was stirred for 1 h at room temperature under H_2 atmosphere. The mixture was filtered and concentrated. The crude product was purified by Preparative HPLC on a XSelect CSH Prep C18 OBD Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-ethyloxazole-2-carboxamide (trifluoroacetic acid salt) (**Compound 57**) (5.9 mg, 16%) as an off-white solid. MS (ESI) calcd. for $C_{29}H_{25}N_9O_2$: 531.21 m/z, found 532.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.31 - 8.52 (m, 2H), 7.93 - 8.12 (m, 3H), 7.75 - 7.90 (m, 1H), 7.65 - 7.74 (m, 1H), 7.40 - 7.51 (m, 1H), 7.25 - 7.39 (m, 2H), 6.68 - 6.89 (m, 1H), 6.48 - 6.64 (m, 1H),

5.47 - 5.64 (m, 1H), 2.98 - 3.18 (m, 1H), 2.80 - 2.97 (m, 1H), 2.56 - 2.68 (m, 3H), 2.08 - 2.27 (m, 1H), 1.10 - 1.30 (m, 3H).

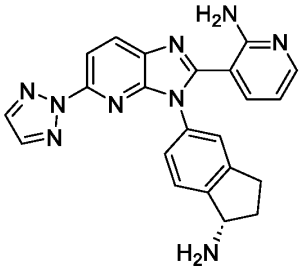
[00393] Example 58: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)nicotinamide (Compound 58)



Compound 58

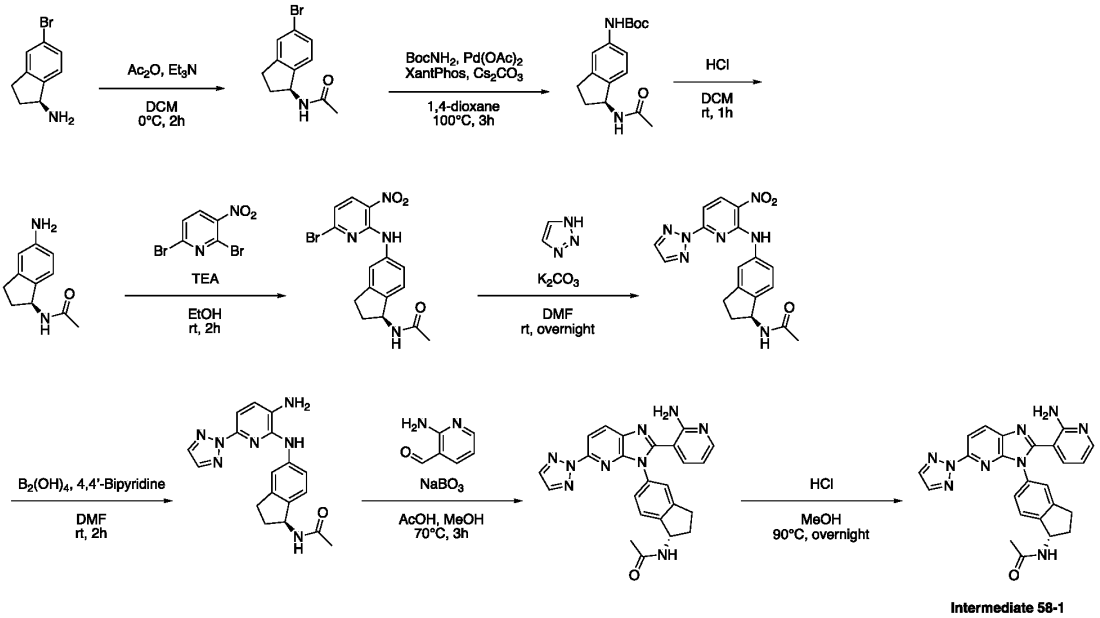
[00394] **Compound 58** was prepared in a manner analogous to **Compound 3** using nicotinic acid in place of 3,4-difluoro-5-anisic acid and **Intermediate 58-1** in place of **Compound 2**. MS (ESI) calcd. for $C_{28}H_{22}N_{10}O$: 514.20 m/z, found 515.15 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm): 9.10 - 9.11 (m, 1H), 8.76 - 8.77 (m, 1H), 8.50 - 8.52 (m, 1H), 8.37 - 8.38 (m, 1H), 8.05 - 8.11 (m, 4H), 7.85 - 7.87 (m, 1H), 7.61 - 7.63 (m, 1H), 7.45 - 7.48 (m, 2H), 7.36 - 7.38 (m, 1H), 6.85 - 6.87 (m, 1H), 5.63 - 5.67 (m, 1H), 3.03 - 3.05 (m, 1H), 2.94 - 2.96 (m, 1H), 2.50 - 2.51 (m, 1H), 2.10 - 2.12 (m, 1H). (TFA salt)

[00395] Intermediate 58-1: (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-(2*H*-1,2,3-triazol-2-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine



Intermediate 58-1

[00396] Synthetic Route:



Intermediate 58-1

[00397] Step 1: Synthesis of (*S*)-*N*-(5-bromo-2,3-dihydro-1*H*-inden-1-yl)acetamide

[00398] To a mixture of (S)-5-bromo-2,3-dihydro-1H-inden-1-amine (74 g, 350 mmol, 1 equiv) and triethylamine (106 g, 1.05 mol, 3 equiv) in dichloromethane (1.5 L) was added acetic anhydride (55.2 g, 526 mmol, 1.5 equiv) at 0°C and the mixture was stirred at 0°C for 2 h. The reaction mixture was quenched by addition of water and extracted 3 times with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was re-crystallized from petroleum ether to afford (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)acetamide (90 g, 83% yield) as a white solid. MS (ESI) calculated for $C_{11}H_{12}BrNO$: 253.01, found 254.00 $[M+H]^+$, 256.00 $[M+H+2]^+$.

[00399] **Step 2: Synthesis of *tert*-butyl (*S*)-(1-acetamido-2,3-dihydro-1*H*-inden-5-yl)carbamate**

[00400] To a mixture of *N*-[(1S)-5-bromo-2,3-dihydro-1*H*-inden-1-yl]acetamide (40 g, 157 mmol, 1 equiv), *tert*-butyl carbamate (27.66 g, 236 mmol, 1.5 equiv), XantPhos (9.11 g, 15.7 mmol, 10 mol%), palladium (II) acetate (3.54g, 15.7 mmol, 10 mol%), and cesium carbonate (154 g, 472 mmol, 10 mol%) was added 1,4-dioxane (300 mL) under nitrogen atmosphere. The resulting mixture was stirred for 3 h at 100°C. The reaction mixture was quenched by addition of water and extracted 3 times with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using an eluent of petroleum ether/dichloromethane/methanol (70:27:3) to afford *tert*-butyl *N*-[(1S)-1-acetamido-2,3-dihydro-1*H*-inden-5-yl]carbamate (43.1 g, 48%). MS (ESI) calculated for $C_{16}H_{22}N_2O_3$: 290.16 m/z, found 289.05 $[M-H]^-$.

[00401] Step 3: Synthesis of (S)-*N*-(5-amino-2,3-dihydro-1*H*-inden-1-yl)acetamide

[00402] To a stirred solution of *tert*-butyl *N*-[(1S)-1-acetamido-2,3-dihydro-1*H*-inden-5-yl]carbamate (43.1 g, 148 mmol, 1 equiv) in dichloromethane (180 mL) was added 4N hydrochloric acid in 1,4-dioxane (185 mL, 742 mmol, 5 equiv). The reaction mixture was stirred for 1h at room temperature. The reaction mixture was concentrated *in vacuo* and re-crystallized from ethyl acetate to afford *N*-[(1S)-5-amino-2,3-dihydro-1*H*-inden-1-yl]acetamide (hydrochloride salt) (23 g, 81%) as a white solid. MS (ESI) calculated for $C_{11}H_{14}N_2O$: 190.11 m/z, found 191.15 $[M+H]^+$.

[00403] Step 4: Synthesis of (S)-N-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide

[00404] A solution of (S)-N-(5-amino-2,3-dihydro-1H-inden-1-yl)acetamide (17 g, 89 mmol), 2,6-dibromo-3-nitropyridine (25.19 g, 89.36 mmol) and triethylamine (45.21 g, 446.8 mmol) in EtOH (200 mL) was stirred at room temperature for 2 h. The reaction was quenched with water and the precipitated solids were collected by filtration, washing with EtOH/H_2O=1:1 to afford (S)-N-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (26 g, 74.37% yield) as an orange solid. MS (ESI) calcd. for $C_{16}H_{15}BrN_4O_3$: 390.03, found 413.00 $[M+Na]^+$, 415.00 $[M+Na+2]^+$.

[00405] Step 5: Synthesis of (S)-N-(5-((3-nitro-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide

[00406] To a solution of (S)-N-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (50.0 g, 128 mmol) in DMF (1.5 L) was added K_2CO_3 (52.99 g, 383.4 mmol) and 1H-1,2,3-triazole (17.65 g, 255.6 mmol). The resulting mixture was stirred at room temperature overnight. The product was precipitated by the addition of H_2O. The precipitated solids were collected by filtration and washed with water. The crude product was re-crystallized from petroleum ether to afford (S)-N-(5-((3-nitro-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (45 g, 93%) as a yellow solid. MS (ESI) calculated for $C_{18}H_{17}N_7O_3$: 379.14 m/z, found 380.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.98 (s, 2H), 7.79 (d, J = 2.1 Hz, 1H), 7.68 (dd, J = 8.3, 2.1 Hz, 1H), 7.17 (d, J = 8.1 Hz, 1H), 7.13 – 7.04 (m, 2H), 5.18 (t, J = 7.4 Hz, 1H), 2.93 – 2.85 (m, 1H), 2.80 – 2.70 (m, 1H), 2.43 – 2.31 (m, 1H), 1.87 (s, 3H), 1.82 – 1.71 (m, 1H).

[00407] Step 6: Synthesis of (S)-N-(5-((3-amino-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide

[00408] To a cooled (0°C) solution of (S)-N-(5-((3-nitro-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (1.3 g, 3.4 mmol) and 4,4-bypyridine (27 mg, 0.17 mmol) in DMF (25 mL) was added $B_2(OH)_4$ (0.92 g, 10 mmol). The resulting mixture was

stirred at room temperature for 2 h. The reaction was quenched with H_2O. The resulting mixture was extracted with ethyl acetate 3 times. The organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The residue obtained was purified by silica gel column chromatography using a gradient of ethyl acetate in petroleum ether to afford (S)-N-(5-((3-amino-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (800 mg, 67%) as a yellow solid. MS (ESI) calcd. for $C_{18}H_{19}N_7O$: 349.17 m/z, found 350.15 $[M+H]^+$.

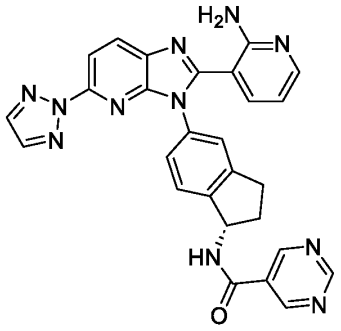
[00409] Step 7: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide

[00410] To a solution of (S)-N-(5-((3-amino-6-(2H-1,2,3-triazol-2-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (700 mg, 2.00 mmol) in AcOH (10 mL) and MeOH (2 mL) was added 2-aminonicotinaldehyde (269 mg, 2.20 mmol) and sodium perborate (328 mg, 4.00 mmol). The resulting mixture was stirred at 70°C for 3 h. The solvent was removed by distillation under vacuum. The resulting mixture was purified by reverse-phase flash column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (520 mg, 57%) as a reddish brown solid. MS (ESI) calcd. for $C_{24}H_{21}N_9O$: 451.19 m/z, found 452.20 $[M+H]^+$.

[00411] Step 8: Synthesis of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Intermediate 58-1)

[00412] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (520 mg, 1.152 mmol) in HCl (20 mL, concentrated) and MeOH (20 mL) was stirred at 90°C overnight. The solvent was removed by distillation under vacuum to afford (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Intermediate 58-1**) (400 mg, 85%) crude as a yellow solid. MS (ESI) calcd. for $C_{22}H_{19}N_9$: 409.18 m/z, found 410.20 $[M+H]^+$.

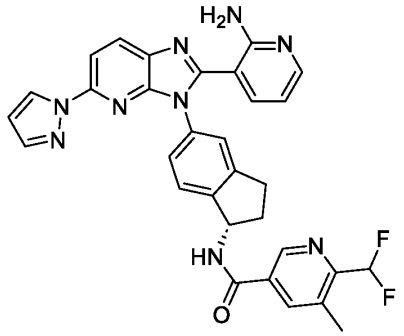
[00413] Example 59: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyrimidine-5-carboxamide (Compound 59)



Compound 59

[00414] **Compound 59** was prepared in a manner analogous to **Compound 3** using pyrimidine-5-carboxylic acid in place of 3,4-difluoro-5-anisic acid, **Intermediate 58-1** in place of **Compound 2**, and PyBOP in place of HATU. MS (ESI) calcd. for $C_{27}H_{21}N_{11}O$: 515.19 m/z, found 516.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.23 - 9.33 (m, 3H), 8.49 - 8.52 (m, 1H), 8.04 - 8.15 (m, 4H), 7.80 - 7.83 (m, 1H), 7.37 - 7.51 (m, 3H), 6.80 - 6.84 (m, 1H), 5.62 - 5.67 (m, 1H), 2.89 - 3.15 (m, 2H), 2.51 - 2.53 (m, 1H), 2.06 - 2.13 (m, 1H). (TFA salt)

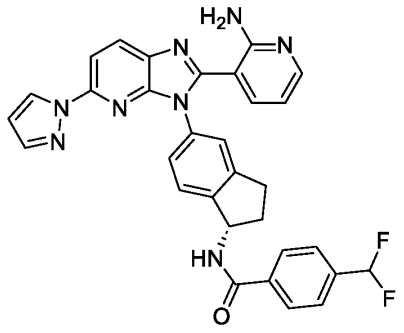
[00415] **Example 60: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)-5-methylnicotinamide (Compound 60)**



Compound 60

[00416] **Compound 60** was prepared in a manner analogous to **Compound 56** (via **Intermediate 56-1**) using 6-bromo-5-methylnicotinic acid in place of 6-bromo-4-methylnicotinic acid. MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$: 577.22 m/z, found 578.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.88 (s, 1H), 8.24 - 8.40 (m, 2H), 8.19 (s, 1H), 7.95 - 8.02 (m, 1H), 7.82 - 7.94 (m, 1H), 7.67 - 7.81 (m, 1H), 7.31 - 7.45 (m, 2H), 7.12 - 7.30 (m, 2H), 6.65 - 7.11 (m, 1H), 6.47 - 6.56 (m, 1H), 6.37 - 6.46 (m, 1H), 5.48 - 5.68 (m, 1H), 2.77 - 3.13 (m, 2H), 2.52 - 2.61 (m, 1H), 2.38 - 2.48 (m, 3H), 1.90 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -116.07.

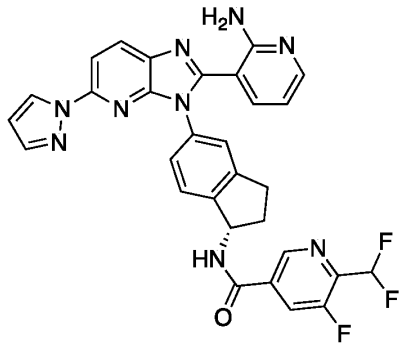
[00417] Example 61: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-4-(difluoromethyl)benzamide (Compound 61)



Compound 61

[00418] Compound 61 was prepared in a manner analogous to **Compound 3** using 4-(difluoromethyl)benzoic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{24}F_2N_8O$: 562.20 m/z, found 563.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.42 - 8.44 (m, 1H), 8.37 - 8.38 (m, 1H), 8.05 - 8.07 (m, 4H), 7.93 - 7.96 (m, 2H), 7.79 - 7.82 (m, 2H), 7.67 - 7.69 (m, 1H), 7.40 - 7.46 (m, 2H), 7.22 - 7.38 (m, 1H), 6.85 - 6.94 (m, 1H), 6.56 - 6.57 (m, 1H), 5.61 - 5.65 (m, 1H), 3.03 - 3.05 (m, 1H), 2.94 - 2.96 (m, 1H), 2.50 - 2.51 (m, 1H), 2.10 - 2.12 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm): -110.38. (TFA salt)

[00419] Example 62: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)-5-fluoronicotinamide (Compound 62)

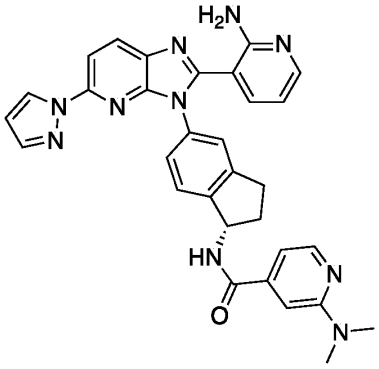


Compound 62

[00420] Compound 62 was prepared in a manner analogous to **Compound 60** (via **Intermediate 56-1**) using TCFH in place of HATU, N-methyl imidazole in place of N,N-diisopropylethylamine, acetonitrile in place of N,N-dimethylformamide and 6-bromo-5-fluoronicotinic acid in place of 6-bromo-5-methylnicotinic acid. MS (ESI) calcd. for

$C_{30}H_{22}F_3N_9O$: 581.19 m/z, found 582.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.33 - 9.36 (m, 1H), 9.01 (s, 1H), 8.34 - 8.58 (m, 3H), 8.00 - 8.15 (m, 2H), 7.82 - 7.83 (m, 1H), 7.73 - 7.76 (m, 1H), 7.45 - 7.48 (m, 2H), 7.04 - 7.39 (m, 2H), 6.77 - 6.81 (m, 1H), 6.58 - 6.59 (m, 1H), 5.61 - 5.68 (m, 1H), 2.89 - 3.12 (m, 2H), 2.51 - 2.53 (m, 1H), 2.07 - 2.18 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm): -117.82, -126.49. (TFA salt)

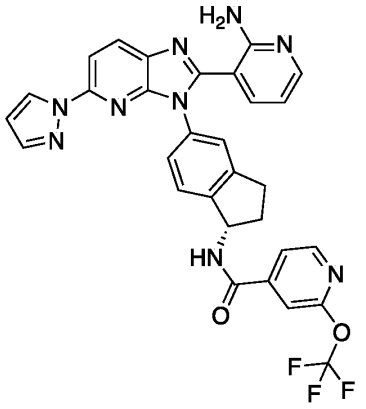
[00421] Example 63: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(dimethylamino)isonicotinamide (Compound 63)



Compound 63

[00422] **Compound 63** was prepared in a manner analogous to **Compound 3** using 2-(dimethylamino)isonicotinic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{31}H_{28}N_{10}O$: 556.24 m/z, found 557.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.31 - 8.39 (m, 2H), 8.13 - 8.18 (m, 1H), 7.96 - 8.07 (m, 2H), 7.79 - 7.87 (m, 1H), 7.31 - 7.49 (m, 4H), 6.97 - 7.05 (m, 2H), 6.43 - 6.58 (m, 2H), 5.57 - 5.69 (m, 1H), 2.98 - 3.13 (m, 6H), 2.81 - 2.97 (m, 2H), 2.53 - 2.59 (m, 1H), 2.07 - 2.13 (m, 1H).

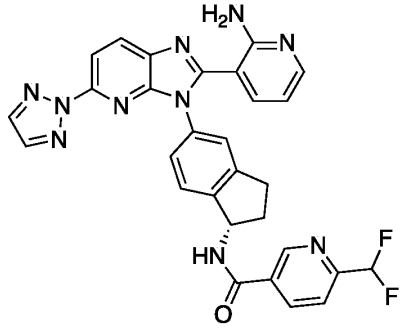
[00423] Example 64: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(trifluoromethoxy)isonicotinamide (Compound 64)



Compound 64

[00424] **Compound 64** was prepared in a manner analogous to **Compound 3** using 2-(trifluoromethoxy)isonicotinic acid in place of 3,4-difluoro-5-anisic acid and PyBOP in place of HATU. MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O_2$: 597.18 m/z, found 598.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.48 - 8.55 (m, 1H), 8.30 - 8.40 (m, 2H), 7.97 - 8.05 (m, 1H), 7.89 - 7.97 (m, 1H), 7.80 - 7.89 (m, 1H), 7.75 - 80 (m, 1H), 7.67 (s, 1H), 7.36 - 7.42 (m, 2H), 7.22 - 7.33 (m, 2H), 6.51 - 6.58 (m, 1H), 6.41 - 6.50 (m, 1H), 5.55 - 5.66 (m, 1H), 2.82 - 3.11 (m, 2H), 2.53 - 2.61 (m, 1H), 2.00 - 2.17 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -55.18. (formic acid salt)

[00425] **Example 65: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(2H-1,2,3-triazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 65)**

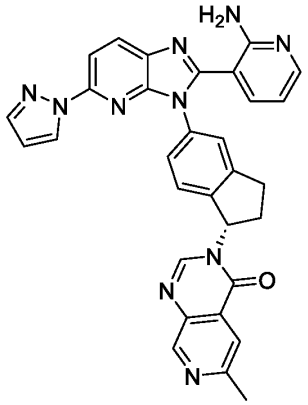


Compound 65

[00426] **Compound 65** was prepared in a manner analogous to **Compound 3** using 6-(difluoromethyl)nicotinic acid in place of 3,4-difluoro-5-anisic acid, PyBOP in place of HATU and **Intermediate 58-1** in place of **Compound 2**. MS (ESI) calcd. for $C_{29}H_{22}F_2N_{10}O$: 564.19 m/z, found 565.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.15 - 9.25 (m, 1H), 8.38 - 8.52 (m, 2H), 8.13 (s, 2H), 7.97 - 8.08 (m, 2H), 7.78 - 7.85 (m, 1H), 7.39 - 7.48 (m, 2H), 7.24 - 7.35 (m, 2H), 7.85 - 7.03 (m, 1H), 6.40 - 6.50 (m, 1H), 5.61 - 5.72 (m, 1H), 2.85 - 3.15 (m, 2H),

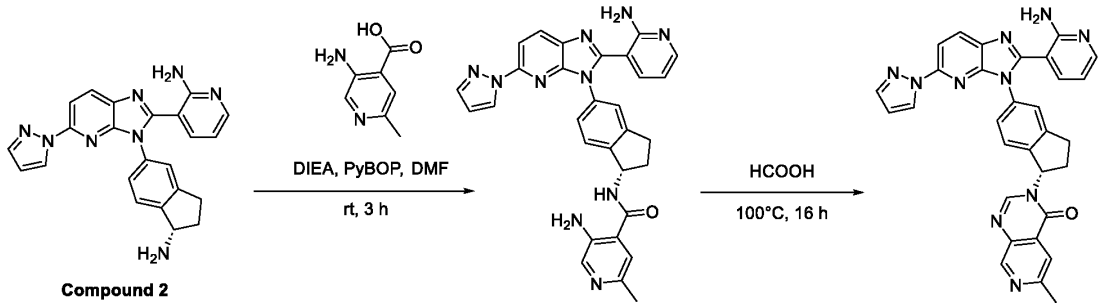
2.52 - 2.64 (m, 1H), 2.00 - 2.19 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -116.04. (formic acid salt).

[00427] Example 66: (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylpyrido[3,4-d]pyrimidin-4(3H)-one (Compound 81)



Compound 81

[00428] Synthetic Route:



Compound 2 **Compound 81**

[00429] Step 1: Synthesis of (S)-5-amino-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-methylisonicotinamide

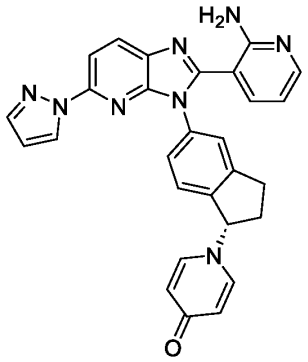
[00430] To a solution of 5-amino-2-methylpyridine-4-carboxylic acid hydrochloride (41.6 mg, 0.220 mmol) in DMF (1 mL) was added DIEA (85.4 mg, 0.660 mmol), 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (90 mg, 0.22 mmol) and HATU (101 mg, 0.264 mmol). The resulting mixture was maintained under nitrogen and stirred at room temperature for 3 h. The reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by reverse-phase flash column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-5-amino-N-

(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-methylisonicotinamide (90 mg, 75% yield) as a yellow solid. MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found: 543.15 $[M+H]^+$.

[00431] Step 2: Synthesis of (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylpyrido[3,4-d]pyrimidin-4(3H)-one (Compound 81)

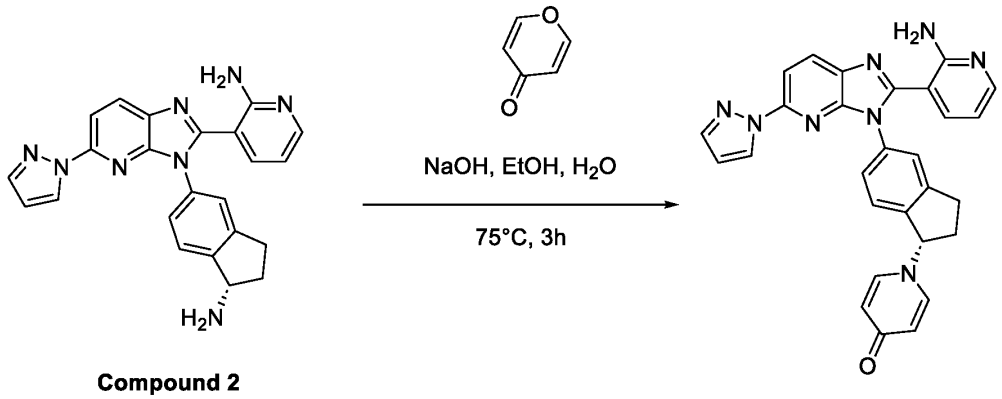
[00432] A solution of 5-amino-N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-methylpyridine-4-carboxamide (80 mg, 0.15 mmol) in formic acid (2 mL) was stirred for 16 h at 100°C. The reaction mixture was cooled to room temperature and purified by Prep-HPLC on a XBridge Prep OBD C18 Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylpyrido[3,4-d]pyrimidin-4(3H)-one (Compound 81) (TFA salt) (16.2 mg, 16% yield) as a yellow solid. MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found 553.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 8.96 - 9.04 (m, 1H), 8.37 - 8.52 (m, 2H), 8.15 - 8.25 (m, 1H), 8.04 - 8.12 (m, 1H), 8.00 - 8.03 (m, 1H), 7.88 - 7.95 (m, 1H), 7.80 - 7.87 (m, 1H), 7.74 - 7.86 (m, 1H), 7.53 - 7.64 (m, 1H), 7.28 - 7.42 (m, 2H), 6.80 - 6.93 (m, 1H), 6.53 - 6.62 (m, 1H), 6.26 - 6.40 (m, 1H), 3.19 - 3.37 (m, 1H), 2.98 - 3.17 (m, 1H), 2.68 - 2.87 (m, 1H), 2.60 - 2.67 (m, 3H), 2.25 - 2.50 (m, 1H).

[00433] Example 67: (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyridin-4(1H)-one (Compound 83)



Compound 83

[00434] Synthetic Route:



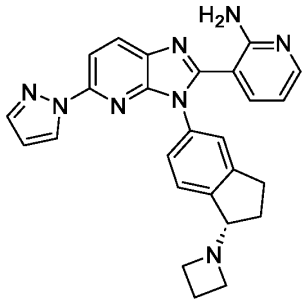
Compound 2

Compound 83

[00435] Step 1: Synthesis of (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyridin-4(1H)-one (Compound 83)

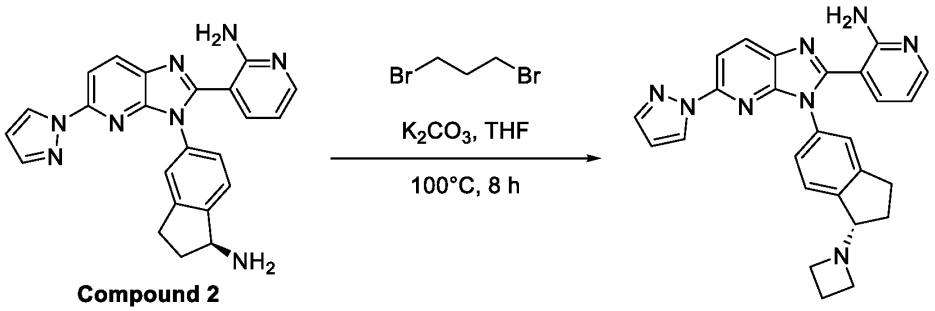
[00436] A mixture of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol) and pyran-4-one (25.9 mg, 0.270 mmol) in EtOH (5 mL) was treated with NaOH (14.7 mg, 0.367 mmol) in water (2 mL) at room temperature. The resulting mixture was stirred for 3 h at 75 °C. The reaction was quenched by the addition of water (20 mL), extracted with EtOAc (3 x 30 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a YMC-Actus Triart C18 ExRS column using a gradient of acetonitrile in water (+ 10 mmol/L NH_4HCO_3) to (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)pyridin-4(1H)-one (**Compound 83**) (19.2 mg, 16% yield) as an off-white solid. MS (ESI) calcd. for $C_{28}H_{22}N_8O$, 486.19 m/z, found 487.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm): 8.33 - 8.42 (m, 2H), 8.02 - 8.10 (m, 1H), 7.96 - 8.01 (m, 1H), 7.80 - 7.88 (m, 1H), 7.67 - 7.73 (m, 2H), 7.52 - 7.58 (m, 1H), 7.31 - 7.38 (m, 1H), 7.25 - 7.30 (m, 1H), 7.19 - 7.24 (m, 1H), 6.54 - 6.60 (m, 1H), 6.46 - 6.51 (m, 1H), 6.18 - 6.25 (m, 2H), 5.77 - 5.86 (m, 1H), 3.15 - 3.27 (m, 1H), 2.94 - 3.08 (m, 1H), 2.73 - 2.86 (m, 1H), 2.19 - 2.28 (m, 1H).

[00437] Example 68: (S)-3-(3-(1-(azetidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 87)



Compound 87

[00438] Synthetic Route:



Compound 2 **Compound 87**

[00439] **Step 1: Synthesis of (S)-3-(3-(1-(azetidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 87)**

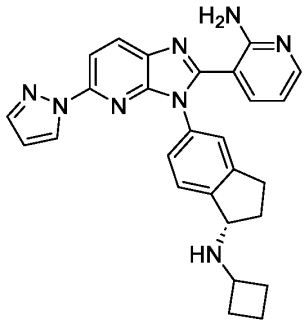
[00440] To a solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol) in THF (2 mL) was added K_2CO_3 (102 mg, 0.735 mmol) and 1,3-dibromopropane (98.9 mg, 0.490 mmol). Then the reaction mixture was stirred at 100°C for 8 h. After cooling to room temperature the reaction was quenched with water (50 mL). The resulting mixture was extracted with ethyl acetate (3 x 50 mL). The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC on a YMC Triart C18 ExRs column using a gradient of acetonitrile in water (+ 10 mmol/L NH_4HCO_3) to afford (S)-3-(3-(1-(azetidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 87**) (6.3 mg, 6% yield) as a white solid. MS (ESI) calcd. for $C_{26}H_{24}N_8$, 448.21, found 449.20. $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.30 - 8.40 (m, 2H), 7.90 - 8.03 (m, 2H), 7.75 - 7.85 (m, 1H), 7.38 - 7.44 (m, 1H), 7.31 - 7.37 (m, 1H), 7.15 - 7.19 (m, 2H), 6.50 - 6.57 (m, 1H), 6.38 - 6.45 (m, 1H), 3.83 - 3.89 (m, 1H), 3.31- 3.39 (Sm, 2H), 3.15 - 3.25 (m, 2H), 2.91 - 3.01 (m, 1H), 2.69 - 2.84 (m, 1H), 2.02 - 2.17 (m, 1H), 1.92 - 2.07 (m, 2H), 1.83 - 1.90 (m, 1H).

[00441] The following compounds were prepared analogous to the synthetic preparation in Example 68 (Compound 87).

[00442] **Table 4A.** Characterization data of compounds prepared analogously to compound 87.

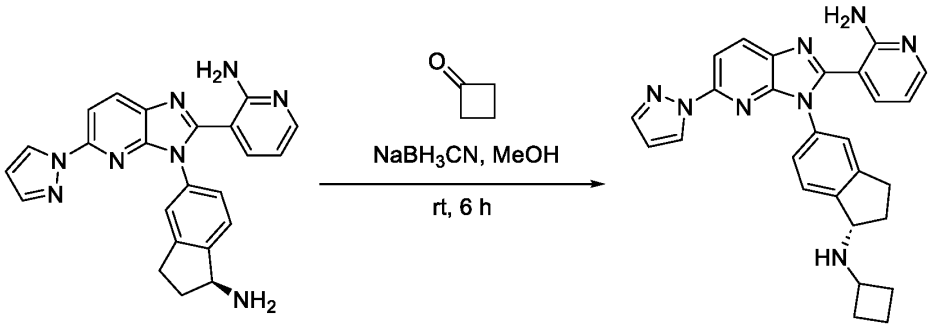
Cpd ID	Characterization Data
330	MS (ESI) calcd. for $C_{27}H_{26}N_8$: 462.22 m/z, found, 463.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.45 (m, 2H), 7.89 - 8.09 (m, 2H), 7.75 - 7.87 (m, 1H), 7.45 - 7.58 (m, 1H), 7.33 - 7.42 (m, 1H), 7.22 - 7.32 (m, 1H), 7.13 - 7.21 (m, 1H), 6.51 - 6.61 (m, 1H), 6.35 - 6.45 (m, 1H), 4.18 - 4.41 (m, 1H), 2.93 - 3.15 (m, 1H), 2.73 - 2.92 (m, 1H), 2.57 - 2.72 (m, 4H), 1.99 - 2.35 (m, 2H), 1.61 - 1.83 (m, 4H).
457	MS (ESI) calcd. for $C_{27}H_{28}N_8O$, 480.24 m/z, found, 481.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.40 (m, 2H), 7.98 - 8.04 (m, 1H), 7.92 - 7.98 (m, 1H), 7.79 - 7.85 (m, 1H), 7.43 - 7.51 (m, 1H), 7.29 - 7.36 (m, 1H), 7.16 - 7.28 (m, 2H), 6.53 - 6.61 (m, 1H), 6.40 - 6.49 (m, 1H), 4.41 - 4.49 (m, 1H), 3.40 - 3.51 (m, 2H), 3.23 (s, 3H), 2.77 - 2.96 (m, 2H), 2.49 - 2.54 (m, 2H), 2.19 (s, 3H), 2.09 - 2.18 (m, 1H), 1.97 - 2.10 (m, 1H).

[00443] **Example 69: (S)-3-(3-(1-(cyclobutylamino)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 88)**



Compound 88

[00444] Synthetic Route:



Compound 2 **Compound 88**

[00445] **Step 1: Synthesis of (S)-3-(3-(1-(cyclobutylamino)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine**

[00446] To a cooled (0°C) solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Example 2**) (60 mg, 0.15 mmol) and cyclobutanone (20.7 mg, 0.294 mmol) in MeOH (2 mL) was added $NaBH_3CN$ (18.6

mg, 0.294 mmol). The resulting mixture was stirred at room temperature for 3 h. The reaction was quenched by the addition of water (30 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 50 mL) and dried over anhydrous Na_2SO_4. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC on XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-(cyclobutylamino)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (TFA salt) (32.7 mg, 48% yield) as an off-white solid. MS (ESI) calcd. for $C_{27}H_{26}N_8$: 462.23 m/z, found: 463.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.38 - 8.46 (m, 1H), 8.31 - 8.37 (m, 1H), 8.02 - 8.09 (m, 1H), 7.96 - 8.01 (m, 1H), 7.79 - 7.85 (m, 1H), 7.64 - 7.76 (m, 2H), 7.52 - 7.59 (m, 1H), 7.37 - 7.47 (m, 1H), 6.66 - 6.76 (m, 1H), 6.53 - 6.60 (m, 1H), 4.71 - 4.81 (m, 1H), 3.81 - 3.94 (m, 1H), 3.07 - 3.23 (m, 1H), 2.86 - 3.03 (m, 1H), 2.45 - 2.50 (m, 1H), 2.06 - 2.25 (m, 5H), 1.72 - 1.88 (m, 2H).

[00447] The following compounds were prepared analogous to the synthetic preparation in Example 69 (Compound 88).

[00448] **Table 5A.** Characterization data of compounds prepared analogously to compound 88.

Cpd ID	Characterization Data
70	MS (ESI) calcd. for $C_{30}H_{27}N_9$, 513.24 m/z, found 514.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.46 (m, 3H), 7.99 - 8.07 (m, 1H), 7.92 - 7.98 (m, 1H), 7.82 - 7.88 (m, 1H), 7.74 - 7.81 (m, 1H), 7.49 - 7.55 (m, 1H), 7.27 - 7.36 (m, 3H), 7.18 - 7.26 (m, 1H), 6.55 - 6.62 (m, 1H), 6.49 - 6.54 (m, 1H), 4.28 - 4.31 (m, 1H), 3.72 - 3.86 (m, 2H), 2.94 - 3.06 (m, 1H), 2.71 - 2.88 (m, 1H), 2.36 - 2.47 (m, 4H), 1.88 - 2.04 (m, 1H).
84	MS (ESI) calcd. for $C_{30}H_{25}F_2N_9$, 549.22 m/z, found 550.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.69 - 8.72 (m, 1H), 8.31 - 8.42 (m, 2H), 7.96 - 8.10 (m, 3H), 7.78 - 7.83 (m, 1H), 7.64 - 7.73 (m, 1H), 7.46 - 7.55 (m, 1H), 7.31 - 7.39 (m, 1H), 7.09 - 7.24 (m, 2H), 6.77 - 6.92 (m, 1H), 6.53 - 6.60 (m, 1H), 6.44 - 6.51 (m, 1H), 4.12 - 4.26 (m, 1H), 3.81 - 3.96 (m, 2H), 2.91 - 3.08 (m, 1H), 2.73 - 2.88 (m, 1H), 2.34 - 2.43 (m, 1H), 1.82 - 1.98 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -114.54.
89	MS (ESI) calcd. for $C_{28}H_{28}N_8O_2S$, 540.21 m/z, found 541.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.41 (m, 2H), 8.00 - 8.08 (m, 1H), 7.89 - 8.00 (m, 1H), 7.76 - 7.85 (m, 1H), 7.50 - 7.58 (m, 1H), 7.30 - 7.38 (m, 1H), 7.22 - 7.30 (m, 2H), 6.52 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 4.20 - 4.35 (m, 1H), 3.15 - 3.30 (m, 2H), 2.90 - 3.15 (m, 4H), 2.70 - 2.88 (m, 1H), 2.35 - 2.50 (m, 1H), 2.10 - 2.25 (m, 2H), 1.90 - 2.10 (m, 2H), 1.68 - 1.85 (m, 1H).
109	MS (ESI) calcd. for $C_{30}H_{31}N_9O$, 533.27 m/z, found, 534.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.38 - 8.47 (m, 1H), 8.32 - 8.37 (m, 1H), 7.96 - 8.08 (m, 2H), 7.79 - 7.85 (m, 1H), 7.66 - 7.79 (m, 2H), 7.52 - 7.59 (m, 1H), 7.37 - 7.47 (m, 1H), 6.71 - 6.81 (m, 1H), 6.53 - 6.61 (m, 1H), 4.93 - 5.01 (m, 1H), 4.40 - 4.51 (m, 1H), 3.45 - 3.52 (m, 2H), 3.08 - 3.25 (m, 2H), 2.85 - 3.02 (m, 1H), 2.55 - 2.63 (m, 2H), 2.45 - 2.54 (m, 2H), 2.15 - 2.25 (m, 1H), 2.00 - 2.06 (m, 3H), 1.35 - 1.65 (m, 2H).

Cpd ID	Characterization Data
111	MS (ESI) calcd. for $C_{26}H_{24}N_8O$, 464.21 m/z, found, 465.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.31 - 8.39 (m, 2H), 7.98 - 8.01 (m, 1H), 7.92 - 7.97 (m, 1H), 7.80 (s, 1H), 7.41 - 7.48 (m, 1H), 7.32 - 7.34 (m, 1H), 7.20 - 7.28 (m, 2H), 6.54 (s, 1H), 6.39 - 6.45 (m, 1H), 4.58 - 4.69 (m, 2H), 4.30 - 4.40 (m, 2H), 4.13 - 4.18 (m, 1H), 4.00 - 4.10 (m, 1H), 2.95 - 3.01 (m, 1H), 2.70 - 2.80 (m, 1H), 2.21 - 2.31 (m, 1H), 1.69 - 1.75 (m, 1H).
131	MS (ESI) calcd. for $C_{29}H_{25}N_9$, 499.22 m/z, found 500.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.50 - 8.58 (m, 1H), 8.32 - 8.46 (m, 2H), 7.90 - 8.10 (m, 2H), 7.80 - 7.90 (m, 2H), 7.50 - 7.65 (m, 2H), 7.30 - 7.45 (m, 2H), 7.22 - 7.30 (m, 2H), 6.57 (s, 1H), 6.45 - 6.55 (m, 1H), 4.25 - 4.37 (m, 1H), 3.92 - 4.00 (m, 2H), 2.90 - 3.15 (m, 1H), 2.75 - 2.90 (m, 1H), 2.35 - 2.45 (m, 1H), 1.82 - 2.00 (m, 1H). (formic acid salt)
140	MS (ESI) calcd. for $C_{30}H_{27}N_9$: 513.24 m/z, found, 514.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm) : 8.31 - 8.39 (m, 2H), 8.25 - 8.30 (m, 1H), 7.96 - 8.03 (m, 1H), 7.90 - 7.96 (m,1H), 7.78 - 7.83 (m, 1H), 7.72 - 7.78 (m, 1H), 7.49 - 7.57 (m, 1H), 7.30 - 7.37 (m, 1H), 7.15 - 7.29 (m, 3H), 6.49 - 6.56 (m, 1H), 6.37 - 6.48 (m, 1H), 4.20 - 4.30 (m, 1H), 3.79 (s, 2H), 2.91 - 3.05 (m, 1H), 2.73 - 2.86 (m, 1H), 2.49 (s, 3H), 2.28 - 2.44 (m, 1H),1.80 - 1.98 (m, 1H).
141	MS (ESI) calcd. for $C_{29}H_{25}N_9$: 499.22 m/z, found, 500.05 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.55 - 8.63 (m, 1H), 8.40 - 8.48 (m, 1H), 8.31 - 8.40 (m, 2H), 7.97 - 8.04 (m, 1H), 7.90 - 7.96 (m, 1H), 7.82 - 7.89 (m, 1H), 7.77 - 7.82 (m, 1H), 7.49 - 7.57 (m, 1H), 7.30 - 7.41 (m, 2H), 7.18 - 7.30 (m, 2H), 6.50 - 6.57 (m, 1H), 6.36 - 6.47 (m, 1H), 4.15 - 4.16 (m, 1H), 3.75 - 3.92 (m, 2H), 2.89 - 3.05 (m, 1H), 2.70 - 2.87 (m, 1H), 2.31 - 2.47 (m, 1H), 1.77 - 1.96 (m, 1H).
142	MS (ESI) calcd. for $C_{29}H_{25}N_9$: 499.22 m/z, found, 500.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.50 - 8.54 (m, 2H), 8.34 - 8.38 (m, 2H), 8.00 - 8.05 (m, 1H), 7.93 - 7.96 (m, 1H), 7.81 - 7.82 (m, 1H), 7.53 - 7.55 (m, 1H), 7.46 - 7.49 (m, 2H), 7.33 - 7.35 (m, 1H), 7.22 - 7.27 (m, 2H), 6.57 - 6.59 (m, 1H), 6.42 - 6.48 (m, 1H), 4.21 - 4.27 (m, 1H), 3.85 (s, 2H), 2.98 - 3.08 (m, 1H), 2.71 - 2.81 (m, 1H), 2.38 - 2.45 (m, 1H), 1.82 - 2.00 (m, 1H).
153	MS (ESI) calcd. for $C_{31}H_{29}N_9$, 527.25 m/z, found 528.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.45 - 8.47 (s, 1H), 8.28 - 8.38 (m, 2H), 7.99 - 8.02 (m, 1H), 7.91 - 7.95 (m, 1H), 7.81 - 7.86 (m, 1H), 7.72 - 7.76 (m, 1H), 7.48 - 7.51 (m, 1H), 7.16 - 7.28 (m, 4H), 6.53 - 6.68 (m, 1H), 6.41 - 6.51 (m, 1H), 4.02 - 4.15 (m, 2H), 2.89 - 2.96 (m, 1H), 2.67 - 2.69 (m, 1H), 2.45 (s, 3H), 2.05 - 2.29 (m, 1H), 1.65 - 1.80 (m, 1H), 1.25 - 1.40 (m, 3H).
154	MS (ESI) calcd. for $C_{31}H_{29}N_9$, 527.25 m/z, found 528.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.47 - 8.45 (s, 1H), 8.28 - 8.38 (m, 2H), 7.89 - 8.02 (m, 2H), 7.75 - 7.86 (m, 2H), 7.48 - 7.51 (m, 1H), 7.16 - 7.28 (m, 4H), 6.53 - 6.68 (m, 1H), 6.41 - 6.51 (m, 1H), 3.95 - 4.02 (m, 1H), 3.68 - 3.72 (m, 1H), 2.90 - 2.92 (m, 1H), 2.67 - 2.69 (m, 1H), 2.43 (s, 3H), 2.36 - 2.39 (m, 1H), 1.70 - 1.88 (m, 1H), 1.30 - 1.40 (m, 3H).
168	MS (ESI) calcd. for $C_{31}H_{29}N_9$ 527.25 m/z, found, 528.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.25 - 8.39 (m, 3H), 7.88 - 7.99 (m, 2H), 7.73 - 7.80 (m, 1H), 7.60 - 7.70 (m, 1H), 7.45 - 7.53 (m, 1H), 7.30 - 7.34 (m, 1H), 7.19 - 7.28 (m, 2H), 7.08 - 7.18 (m, 1H), 6.47 - 6.54 (m, 1H), 6.28 - 6.36 (m, 1H), 4.41 - 4.52 (m, 1H), 3.49 (s, 2H), 2.80 - 3.01 (m, 2H), 2.40 (s, 3H), 2.08 - 2.0 (m, 2H), 2.08 (s, 3H).

Cpd ID	Characterization Data
206	MS (ESI) calcd. for $C_{28}H_{26}N_{10}$ 502.23 m/z, found, 503.30 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.43 - 8.45 (m, 1H), 8.37 - 8.38 (m, 1H), 8.07 - 8.09 (m, 1H), 8.01 - 8.02 (m, 1H), 7.83 - 7.84 (m, 1H), 7.81 - 7.82 (m, 1H), 7.77 - 7.78 (m, 1H), 7.61 - 7.63 (m, 1H), 7.57 - 7.58 (m, 1H), 7.43 - 7.46 (m, 1H), 6.68 - 6.71 (m, 1H), 6.57 - 6.58 (m, 1H), 6.41 - 6.42 (m, 1H), 4.86 - 4.89 (m, 1H), 4.20 - 4.22 (m, 2H), 3.86 - 3.88 (m, 3H), 3.18 - 3.20 (m, 1H), 2.96 - 2.98 (m, 1H), 2.58 - 2.61 (m, 1H), 2.25 - 2.33 (m, 1H). (TFA salt)
208	MS (ESI) calcd. for $C_{31}H_{27}FN_{10}$ 558.24 *m/z*. found,559.30 [M+H]+. ^{1}H NMR (400 MHz, DMSO-*d6*) δ(ppm) 8.30 - 8.46 (m, 2H), 8.01 - 8.12 (m, 2H), 7.90 - 8.00 (m, 1H), 7.81 (d, *J* = 1.2 Hz, 1H), 7.45 - 7.60 (m, 2H), 7.38 - 7.44 (m, 1H), 7.31 - 7.37 (m, 1H), 7.19 - 7.30 (m, 1H), 6.59 - 6.70 (m, 1H), 6.51 - 6.58 (m, 1H), 6.35 - 6.48 (m, 2H), 5.21 - 5.50 (m, 1H), 4.25 - 4.43 (m, 1H), 4.11 - 4.24 (m, 2H), 3.97 - 4.10 (m, 1H), 3.75 - 3.85 (m, 1H), 3.65 - 3.73 (m, 1H), 3.15 - 3.30 (m, 1H), 3.12 (s, 1H). ^{19}F NMR (376 MHz, DMSO-*d6*) δ (ppm); -194.779.
234	MS (ESI) calcd. for $C_{29}H_{24}F_2N_{10}$, 550.22 m/z, found 551.20 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.80 - 8.91 (m, 1H), 8.49 - 8.57 (m, 1H), 8.19 - 8.26 (m, 3H), 8.12 - 8.18 (m, 1H), 8.06 - 8.11 (m, 1H), 7.81 - 7.92 (m, 2H), 7.71 - 7.80 (m, 1H), 7.62 - 7.69 (m, 1H), 7.45 - 7.54 (m, 1H), 6.84 - 7.20 (m, 1H), 6.73 - 6.81 (m, 1H), 4.94 - 5.09 (m, 1H), 4.39 - 4.57 (m, 2H), 3.16 - 3.30 (m, 1H), 2.97 - 3.11 (m, 1H), 2.62 - 2.74 (m, 1H), 2.35 - 2.49 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -115.51. (TFA salt)
274	MS (ESI) calcd. for $C_{29}H_{31}N_9$, 505.27. found, 506.35 $[M+H]^+$, ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 – 8.00 (m, 2H), 7.93 – 7.99 (m, 2H), 7.80 (s, 1H), 7.47 -7.44 (m, 1H), 7.25 – 7.32 (m, 1H), 7.23 – 7.20 (m. 2H), 6.97 (s, 2H), 6.53 (s, 1H), 6.43 – 6.39 (m, 1H),4.32 - 4.23 (m, 1H), 2.97- 2.90 (m, 1H), 2.89 – 2.71 (m, 3H), 2.57 – 2.50 (m, 1H), 2.39 -2.49 (m, 1H), 2.14 (s, 3H), 1.91 - 1.80 (m, 4H), 1.78 - 1.71 (m, 2H), 1.40 – 1.29 (m, 2H). (formic acid salt)
276	MS (ESI) calcd. for $C_{32}H_{33}N_{11}$, 571.29 m/z, found 572.15 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.41 – 8.30 (m, 2H), 8.03 – 7.91 (m, 2H), 7.81 (d, J = 1.6 Hz, 1H), 7.50 – 7.31 (m, 3H), 7.31 – 7.18 (m, 2H), 6.95 (s, 2H), 6.54 (t, *J* = 2.1 Hz, 1H), 6.48 – 6.38 (m, 1H), 5.65 (d, *J* = 2.3 Hz, 1H), 4.41 – 4.28 (m, 1H), 3.75 – 3.49 (m, 5H), 3.01 – 2.87 (m, 1H), 2.87 – 2.71 (m, 2H), 2.71 – 2.55 (m, 2H), 2.47 – 2.41 (m, 1H), 2.08 – 1.93 (m, 2H), 1.91 – 1.80 (m, 1H), 1.80 – 1.72 (m, 1H), 1.50 – 1.32 (m, 2H).
277	MS (ESI) calcd. for $C_{33}H_{32}N_{10}$, 568.28 m/z, found, 569.40 $[M+H]^+$; 1H NMR (400 MHz, DMSO-d6) δ 8.41 - 8.32 (m, 2H), 8.13 - 8.06 (m, 1H), 8.03 - 7.91 (m, 2H), 7.81 (d, J = 1.6 Hz, 1H), 7.54 - 7.44 (m, 2H), 7.33 (d, J = 1.9 Hz, 1H), 7.29 - 7.19 (m, 2H), 6.94 (s, 2H), 6.83 (d, J = 8.6 Hz, 1H), 6.62 - 6.51 (m, 2H), 6.43 (dd, J = 7.6, 4.8 Hz, 1H), 4.41 - 4.33 (m, 1H), 4.27 - 4.16 (m, 2H), 2.99 - 2.86 (m, 4H), 2.85 - 2.72 (m, 1H), 2.50 - 2.52 (m, 1H), 2.09 - 1.96 (m, 2H), 1.92 - 1.85 (m, 1H), 1.85 - 1.72 (m, 1H), 1.40 - 1.24 (m, 2H).
279	MS (ESI) calcd for $C_{32}H_{33}N_9O$ 559.68 m/z, found 560.35 $[M+H]^+$. 1H NMR (500 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.92 (s, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.36 (d, J = 2.6 Hz, 1H), 8.07 (dd, J = 5.3, 1.8 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 1.7 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 1.9 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.45 (dd, J = 8.1, 2.0 Hz, 1H), 6.64 – 6.56 (m, 2H), 5.04 (s, 1H), 4.48 (s, 1H), 4.41 (s, 1H), 3.50 – 3.58 (m, 1H), 3.23 – 3.17 (m, 2H), 3.01 – 2.95 (m, 1H), 2.67 (s, 2H), 2.63 – 2.56 (m, 2H), 2.26 – 2.20 (m, 1H), 2.05 (s, 2H), 1.59 (s, 1H), 1.47 (s, 1H), 0.74 (s, 4H).

Cpd ID	Characterization Data
305	MS (ESI) calcd for $C_{30}H_{24}F_3N_9O$: 583.21 m/z, found: 584.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.36 - 8.41 (m, 1H), 8.33 - 8.36 (m, 1H), 8.26 - 8.32 (m, 1H), 7.93 - 8.04 (m, 2H), 7.79 - 7.84 (m, 1H), 7.45 - 7.59 (m, 2H), 7.31 - 7.37 (m, 2H), 7.21 - 7.28 (m, 2H), 6.51 - 6.62 (m, 1H), 6.40 - 6.50 (m, 1H), 4.14 - 4.30 (m, 1H), 3.92 (s, 2H), 2.88 - 3.04 (m, 1H), 2.66 - 2.88 (m, 1H), 2.30 - 2.43 (m, 1H), 1.77 - 1.93 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -54.93.
339	MS (ESI) calcd. for $C_{24}H_{22}N_8$, 422.20 m/z, found, 423.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.38 (m, 2H), 8.02 - 8.06 (m, 1H), 7.94 - 7.99 (m, 1H), 7.82 - 7.84 (m, 1H), 7.65 - 7.68 (m, 1H), 7.45 - 7.48 (m, 1H), 7.31 - 7.34 (m, 1H), 7.22 - 7.28 (m, 1H), 6.92 (s, 2H), 6.52 - 6.54 (m, 1H), 6.40 - 6.45 (m, 1H), 4.42 - 4.49 (m, 1H), 3.02 - 3.10 (m, 1H), 2.82 - 2.91 (m, 1H), 2.50 - 2.52 (m, 3H), 2.39 - 2.42 (m, 1H), 2.00 - 2.09 (m, 1H).
340	MS (ESI) calcd. for $C_{25}H_{24}N_8$, 436.21 m/z, found, 437.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.34 - 8.37 (m, 2H), 7.94 - 8.10 (m, 2H), 7.77 - 7.82 (m, 1H), 7.38 - 7.49 (m, 2H), 7.31 - 7.36 (m, 1H), 7.19 - 7.28 (m, 1H), 6.95 - 7.11 (m, 2H), 6.54 (s, 1H), 6.35 - 6.38 (m, 1H), 4.30 - 4.39 (m, 1H), 2.82 - 3.00 (m, 2H), 1.90 - 2.30 (m, 8H).
366	MS (ESI) calcd. for $C_{32}H_{31}N_{11}$ 569.28 m/z, found, 570.20 $[M+H]^-$. ^1H-NMR (400 MHz, DMSO) δ (ppm); 8.45 - 8.55 (m, 1H), 8.05 - 8.20 (m, 5H), 7.81 - 7.95 (m, 1H), 7.72 - 7.80 (m, 2H), 7.52 - 7.60 (m, 1H), 7.41 - 7.50 (m, 1H), 7.21 - 7.30 (m, 1H), 6.85 - 6.95 (m, 1H), 6.72 - 6.81 (m, 1H), 5.00 - 5.10 (m, 1H), 4.30 - 4.41 (m, 2H), 3.60 - 3.69 (m, 1H), 3.11 - 3.23 (m, 3H), 2.90 - 3.05 (m, 1H), 2.58 - 2.70 (m, 1H), 2.12 - 2.35 (m, 3H), 1.61 - 1.78 (m, 2H). (TFA salt)
367	MS (ESI) calcd. for $C_{33}H_{31}FN_{10}$ 586.27 m/z, found, 587.20 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO) δ (ppm); 8.40 - 8.48 (m, 1H), 8.25 - 8.35 (m, 1H), 8.02 - 8.13 (m, 2H), 7.81 - 7.92 (m, 2H), 7.71 - 7.80 (m, 2H), 7.55 - 7.61 (m, 1H), 7.40 - 7.48 (m, 1H), 7.25 - 7.32 (m, 1H), 6.85 - 6.95 (m, 1H), 6.75 - 6.84 (m, 1H), 6.35 - 6.41 (m, 1H), 4.98 - 5.06 (m, 1H), 4.27 - 4.42 (m, 2H), 3.60 - 3.65 (m, 1H), 3.12 - 3.26 (m, 3H), 2.91 - 3.05 (m, 1H), 2.55 - 2.70 (m, 1H), 2.14 - 2.35 (m, 3H), 1.61 - 1.80 (m, 2H).^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -126.83, -74.05. (TFA salt)
368	MS (ESI) calcd. for $C_{33}H_{32}N_{10}$ 568.28m/z, found, 569.20$[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.29 - 8.37 (m, 3H), 7.93 - 8.02 (m, 3H), 7.79 - 7.81 (m, 1H), 7.48 - 7.51 (m, 1H), 7.18 - 7.35 (m, 5H), 6.52 - 6.55 (m, 1H), 6.40 - 6.45 (m, 1H), 4.30 - 4.38 (m, 1H), 3.65 - 3.78 (m, 2H), 2.91 - 2.99 (m, 1H), 2.72 - 2.88 (m, 4H), 2.39 - 2.43 (m, 1H), 1.99 - 2.06 (m, 1H), 1.89 - 1.98 (m, 1H), 1.72 - 1.83 (m, 1H), 1.34 - 1.50 (m, 2H).
387	MS (ESI) calcd. For $C_{32}H_{30}N_{10}$, 554.27 m/z, found 555.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6 + CF_3COOD) δ (ppm); 8.49 (d, J = 8.8 MHz, 1H), 8.37 - 8.38 (m, 1H), 8.05 - 8.15 (m, 4H), 7.81 - 7.94 (m, 3H), 7.66 (s, 1H), 7.47 - 7.50 (m, 1H), 7.19 (d, J = 9.2 MHz, 1H), 6.99 - 7.02 (m, 1H), 6.87 - 6.90 (m, 1H), 6.57 - 6.58 (m, 1H), 5.02 - 5.05 (m, 1H), 4.29 - 4.30 (m, 1H), 4.01 - 4.04 (m, 1H), 3.81 - 3.91 (m, 2H), 3.68 - 3.70 (m, 1H), 3.19 - 3.27 (m, 1H), 2.95 - 3.03 (m, 1H), 2.55 - 2.62 (m, 3H), 2.30 - 2.35 (m, 1H).
388	MS (ESI) calcd. For $C_{32}H_{30}N_{10}$, 554.27 m/z, found 555.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6 + CF_3COOD) δ (ppm); 8.49 (d, J = 8.8 MHz, 1H), 8.37 - 8.38 (m, 1H), 8.05 - 8.15 (m, 4H), 7.81 - 7.94 (m, 3H), 7.66 (s, 1H), 7.47 - 7.50 (m, 1H), 7.19 (d, J = 9.2 MHz, 1H), 6.99 - 7.02 (m, 1H), 6.87 - 6.90 (m, 1H), 6.57 - 6.58 (m, 1H), 5.02 - 5.05 (m, 1H), 4.29 - 4.30 (m, 1H), 4.01 - 4.04 (m, 1H), 3.81 - 3.91 (m, 2H), 3.68 - 3.70 (m, 1H), 3.19 - 3.27 (m, 1H), 2.95 - 3.03 (m, 1H), 2.55 - 2.62 (m, 3H), 2.30 - 2.35 (m, 1H).

Cpd ID	Characterization Data
393	MS (ESI) calcd. for $C_{31}H_{33}N_9O_2S$, 595.25 m/z, found, 596.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ 8.43 - 8.22 (m, 2H), 8.08 - 7.91 (m, 2H), 7.81 (s, 1H), 7.60 - 7.41 (m, 1H), 7.36 - 7.31 (m, 1H), 7.27 - 7.18 (m, 2H), 6.95 (s, 2H), 6.55 (s, 1H), 6.45 - 6.39 (m, 1H), 4.43 - 4.16 (m, 1H), 3.63 - 3.54 (m, 2H), 3.01 - 2.89 (m, 3H), 2.86 - 2.73 (m, 2H), 2.61 - 2.57 (m, 1H), 2.49 - 2.25 (m, 1H), 2.20 - 2.04 (m, 1H), 2.03 - 1.89 (m, 2H), 1.82 - 1.69 (m, 1H), 1.42 (s, 2H), 1.03 - 0.88 (m, 4H).
394	MS (ESI) calcd. for $C_{31}H_{34}N_{10}O$, 562.29 m/z, found, 563.40 [M+H]+. ^1H NMR (400 MHz, DMSO-d6) δ 8.44 - 8.24 (m, 2H), 8.05 - 7.91 (m, 2H), 7.85 - 7.74 (m, 1H), 7.56 - 7.43 (m, 1H), 7.37 - 7.30 (m, 1H), 7.28 - 7.19 (m, 2H), 6.99 - 6.89 (m, 2H), 6.59 - 6.51 (m, 1H), 6.45 - 6.38 (m, 1H), 4.36 (s, 1H), 3.59 - 3.44 (m, 2H), 3.04 - 2.87 (m, 1H), 2.85 - 2.71 (m, 10H), 2.50 - 2.30 (m, 2H), 2.00 - 1.89 (m, 1H), 1.87 - 1.70 (m, 2H), 1.38 - 1.20 (m, 2H).
434	MS (ESI) calcd. for $C_{33}H_{33}F_2N_9O$, 609.28 m/z, found 610.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.68 - 8.74 (m, 1H), 8.25 - 8.33 (m, 1H), 8.19 - 8.24 (m, 1H), 7.68 - 8.04 (m, 3H), 7.44 - 7.51 (m, 1H), 7.29 - 7.35 (m, 1H), 7.19 - 7.27 (m, 2H), 6.96 - 7.05 (m, 2H), 6.39 - 6.48 (m, 1H), 4.32 - 4.46 (m, 1H), 4.12 - 4.29 (m, 2H), 3.16 - 3.27 (m, 1H), 2.88 - 3.01 (m, 2H), 2.72 - 2.86 (m, 2H), 2.41 - 2.49 (m, 1H), 1.78 - 2.13 (m, 5H), 1.15 - 1.36 (m, 2H), 0.67 - 0.74 (m, 4H). ^{19}F NMR (282 MHz, DMSO-d_6) δ(ppm) -94.38.
437	MS (ESI) calcd. for $C_{28}H_{28}N_8$, 476.24 m/z, found, 477.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.38 (m, 2H), 7.93 - 8.01 (m, 2H), 7.81 - 7.83 (m, 1H), 7.43 - 7.46 (m, 1H), 7.31 - 7.33 (m, 1H), 7.22 - 7.25 (m, 1H), 7.16 - 7.19 (m, 1H), 6.57 - 6.58 (m, 1H), 6.33 - 6.39 (m, 1H), 4.51 - 4.56 (m, 1H), 2.73 - 2.92 (m, 2H), 2.22 - 2.32 (m, 2H), 2.21 (s, 3H), 2.01 - 2.14 (m, 2H), 0.81 - 0.89 (m, 1H), 0.39 - 0.56 (m, 2H), 0.02 - 0.13 (m, 2H).
439	MS (ESI) calcd. For $C_{31}H_{28}N_{10}$, 540.25 m/z, found 541.40 $[M+H]^+$. ^1H NMR NMR (300 MHz, DMSO-d_6) δ 8.35 - 8.37 (m, 2H), 8.04 - 8.06 (m, 1H), 8.00 - 8.02 (m, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.80 - 7.81 (m, 1H), 7.46 - 7.51 (m, 2H), 7.35 - 7.36 (m, 1H), 7.21 - 7.28 (m, 2H), 6.98 (s, 2H), 6.58 - 6.62 (m, 1H), 6.52 - 6.53 (m, 1H), 6.44 - 6.48 (m, 1H), 6.34 - 6.37 (m, 1H), 4.23 - 4.27 (m, 1H), 4.07 - 4.13 (m, 2H), 3.87 - 3.91 (m, 1H), 3.60 - 3.65 (m, 2H), 2.95 - 3.05 (m, 1H), 2.74 - 2.85 (m, 1H), 2.31 - 2.42 (m, 1H), 1.77 - 1.89 (m, 1H).
440	MS (ESI) calcd. for $C_{33}H_{35}N_9O_2$, 589.29 m/z, found, 590.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ(ppm) 8.34 – 8.26 (m, 1H), 8.20 – 8.14 (m, 1H), 8.03 – 7.96 (m, 1H), 7.82 – 7.72 (m, 1H), 7.52 – 7.42 (m, 1H), 7.32 (s, 1H), 7.28 – 7.16 (m, 2H), 6.95 (s, 2H), 6.46 – 6.35 (m, 1H), 6.13 – 5.98 (m, 1H), 4.34 (s, 1H), 4.19 (s, 2H), 3.92 (s, 3H), 3.22 (s, 1H), 2.92 (s, 2H), 2.86 – 2.69 (m, 2H), 2.48 – 2.36 (m, 1H), 2.08 (s, 1H), 2.04 – 1.69 (m, 4H), 1.39 – 1.22 (m, 1H), 1.19 (s, 1H), 0.77 – 0.62 (m, 4H).
442	MS (ESI) calcd. for $C_{35}H_{37}N_9O$, 599.31 m/z, found 600.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d6) δ (ppm); 8.24 - 8.37 (m, 2H), 7.78 - 8.04 (m, 2H), 7.48 - 7.60 (m, 1H), 7.16 - 7.38 (m, 3H), 6.38 - 6.49 (m, 1H), 6.20 - 6.30 (m, 1H), 4.40 - 4.53 (m, 1H), 4.25 (s, 2H), 3.15 - 3.28 (m, 1H), 2.91 - 3.12 (m, 2H), 2.75 - 2.87 (m, 2H), 2.40 - 2.51 (m, 1H), 1.69 - 2.14 (m, 5H), 1.20 - 1.36 (m, 2H), 0.87 - 1.03 (m, 2H), 0.62 - 0.87 (m, 6H).
458	MS (ESI) calcd. for $C_{29}H_{30}N_8$, 490.26 m/z, found, 491.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.32 - 8.39 (m, 2H), 7.96 - 8.03 (m, 2H), 7.79 - 7.82 (m, 1H), 7.43 - 7.47 (m, 1H), 7.34 - 7.36 (m, 1H), 7.17 - 7.29 (m, 2H), 6.56 - 6.58 (m, 1H), 6.35 - 6.39 (m, 1H), 4.43 - 4.51 (m, 1H), 2.77 - 2.94 (m, 2H), 2.41 - 2.49 (m, 2H), 2.21 (s, 3H), 1.95 - 2.13 (m, 2H), 1.31 - 1.41 (m, 2H), 0.64 - 0.72 (m, 1H), 0.32 - 0.41 (m, 2H), 0.01 - 0.03 (m, 2H).
461	MS (ESI) calcd. for $C_{31}H_{31}N_9O$, 545.26 m/z, found, 546.25 $[M+H]^+$. ^1H NMR (300 MHz,

Cpd ID	Characterization Data
	DMSO-d_6) δ (ppm); 8.30 - 8.40 (m, 2H), 7.93 - 8.02 (m, 2H), 7.79 - 7.81 (m, 1H), 7.42 - 7.48 (m, 1H), 7.30 - 7.39 (m, 1H), 7.20 - 7.29 (m, 2H), 6.89 - 6.99 (m, 2H), 6.50 - 6.52 (m, 1H), 6.38 - 6.42 (m, 1H), 4.18 - 4.31 (m, 1H), 3.71 - 3.88 (m, 1H), 3.38 - 3.62 (m, 3H), 3.10 - 3.18 (m, 1H), 2.89 - 2.98 (m, 1H), 2.70 - 2.81 (m, 1H), 2.40 - 2.45 (m, 1H), 1.91 - 2.10 (m, 1H), 1.79 - 1.88 (m, 1H), 1.69 - 1.75 (m, 2H), 1.13 - 1.25 (m, 1H), 0.65 - 0.73 (m, 4H).
462	MS (ESI) calcd. for $C_{31}H_{31}N_9O$, 545.26 m/z, found, 546.20 $[M+H]^+$.^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.40 (m, 2H), 7.93 - 8.02 (m, 2H), 7.79 - 7.83 (m, 1H), 7.55 - 7.62 (m, 1H), 7.31 - 7.36 (m, 1H), 7.18 - 7.26 (m, 2H), 6.92 - 7.00 (m, 2H), 6.53 - 6.56 (m, 1H), 6.39 - 6.46 (m, 1H), 4.21 - 4.31 (m, 1H), 3.70 - 3.86 (m, 1H), 3.45 - 3.65 (m, 3H), 3.09 - 3.15 (m, 1H), 2.90 - 3.00 (m, 1H), 2.71 - 2.81 (m, 1H), 2.40- 2.45 (m, 1H), 1.64 - 2.10 (m, 4H), 1.12 - 1.25 (m, 1H), 0.65 - 0.73 (m, 4H).
463	MS (ESI) calcd. for $C_{32}H_{29}N_9$, 539.25 m/z, found, 540.40 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.34 - 8.36 (m, 2H), 8.28 - 8.33 (m, 1H), 8.21 - 8.22 (m, 1H), 7.99 (d, J = 4.8 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 1.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.29 - 7.33 (m, 1H), 7.20 - 7.25 (m, 2H), 7.08 (d, J = 5.1 Hz, 1H), 6.94 (s, 2H), 6.53 (d, J = 2.4 Hz, 1H), 6.40(d, J = 7.5, 1H), 4.30 - 4.45 (m, 1H), 3.07 - 3.20 (m, 2H), 2.91 - 2.93 (m, 1H), 2.80 - 2.85 (m, 1H), 2.73 - 2.78 (m, 2H), 2.57 - 2.59 (m, 1H), 2.00 - 2.10 (m, 1H), 1.72 - 1.89 (m, 1H), 1.55 - 1.66 (m, 1H), 1.15 - 1.22 (m, 1H).
464	MS (ESI) calcd. for $C_{32}H_{29}N_9$, 539.25 m/z, found, 540.40 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.34 - 8.37 (m, 2H), 8.28 - 8.33 (m, 1H), 8.21 - 8.23 (m, 1H), 8.00 (d, J = 4.8 Hz, 1H), 7.95 (d, J = 8.7 Hz, 1H), 7.79 (d, J = 1.2 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.36 - 7.45 (m, 1H), 7.22 - 7.27 (m, 2H), 7.08 (d, J = 5.1 Hz, 1H), 6.94 (s, 2H), 6.54 (d, J = 4.2 Hz, 1H), 6.42(d, J = 7.5, 1H), 4.36 - 4.47 (m, 1H), 3.10 - 3.21 (m, 1H), 2.91 - 3.00 (m, 3H), 2.76 - 2.85 (m, 2H), 2.55 - 2.71 (m, 2H), 2.01 - 2.16 (m, 1H), 1.75 - 1.92 (m, 1H), 1.60 - 1.74 (m, 1H), 1.20 - 1.28 (m, 1H).
469	MS (ESI) calcd. for $C_{33}H_{31}N_9$, 553.27 *m/z*, found, 554.35 $[M+H]^+$ / ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.35 (m, 2H), 7.95 - 8.01 (m, 2H), 7.81 (s, 1H), 7.52 (d, J = 5.2 Hz, 1H), 7.34 (s, 1H), 7.25 (d, J = 5.2 Hz, 2H), 7.15 - 7.18 (m, 2H), 6.52 - 6.60 (m, 4H), 6.43 - 6.46 (m, 1H), 4.30 - 4.31 (m, 1H), 3.59 - 3.62 (m, 1H), 3.51 - 3.55 (m, 1H), 3.33 - 3.37 (m, 1H), 3.22 - 3.27 (m, 1H), 2.96 - 3.07 (m, 2H), 2.76 - 2.84 (m, 1H), 2.48 - 2.49 (m, 1H), 2.20 - 2.22 (m, 1H), 1.85 - 1.89 (m, 2H).
470	MS (ESI) calcd. for $C_{33}H_{31}N_9$, 553.27 *m/z*, found, 554.35 $[M+H]^+$ / ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.33 - 8.35 (m, 2H), 7.95 - 8.01 (m, 2H), 7.81 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.34 (s, 1H), 7.23 - 7.27 (m, 2H), 7.14 - 7.18 (m, 2H), 6.51 - 6.60 (m, 4H), 6.42 - 6.45 (m, 1H), 4.30 - 4.33 (m, 1H), 3.59 - 3.62 (m, 1H), 3.49 - 3.52 (m, 1H), 3.35 - 3.37 (m, 1H), 3.23 - 3.26 (m, 1H), 2.96 - 3.07 (m, 2H), 2.76 - 2.83 (m, 1H), 2.48 - 2.49 (m, 1H), 2.20 - 2.22 (m, 1H), 1.84 - 1.90 (m, 2H).
471	MS (ESI) calcd. for $C_{32}H_{30}N_{10}$ 8.33 - 8.36 (m, 2H), 7.92 - 8.10 (m, 3H), 7.70 -7.80 (m, 2H), 7.47 (d, J =7.8 Hz, 1H), 7.34 (s, 1H), 7.24 (t, J = 8.0 Hz, 2H), 7.11 - 715 (m, 1H), 6.85 - 6.94 (m, 3H), 6.53 (s, 1H), 6.38 - 6.42 (m, 1H), 4.30 (s, 1H), 3.51 - 3.86 (m, 2H), 3.32 - 3.39 (m, 1H), 3.23 - 3.28 (m, 1H), 3.10 - 3.12 (m, 1H), 2.93 - 2.95 (m, 1H), 2.73 - 2.81 (m, 1H), 2.58 - 2.69 (m, 2H), 2.18 - 2.20 (m, 1H), 1.83 - 1.90 (m, 2H).554.27 *m/z*, found, 555.20 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-*d6*) δ(ppm)
472	MS (ESI) calcd. for $C_{32}H_{30}N_{10}$ 554.27 *m/z*, found, 555.20 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-*d6*) δ(ppm) 8.33 - 8.36 (m, 2H), 7.98 - 8.00 (m, 1H), 7.90 -7.97 (m, 2H), 7.79 - 7.81 (m, 2H), 7.49 - 7.51 (m, 1H), 7.34 (s, 1H), 7.20 - 7.26 (m, 2H), 711 - 715 (m, 1H), 6.94 (s, 2H), 6.84 - 6.87 (m, 1H), 6.51 - 6.53 (m, 1H), 6.38 - 6.42 (m, 1H), 4.29 - 4.32 (m, 1H), 3.60 -

Cpd ID	Characterization Data
	3.64 (m, 1H), 3.50 - 3.55 (m, 1H), 3.40 - 3.41 (m, 1H), 3.26 - 3.29 (m, 1H), 2.94 - 3.08 (m, 2H), 2.73 - 2.84 (m, 1H), 2.41 - 2.43 (m, 2H), 2.13 - 2.23 (m, 1H), 1.79 - 1.98 (m, 2H).
473	MS (ESI) calcd. for $C_{31}H_{27}N_9$, 525.24. Found, 526.35 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm);8.50-8.60 (m, 1H),8.50 - 8.40 (m, 2H), 8.40 - 8.30 (m, 1H), 8.20 - 8.30 (m, 1H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H),7.75 - 7.90 (m, 1H), 7.60- 7.70 (m, 1H), 7.50 - 7.60 (m, 1H), 7.35 - 7.40 (m, 2H), 6.90 - 7.05 (m, 2H), 6.50 - 6.60 (m, 1H), 6.30 - 6.50 (m, 1H), 4.30 - 4.70 (m, 2H), 3.00 - 3.10 (m, 2H), 2.80 - 2.95 (m, 2H), 2.50 - 2.55 (m, 1H), 1.80 - 2.15 (m, 2H),1.20 - 1.30 (m, 1H)
474	MS (ESI) calcd. for $C_{31}H_{27}N_9$, 525.24. Found, 526.35 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d6) δ (ppm);8.50-8.60 (m, 1H),8.50 - 8.40 (m, 1H), 8.40 - 8.30 (m, 2H), 8.20 - 8.30 (m, 1H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H),7.75 - 7.90 (m, 1H), 7.60- 7.70 (m, 1H), 7.50 - 7.60 (m, 1H), 7.40 - 7.50 (m, 1H), 7.35 - 7.40 (m, 2H), 6.90 - 7.05 (m, 2H), 6.60 - 6.70 (m, 1H), 6.50 - 6.60 (m, 1H), 4.40 - 4.65 (m, 2H), 3.00 - 3.10 (m, 2H), 2.75 - 2.95 (m, 2H), 2.50 - 2.60 (m, 1H), 2.40 - 2.50 (m, 1H),1.80 - 2.00 (m, 2H).
480	MS (ESI) calcd. for $C_{35}H_{36}FN_9O$, 617.30 m/z, found 618.30 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm) 8.38 - 8.40 (m, 1H), 8.18 - 8.19 (m, 1H), 8.05 - 8.07 (m, 1H), 7.91 - 7.94 (m, 1H), 7.75 - 7.77 (m, 2H), 7.59 - 7.60 (m, 1H), 7.51 - 7.53 (m, 1H), 6.74 - 6.78 (m, 1H), 6.27 - 6.28 (m, 1H), 5.79 - 5.92 (m, 1H), 5.20 - 5.26 (m, 1H), 4.41 - 4.48 (m, 2H), 3.78 - 3.80 (m, 3H), 3.20 - 3.38 (m, 3H), 2.67 - 2.71 (m, 1H), 2.29 - 2.38 (m, 1H), 2.12 - 2.20 (m, 1H), 1.99 - 2.09 (m, 2H), 1.45 - 1.55 (m, 2H), 0.99 - 1.00 (m, 2H), 0.75 - 0.80 (m, 4H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -74.01, -195.70. (TFA salt)
481	MS (ESI) calcd. for $C_{31}H_{26}FN_9$, 543.23 m/z, found, 544.20 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d6) δ (ppm); 8.42 - 8.59 (m, 1H), 8.21 - 8.42 (m, 3H), 7.89 - 8.15 (m, 2H), 7.68 - 7.89 (m, 1H), 7.45 - 7.68(m, 2H), 7.15 - 7.45 (m, 3H), 6.51 - 6.69 (m, 1H), 6.35 - 6.51 (m, 1H), 5.42 - 5.73 (m, 1H),4.52 - 4.69 (m, 1H), 4.22 - 4.52 (m, 1H), 2.95 - 3.38 (m, 3H), 2.78 - 2.95 (m, 1H), 2.42 - 2.52 (m, 1H), 1.85 - 2.15 (m, 1H).
482	MS (ESI) calcd. for $C_{31}H_{26}FN_9$, 543.23 m/z, found, 544.20 [M+H]+. ^{1}H-NMR (400 MHz, DMSO-d6) δ (ppm); 8.42 - 8.58 (m, 1H), 8.22 - 8.42 (m, 3H), 7.89 - 8.15 (m, 2H), 7.71 - 7.89 (m, 1H), 7.49 - 7.71(m, 2H), 7.31 - 7.49 (m, 2H), 7.15 - 7.31 (m, 1H), 6.51 - 6.69 (m, 1H), 6.33 - 6.51 (m, 1H), 5.22 - 5.73 (m, 1H),4.37 - 4.54 (m, 2H), 3.09 - 3.33 (m, 2H), 2.95 - 3.33 (m, 1H), 2.79 - 2.95 (m, 1H), 2.56 - 2.62 (m, 1H), 1.71 - 2.03 (m, 1H).
493	MS (ESI) calcd. for $C_{31}H_{30}FN_9O_2$: 579.25 m/z, found, 580.40 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO) δ (ppm); 8.35 - 8.42 (m, 1H), 8.18 - 8.22 (m, 1H), 8.03 - 8.08 (m, 1H), 7.82 - 7.88 (m, 1H), 7.75 - 7.80 (m, 1H), 7.65 - 7.73 (m, 1H), 7.59 - 7.65 (m, 1H), 7.48 - 7.55 (m, 1H), 6.70 - 6.80 (m, 1H), 6.08 - 6.12 (m, 1H), 5.62 - 5.82 (m, 1H), 4.98 - 5.10 (m, 1H), 4.58 - 4.70 (m, 1H), 4.35 - 4.50 (m, 2H), 4.15 - 4.25 (m, 1H), 3.99 - 4.06 (m, 1H), 3.87 - 3.95 (m, 3H), 3.28 - 3.42 (m, 2H), 1.50 - 1.62 (m, 1H), 0.70 - 0.85 (m, 4H).^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -194.96, -73.88. (TFA salt)
500	Observed mass (ESI): 560.2 [M+H]+. 1H-NMR (400 MHz, DMSO) δ (ppm): 8.32 - 8.50 (m, 2H), 7.98 - 8.15 (m, 2H), 7.70 - 7.88 (m, 3H), 7.53 - 7.65 (m, 1H), 7.40 - 7.50 (m, 1H), 6.75 - 6.85 (m, 1H), 6.52 - 6.63 (m, 1H), 4.96 - 5.10 (m, 1H), 4.32 - 4.55 (m, 2H), 3.55 - 3.65 (m, 1H), 3.11 - 3.30 (m, 2H), 2.90 - 3.08 (m, 1H), 2.55 - 2.75 (m, 2H), 1.99 - 2.40 (m, 4H), 1.37 - 1.65 (m, 2H), 1.65 - 1.85 (m, 4H).
501	Observed mass (ESI): 540.4 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.35 - 8.38 (m, 3H), 8.00 - 8.01 (m, 1H), 7.95 - 7.99 (m, 1H), 7.80 - 7.81 (m, 1H), 7.51 - 7.54 (m, 2H), 7.36 - 7.37 (m, 1H), 7.18 - 7.28 (m, 3H), 6.53 - 6.54 (m, 1H), 6.40 - 6.43 (m, 1H), 4.44 - 4.48

Cpd ID	Characterization Data
	(m, 1H), 3.98 - 4.00 (m, 1H), 2.98 - 3.05 (m, 1H), 2.77 - 2.84 (m, 3H), 2.52 - 2.53 (m, 1H), 2.12 - 2.18 (m, 1H), 1.94 - 2.05 (m, 1H), 1.85 - 1.93 (m, 1H), 1.74 - 1.76 (m, 2H).
502	Observed mass (ESI): 540.4 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.35 - 8.38 (m, 3H), 8.00 - 8.01 (m, 1H), 7.95 - 7.97 (m, 1H), 7.81 - 7.82 (m, 1H), 7.54 - 7.56 (m, 1H), 7.49 - 7.50 (m, 1H), 7.34 - 7.35 (m, 1H), 7.20 - 7.27 (m, 3H), 6.55 - 6.56 (m, 1H), 6.45 - 6.48 (m, 1H), 4.45 - 4.48 (m, 1H), 3.94 - 3.97 (m, 1H), 2.91 - 3.01 (m, 1H), 2.75 - 2.86 (m, 3H), 2.61 - 2.64 (m, 1H), 2.15 - 2.20 (m, 1H), 2.00 - 2.05 (m, 1H), 1.77 – 1.85 (m, 3H).
503	Observed mass (ESI): 561.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.30 - 8.32 (m, 1H), 8.13 - 8.17 (m, 2H), 7.98 - 7.99 (m, 1H), 7.49 - 7.51 (m, 1H), 7.39 (s, 1H), 7.29 - 7.30 (m, 1H), 7.22 - 7.26 (m, 2H), 6.41 - 6.44 (m, 1H), 4.32 - 4.35 (m, 1H), 4.20 - 4.29 (m, 2H), 3.17 - 3.20 (m, 1H), 2.87 - 2.97 (m, 2H), 2.73 - 2.80 (m, 2H), 2.50 - 2.51 (m, 1H), 1.91 - 2.04 (m, 3H), 1.81 - 1.83 (m, 1H), 1.21 - 1.31 (m, 1H), 1.08 - 1.18 (m, 1H), 0.60 - 0.75 (m, 4H).
506	Observed mass (ESI): 530.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.06 - 8.24 (m, 1H), 7.87 - 8.05 (m, 1H), 7.35 - 7.62 (m, 2H), 7.05 - 7.34 (m, 3H), 6.30 - 6.57 (m, 1H), 4.30 - 4.55 (m, 1H), 4.09 - 4.28 (m, 1H), 3.86 - 4.08 (m, 2H), 3.71 - 3.85 (m, 1H), 3.45 - 3.70 (m, 1H), 2.88 - 3.12 (m, 1H), 2.65 - 2.87 (m, 1H), 2.20 - 2.43 (m, 1H), 1.70 - 1.95 (m, 1H), 1.40 - 1.65 (m, 2H), 0.84 - 1.02 (m, 2H), 0.55 - 0.83 (m, 6H).
507	Observed mass (ESI): 608.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ(ppm): 8.41 (d, J = 11.2 Hz, 1H), 7.89 - 8.12 (m, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.33 (s, 1H), 7.10 - 7.30 (m, 2H), 6.29 - 6.58 (m, 1H), 6.08 (d, J = 2.8 Hz, 1H), 4.37 (t, J = 7.2 Hz, 1H), 4.11 - 4.30 (m, 2H), 3.84 (s, 3H), 3.10 - 3.30 (m, 1H), 2.89 - 3.02 (m, 2H), 2.70 - 2.81 (m, 2H), 2.39 - 2.49 (m, 1H), 1.76 - 2.06 (m, 4H), 1.07 - 1.42 (m, 2H), 0.50 - 0.98 (m, 4H). 19F NMR (376 MHz, DMSO-d6) δ (ppm): -73.527, -112.623. (TFA salt)
508	Observed mass (ESI): 556.15 [M+H]+. 1H-NMR (400 MHz, DMSO-d6) δ (ppm): 8.33 - 8.35 (m, 2H), 7.93 - 8.00 (m, 3H), 7.79 (s, 1H), 7.51 - 7.53 (m, 1H), 7.32 (s, 1H), 7.22 - 7.24 (m, 2H), 7.09 - 7.10 (m, 1H), 6.52 - 6.54 (m, 1H), 6.40 - 6.44 (m, 1H), 4.33 - 4.36 (m, 2H), 3.66 - 3.67 (m, 3H), 2.78 - 3.03 (m, 2H), 2.63 - 2.67 (m, 1H), 2.44 - 2.52 (m, 2H), 1.86 - 1.93 (m, 4H).
509	Observed mass (ESI): 556.15 [M+H]+. 1H-NMR (400 MHz, DMSO-d6) δ (ppm): 8.33 - 8.35 (m, 2H), 7.93 - 8.00 (m, 3H), 7.79 (s, 1H), 7.51 - 7.53 (m, 1H), 7.32 (s, 1H), 7.22 - 7.24 (m, 2H), 7.07 - 7.09 (m, 1H), 6.52 - 6.53 (m, 1H), 6.38 - 6.43 (m, 1H), 4.31 - 4.38 (m, 2H), 3.86 (s, 3H), 2.93 - 2.96 (m, 1H), 2.76 - 2.86 (m, 2H), 2.60 - 2.64 (m, 1H), 2.38 - 2.51 (m, 2H), 1.77 - 1.88 (m, 2H).
510	Observed mass (ESI): 556.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.34 - 8.35 (m, 2H), 7.99 - 8.01 (m, 2H), 7.94 - 7.96 (m, 1H), 7.80 - 7.81 (m, 1H), 7.53 - 7.55 (m, 1H), 7.32 - 7.33 (m, 1H), 7.23 - 7.25 (m, 2H), 6.86 (s, 1H), 6.52 - 6.57 (m, 1H), 6.42 - 6.45 (m, 1H), 4.30 - 4.37 (m, 1H), 4.26 - 4.28 (m, 1H), 3.74 - 3.81 (s, 3H), 2.88 - 3.00 (m, 2H), 2.69 - 2.83 (m, 2H), 2.47 - 2.54 (m, 2H), 1.84 - 1.93(m, 2H).
511	Observed mass (ESI): 556.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.35 - 8.37 (m, 2H), 7.95 - 8.01 (m, 3H), 7.81 (s, 1H), 7.54 - 7.56 (m, 1H), 7.33 - 7.34 (s, 1H), 7.24 - 7.26 (m, 2H), 6.83 (s, 1H), 6.55 (s, 1H), 6.42 - 6.45 (m, 1H), 4.36 - 4.39 (m, 1H), 4.25 - 4.29 (m, 1H), 3.81 (s, 3H), 2.91 - 3.01 (m, 1H), 2.77 - 2.88 (m, 2H), 2.65 - 2.73 (m, 1H), 2.40 - 2.53 (m, 2H), 1.75 - 1.92 (m, 2H).

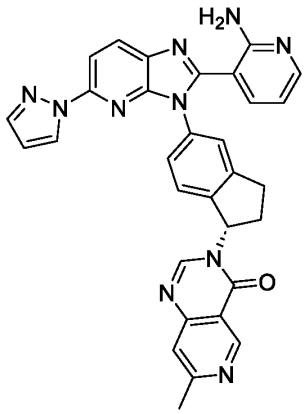
Cpd ID	Characterization Data
512	Observed mass (ESI): 608.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.28 - 8.42 (m, 1H), 8.09 - 8.28 (m, 1H), 7.89 - 8.09 (m, 1H), 7.65 - 7.89 (m, 1H), 7.41 - 7.65 (m, 1H), 7.07 - 7.41 (m, 3H), 6.36 - 6.63 (m, 1H), 5.95 - 6.21 (m, 1H), 4.75 - 4.99 (m, 1H), 4.48 - 4.75 (m, 1H),4.23 - 4.48 (m, 2H), 3.85 - 4.02 (m, 3H), 3.14 - 3.49 (m, 1H), 2.91 - 3.12 (m, 2H), 2.61 - 2.91 (m, 2H), 2.26 - 2.49 (m, 1H), 1.78 - 2.12 (m, 3H), 1.37 - 1.71 (m, 1H), 0.55 - 0.98 (m, 4H).
513	Observed mass (ESI): 608.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.28 - 8.42 (m, 1H), 8.09 - 8.28 (m, 1H), 7.89 - 8.09 (m, 1H), 7.68 - 7.89 (m, 1H), 7.39 - 7.65 (m, 1H), 7.07 - 7.39 (m, 3H), 6.35 - 6.61 (m, 1H), 5.95 - 6.19 (m, 1H), 4.85 - 5.11 (m, 1H), 4.46 - 4.73 (m, 1H),4.16 - 4.46 (m, 2H), 3.87 - 3.95 (m, 3H), 3.12 - 3.49 (m, 1H), 2.89 - 3.12 (m, 2H), 2.61 - 2.89 (m, 2H), 2.40 - 2.49 (m, 1H), 1.91 - 2.15 (m, 1H), 1.79 - 1.91 (m, 1H),1.37 - 1.79 (m, 2H), 0.55 - 0.98 (m, 4H).
514	Observed mass (ESI): 608.15 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.28 - 8.42 (m, 1H), 8.09 - 8.28 (m, 1H), 7.89 - 8.09 (m, 1H), 7.65 - 7.89 (m, 1H), 7.42 - 7.65 (m, 1H), 7.08 - 7.42 (m, 3H), 6.36 - 6.61 (m, 1H), 5.95 - 6.21 (m, 1H), 4.22 - 4.65 (m, 2H), 4.08 - 4.19 (m, 1H),4.01 - 4.08 (m, 1H), 3.88 - 3.93 (m, 3H), 3.66 - 3.82 (m, 1H), 3.41 - 3.59 (m, 1H),3.22 - 3.41 (m, 1H), 3.06 - 3.22 (m, 1H), 2.88 - 3.06 (m, 1H), 2.75 - 2.88 (m, 1H), 2.42 - 2.52 (m, 1H), 1.88 - 2.22 (m, 2H), 1.75 - 1.88 (m, 1H), 1.32 - 1.65 (m, 1H), 0.65 - 0.85 (m, 4H).
515	Observed mass (ESI): 608.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.09 - 8.42 (m, 2H), 7.89 - 8.09 (m, 1H), 7.65 - 7.89 (m, 1H), 7.41 - 7.65 (m, 1H), 7.07 - 7.41 (m, 3H), 6.36 - 6.61 (m, 1H), 5.95 - 6.21 (m, 1H), 4.28 - 4.69 (m, 2H), 4.08 - 4.19 (m, 1H),3.88 - 3.93 (m, 3H), 3.61 - 3.82 (m, 1H), 3.23 - 3.58 (m, 2H), 3.06 - 3.23 (m, 1H), 2.88 - 3.06 (m, 1H), 2.67 - 2.88 (m, 1H), 2.48 - 2.52 (m, 1H), 1.93 - 2.18 (m, 2H), 1.68 - 1.93 (m, 2H), 1.32 - 1.65 (m, 1H),1.06 - 1.32 (m, 1H), 0.69 - 0.89 (m, 4H).
519	Observed mass (ESI): 590.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.35 - 8.38 (m, 2H), 8.00 - 8.02 (m, 1H), 7.94 - 7.96 (m, 1H), 7.81 (s, 1H), 7.48 - 7.50 (m, 1H), 7.41 - 7.42 (m, 1H), 7.33 - 7.37 (m, 2H), 7.22 - 7.25 (m, 1H), 6.93 (s, 2H), 6.54 - 6.55 (m, 1H), 6.41 - 6.44 (m, 1H), 5.66 - 5.67 (m, 1H), 5.40 - 5.54 (m, 1H), 4.42 - 4.50 (m, 1H), 3.59 - 3.65 (m, 5H), 309 - 3.16 (m, 2H), 2.90 (s, 1H), 2.67 - 2.73 (m, 2H), 2.12 - 2.15 (m, 1H), 2.03 - 2.08 (m, 1H), 1.86 - 1.89 (m, 1H), 1.43 - 1.49 (m, 2H).
521	Observed mass (ESI): 576.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.19 - 8.22 (m, 1H), 8.05 - 8.09 (m, 1H), 7.74 - 7.79 (m, 1H), 7.65 - 7.72 (m, 1H), 7.45 - 7.59 (m, 3H),6.66 - 6.71 (m, 1H), 5.77 - 5.97 (m, 1H), 5.21 - 5.29 (m, 1H), 4.35 - 4.57 (m, 2H), 3.61 - 3.62 (m, 1H), 3.35 - 3.38 (m, 1H), 3.32 - 3.34 (m, 1H), 3.15 - 3.31 (m, 1H), 2.63 - 2.81 (m, 1H), 2.28 - 2.45 (m, 1H), 2.11 - 2.23 (m, 1H), 2.01 - 2.09 (m, 1H), 1.41 - 1.73 (m, 3H), 0.89 - 0.94 (m, 2H), 0.71 - 0.83 (m, 6H). (TFA salt)
523	Observed mass (ESI): 632.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ ppm: 8.29 - 8.32 (m, 1H), 8.17 (s, 1H), 8.00 - 8.01 (m, 1H), 7.77 (d, J = 8.7 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.33 (s, 1H), 7.26 - 7.29 (m, 1H), 7.22 - 7.25 (m, 1H), 6.93 (s, 2H), 6.40 - 6.44 (m, 1H), 6.05 (s, 1H), 4.61 - 4.68 (m, 1H), 4.42 - 4.49 (m, 1H), 4.27 - 4.31 (m, 1H), 4.13 - 4.25 (m, 2H), 3.92 (s, 3H), 3.65 - 3.67 (m, 1H), 3.42 - 3.51 (m, 2H), 3.15 - 3.17 (m, 1H), 2.75 - 3.01 (m, 3H), 2.28 - 2.36 (m, 1H), 1.96 - 2.03 (m, 1H), 1.78 - 1.82 (m, 2H), 1.62 - 1.69 (m, 1H), 0.67 - 0.74 (m, 4H).
524	Observed mass (ESI): 632.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ ppm: 8.29 - 8.32 (m, 1H), 8.17 (s, 1H), 8.00 - 8.01 (m, 1H), 7.77 (d, J = 8.7 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.33 (s, 1H), 7.26 - 7.28 (m, 1H), 7.21 - 7.25 (m, 1H), 6.93 (s, 2H), 6.40 - 6.44 (m, 1H), 6.05

Cpd ID	Characterization Data
	(s, 1H), 4.22 - 4.36 (m, 2H), 4.08 - 4.15 (m, 1H), 3.98 - 4.06 (m, 1H), 3.92 (s, 3H), 3.82 - 3.88 (m, 2H), 3.51 - 3.66 (m, 2H), 3.28 - 3.33 (m, 1H), 3.12 - 3.14 (m, 1H), 2.93 - 3.01 (m, 1H), 2.73 - 2.84 (m, 1H), 2.26 - 2.38 (m, 1H), 1.74 - 1.95 (m, 4H), 0.66 - 0.73 (m, 4H).
530	Observed mass (ESI): 526.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.30 - 8.41 (m, 2H), 8.21 - 8.29 (m, 1H), 7.89 - 8.05 (m, 2H), 7.76 - 7.82 (m, 1H), 7.55 - 7.64 (m, 1H), 7.43 - 7.54 (m, 1H), 7.34 - 7.40 (m, 1H), 7.19 - 7.30 (m, 2H), 7.08 - 7.18 (m, 1H), 6.92 - 6.99 (m, 2H), 6.50 - 6.58 (m, 1H), 6.40 - 6.49 (m, 1H), 4.30 - 4.49 (m, 1H), 4.20 - 4.16 (m, 1H), 3.78 - 3.91 (m, 1H), 3.10 - 3.26 (m, 2H), 2.77 - 3.09 (m, 5H), 1.88 - 1.97 (m, 1H).
531	Observed mass (ESI): 526.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.22 - 8.41 (m, 3H), 7.89 - 8.05 (m, 2H), 7.76 - 7.82 (m, 1H), 7.55 - 7.64 (m, 1H), 7.43 - 7.54 (m, 1H), 7.34 - 7.40 (m, 1H), 7.19 - 7.30 (m, 2H), 7.08 - 7.18 (m, 1H), 6.92 - 6.99 (m, 2H), 6.50 - 6.58 (m, 1H), 6.40 - 6.49 (m, 1H), 4.30 - 4.49 (m, 1H), 4.16 - 4.20 (m, 1H), 3.78 - 3.91 (m, 1H), 3.10 - 3.26 (m, 2H), 2.77 - 3.09 (m, 5H), 1.88 - 1.97 (m, 1H).
532	Observed mass (ESI): 579.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.33 - 8.46 (m, 1H), 8.01 - 8.13 (m, 3H), 7.91 - 7.99 (m, 1H), 7.53 - 7.61 (m, 1H), 7.21 - 7.44 (m, 3H), 6.44 - 6.51 (m, 1H), 5.45 - 5.69 (m, 1H), 4.55 - 4.69 (m, 1H), 4.18 - 4.41 (m, 2H), 3.07 - 3.31 (m, 4H), 2.64 - 2.82 (m, 1H), 1.82 - 2.19 (m, 3H), 1.35 - 1.48 (m, 1H), 1.25 - 1.34 (m, 1H), 0.65 - 0.79 (m, 4H).
533	Observed mass (ESI): 579.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.43 - 8.46 (m, 1H), 8.01 - 8.19 (m, 4H), 7.55 - 7.59 (m, 1H), 7.36 - 7.42 (m, 1H), 7.24 - 7.34 (m, 2H), 6.45 - 6.49 (m, 1H), 5.17 - 5.38 (m, 1H), 4.39 - 4.44 (m, 1H), 4.15 - 4.32 (m, 2H), 3.41 - 3.55 (m, 1H), 3.12 - 3.23 (m, 1H), 2.95 - 3.11 (m, 2H), 2.71 - 2.84 (m, 1H), 1.82 - 2.11 (m, 3H), 1.25 - 1.37 (m, 1H), 1.15 - 1.19 (m, 1H), 0.72 - 0.89 (m, 4H).
542	Observed mass (ESI): 580.29 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ 9.35 (s, 1H), 9.34-9.29 (m, 1H), 8.38 (d, J = 2.6 Hz, 1H), 8.08 (d, J =2.0 Hz, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.84 (d, J = 1.6 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.63 (s, 1H), 7.57 (d, J = 7.4 Hz, 1H), 7.50 (d, J =2.0 Hz, 1H), 6.69 – 6.55 (m, 1H), 5.91-5.70 (m, 1H), 5.30-5.26 (m, 1H), 5.92-5.74 (m, 1H), 5.38-5.21 (m, 1H), 4.55-4.26 (m, 1H), 4.19-4.11 (m, 2H), 4.00-3.64(m, 2H), 3.29-3.10 (m, 1H), 2.94-2.91 (m, 1H), 3.18-3.11 (m, 1H), 2.94-2.91 (m, 1H), 2.23-2.18 (m, 2H), 1.70-1.42 (m, 2H), 1.03-1.01 (m, 6H).
543	Observed mass (ESI): 619.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32 (d, J = 8.3 Hz, 1H), 8.25 (d, J = 5.4 Hz, 1H), 8.14 (d, J = 4.0 Hz, 1H), 8.02 (dd, J = 4.8, 1.9 Hz, 1H), 7.61 (dd, J = 5.5, 1.5 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.36 - 7.43 (m, 3H), 7.26 (dd, J = 7.7, 1.9 Hz, 1H), 6.97 (s, 2H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 5.34 - 5.61 (m, 1H), 4.41 - 4.58 (m, 1H), 4.12 - 4.29 (m, 2H), 3.89 (s, 3H), 3.19 - 3.25 (m, 2H), 3.13 - 3.19 (m, 1H), 3.01 - 3.11 (m, 2H), 2.80 - 2.97 (m, 1H), 1.81 - 2.10 (m, 3H), 1.23 - 1.52 (m, 2H), 0.65 - 0.81 (m, 4H).
545	Observed mass (ESI): 619.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm) 8.47 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 7.94 - 8.09 (m, 1H), 7.72 - 7.87 (m, 2H), 7.53 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.16 - 7.29 (m, 1H), 6.98 (s, 2H), 6.77 - 6.86 (m, 1H), 6.37 - 6.47 (m, 1H), 5.31 - 5.61 (m, 1H), 4.36 - 4.57 (m, 1H), 4.10 - 4.27 (m, 2H), 4.01 (s, 3H), 3.15 - 3.31 (m, 2H), 2.68 - 2.98 (m, 3H), 2.14 - 2.28 (m, 1H), 1.73 - 2.11 (m, 3H), 1.20 - 1. 49 (m, 2H), 0.58 - 0.82 (m, 4H).
557	Observed mass (ESI): 600.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.37 - 8.39 (m, 1H), 8.31 - 8.33 (m, 1H), 8.00 - 8.06 (m, 1H), 7.92 - 7.95 (m, 1H), 7.81 - 7.85 (m, 1H), 7.28 - 7.37 (m, 2H), 7.20 - 7.26 (m, 2H), 6.54 - 6.68 (m, 1H), 6.24 - 6.42 (m, 1H), 4.21 - 4.60 (m, 3H), 3.56 - 3.60 (m, 2H), 2.83 - 3.14 (m, 4H), 2.21 - 2.32 (m, 2H), 1.92 - 2.09 (m, 2H),

Cpd ID	Characterization Data
	1.37 - 1.82 (m, 3H), 0.60 - 0.89 (m, 4H), 0.31 - 0.45 (m, 1H), 0.15 - 0.29 (m, 2H), - 0.09 - 0.00 (m, 1H).
560	Observed mass (ESI): 668.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ ppm: 8.36 (d, J = 8.6 Hz, 1H), 8.29 (d, J = 2.7 Hz, 1H), 7.99 (dd, J = 4.9, 1.8 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.20 - 7.73 (m, 5H), 6.90 (s, 2H), 6.38 - 6.47 (m, 1H), 6.30 - 6.37 (m, 1H), 4.18 - 4.38 (m, 2H), 3.95 - 4.16 (m, 2H), 3.76 - 3.93 (m, 2H), 3.51 - 3.69 (m, 2H), 3.21 - 3.29 (m, 2H), 3.10 - 3.20 (m, 1H), 2.70 - 3.04 (m, 2H), 2.24 - 2.38 (m, 1H), 1.70 - 1.98 (m, 4H), 0.60 - 0.75 (m, 4H).
561	Observed mass (ESI): 668.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.36 (d, J = 8.6 Hz, 1H), 8.30 (d, J = 2.7 Hz, 1H), 7.99 (dd, J = 4.8, 1.9 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.70 - 7.21 (m, 5H), 6.90 (s, 2H), 6.38 - 6.47 (m, 1H), 6.34 (d, J = 2.7 Hz, 1H), 4.57 - 4.71 (m, 1H), 4.42 - 4.55 (m, 1H), 4.26 - 4.38 (m, 1H), 4.03 - 4.24 (m, 2H), 3.57 - 3.70 (m, 1H), 3.39 - 3.52 (m, 2H), 3.21 - 3.25 (m, 1H), 3.08 - 3.19 (m, 1H), 2.74 - 3.01 (m, 3H), 2.28 - 2.38 (m, 1H), 1.91 - 2.03 (m, 1H), 1.72 - 1.88 (m, 2H), 1.60 - 1.70 (m, 1H), 0.60 - 0.76 (m, 4H).
579	Observed mass (ESI): 613.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ(ppm): 8.30 - 8.43 (m, 2H), 8.24 (d, J = 6.5 Hz, 1H), 7.91 - 8.06 (m, 2H), 7.80 - 7.83 (m, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.32 - 7.40 (m, 2H), 7.24 (dd, J = 7.7, 1.9 Hz, 1H), 7.16 (d, J = 6.5 Hz, 1H), 6.92 (s, 2H), 6.52 - 6.58 (m, 1H), 6.38 - 6.47 (m, 1H), 5.35 - 5.63 (m, 1H), 4.38 - 4.56 (m, 1H), 3.97 - 4.37 (m, 1H), 3.19 - 3.33 (m, 4H), 3.06 - 3.18 (m, 2H), 2.23 - 2.36 (m, 1H), 2.02 - 2.13 (m, 1H), 1.76 - 2.01 (m, 1H), 1.34 - 1.54 (m, 2H).
580	Observed mass (ESI): 623.4 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.99 - 9.20 (m, 1H), 8.21 - 8.46 (m, 2H), 7.84 - 8.08 (m, 3H), 7.70 - 8.84 (m, 1H), 7.40 - 7.56 (m, 1H), 7.26 - 7.36 (m, 1H), 7.11 - 7.26 (m, 2H), 6.43 - 6.60 (m, 1H), 6.34 - 6.43 (m, 1H), 4.20 - 4.40 (m, 2H), 3.54 - 3.57 (m, 1H), 3.01 - 3.18 (m, 2H), 2.84 - 3.00 (m, 2H), 2.66 - 2.84 (m, 1H), 2.41 - 2.45 (m, 1H), 1.70 - 2.11 (m, 3H), 1.33 - 1.37 (m, 2H).
581	Observed mass (ESI): 567.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.35 - 8.38 (m, 2H), 8.22 (d, J = 6.3 Hz, 1H), 7.94 - 8.03 (m, 2H), 7.81 (s, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.38 (s, 1H), 7.22 - 7.28 (m, 2H), 6.98 (s, 2H), 6.64 (d, J = 6.3 Hz, 1H), 6.53 - 6.54 (m, 1H), 6.45 - 6.48 (m, 1H), 4.22 - 4.31 (m, 3H), 3.93 - 3.95 (m, 1H), 3.79 - 3.84 (m, 2H), 2.95 - 3.05 (m, 1H), 2.80 - 2.82 (m, 1H), 2.49 - 2.51 (m, 1H), 1.72 - 1.80 (m, 1H).
586	Observed mass (ESI): 625.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32 - 8.40 (m, 2H), 8.08 (s, 1H), 7.92 - 8.04 (m, 2H), 7.78 - 7.84 (m, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 1.9 Hz, 1H), 7.18 - 7.29 (m, 2H), 6.94 (s, 2H), 6.52 - 6.58 (m, 1H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 4.32 - 4.50 (m, 3H), 3.93 (s, 3H), 3.18 - 3.25 (m, 2H), 2.90 - 3.04 (m, 2H), 2.73 - 2.84 (m, 1H), 2.39 - 2.46 (m, 1H), 2.00 - 2.10 (m, 1H), 1.91 - 1.99 (m, 1H), 1.76 - 1.90 (m, 2H), 1.32 - 1.47 (m, 2H).
589	Observed mass (ESI): 615.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 8.24 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 2.7 Hz, 1H), 8.01 – 7.93 (m, 1H), 7.75 (d, J = 8.6 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 2.1 Hz, 1H), 7.29 (d, J = 1.8 Hz, 1H), 7.25 – 7.14 (m, 2H), 6.94 (s, 2H), 6.44 – 6.35 (m, 1H), 6.05 (d, J = 2.7 Hz, 1H), 5.64 (d, J = 2.1 Hz, 1H), 4.36 (s, 1H), 3.63 (s, 5H), 2.87 (s, 7H), 2.83 – 2.71 (m, 2H), 2.71 – 2.57 (m, 2H), 2.43 (d, J = 8.1 Hz, 1H), 1.97 (d, J = 12.0 Hz, 1H), 1.90 – 1.68 (m, 2H), 1.48 – 1.30 (m, 2H).
592	Observed mass (ESI): 596.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.70 (s, 1H), 8.31 - 8.40 (m, 2H), 7.92 - 8.04 (m, 2H), 7.81 (d, J = 1.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.34 (s, 1H), 7.19 - 7.30 (m, 2H), 6.94 (s, 2H), 6.52 - 6.58 (m, 1H), 6.38 - 6.46 (m, 1H), 4.29 - 4.51 (m, 3H), 3.26 - 3.31 (m, 2H), 2.91 - 3.09 (m, 2H), 2.73 - 2.84 (m, 1H), 2.40 - 2.45 (m,

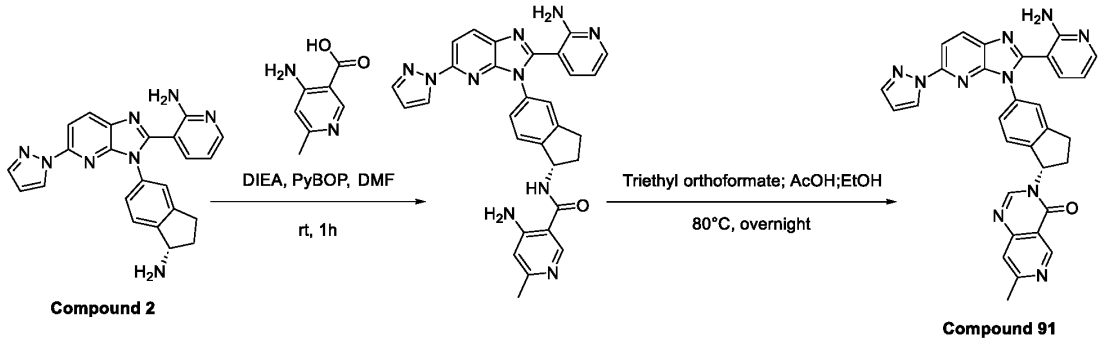
Cpd ID	Characterization Data
	1H), 1.91 - 2.08 (m, 2H), 1.75 - 1.84 (m, 1H), 1.30- 1.45 (m, 2H).
596	Observed mass (ESI): 627.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 8.26 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 2.7 Hz, 1H), 8.03 – 7.94 (m, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.41 (d, J = 2.2 Hz, 1H), 7.32 (s, 1H), 7.28 – 7.16 (m, 2H), 6.94 (s, 2H), 6.45 – 6.37 (m, 1H), 5.86 (d, J = 2.7 Hz, 1H), 5.66 (d, J = 2.3 Hz, 1H), 4.48 – 4.32 (m, 1H), 4.16 – 4.07 (m, 1H), 3.93 – 3.81 (m, 4H), 3.69 – 3.55 (m, 5H), 3.17 (d, J = 5.1 Hz, 4H), 2.99 – 2.90 (m, 1H), 2.86 – 2.77 (m, 1H), 2.74 – 2.64 (m, 1H), 2.40 – 2.29 (m, 2H), 2.04 – 1.93 (m, 1H), 1.92 – 1.79 (m, 1H), 1.51 – 1.35 (m, 1H).
602	Observed mass (ESI): 635.45 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32- 8.42 (m, 2H), 8.02 (dd, J = 4.9, 1.9, 1H), 7.96 (d, J = 8.6, 1H), 7.82 (d, J = 1.6 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.41 (s, 1H), 7.21- 7.33 (m, 2H), 7.12 (s, 1H), 6.92 (s, 2H), 6.56 (dd, J = 2.6, 1.7 Hz, 1H), 6.44 (dd, J = 7.6, 4.8 Hz, 1H), 4.26- 4.59 (m, 3H), 3.00- 3.22 (m, 4H), 2.78- 2.92 (m, 1H), 2.40 - 2.45 (m, 1H),2.05- 2.16 (m, 1H), 1.84- 2.05 (m, 3H), 1.36- 1.45 (m, 2H), 0.94- 1.07 (m, 4H). (formic acid salt)
603	Observed mass (ESI): 635.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.35 - 8.38 (m, 2H), 8.00 - 8.02 (m, 1H), 7.94 - 7.97 (m, 1H), 7.81 (s, 1H), 7.48 - 7.51 (m, 1H), 7.33 (s, 1H), 7.23 - 7.25 (m, 2H), 6.56 (s, 1H), 6.42 - 6.46 (m, 1H), 4.32 - 4.37 (m, 3H), 3.23 - 3.30 (m, 2H), 3.07 - 3.13 (m, 2H), 2.95 - 3.01 (m, 2H), 2.81 - 2.93 (m, 3H), 2.47 - 2.53 (m, 1H), 1.97 - 2.06 (m, 4H), 1.79 - 1.91 (m, 1H), 1.36 - 1.47 (m, 2H).

[00449] Example 70: (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-7-methylpyrido[4,3-d]pyrimidin-4(3H)-one (Compound 91)



Compound 91

[00450] Synthetic Route:



[00451] Step 1: Synthesis of (S)-4-amino-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide

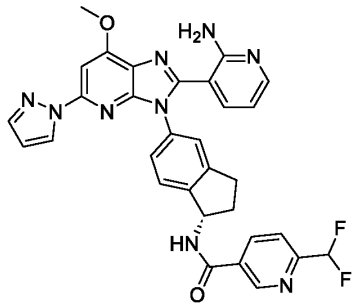
[00452] To a solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol), 4-amino-6-methylpyridine-3-carboxylic acid (37.3 mg, 0.245 mmol) and N,N-diisopropylethylamine (94.9 mg, 0.735 mmol) in DMF (3 mL) was added PyBOP (127 mg, 0.245 mmol) at 0°C. The resulting mixture was stirred at room temperature for 1 h. The reaction was quenched by the addition of H_2O (20 ml). The precipitated solids were collected by filtration and washed with H_2O (3 x 20 ml). The solids were purified by reverse phase column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-4-amino-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (100 mg, 74% yield) as an off-white solid. MS (ESI) calcd. For $C_{30}H_{26}N_{10}O$: 542.23 m/z, found: 543.20 $[M+H]^+$.

[00453] Step 2: Synthesis of (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-7-methylpyrido[4,3-d]pyrimidin-4(3H)-one (Compound 91)

[00454] A solution of (S)-4-amino-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (80 mg, 0.15 mmol), triethyl orthoformate (0.4 mL) and AcOH (0.2 mL) in EtOH (2 mL) was maintained under nitrogen and stirred overnight at 80°C. The solvent was evaporated under vacuum. The residue was purified by Prep-HPLC on a XBridge Prep OBD C18 Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-7-methylpyrido[4,3-d]pyrimidin-4(3H)-one (TFA salt) (12.1 mg, 15% yield) as an off-white solid. MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found 553.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.26 - 9.32 (m, 1H), 8.35 - 8.47 (m, 3H), 7.96 - 8.08 (m, 2H), 7.81 - 7.85 (m, 1H), 7.70 - 7.78 (m, 1H), 7.56 - 7.60 (m, 2H), 7.25 - 7.45 (m, 2H), 6.80 - 6.88 (m, 1H), 6.56 - 6.61 (m, 1H), 6.25

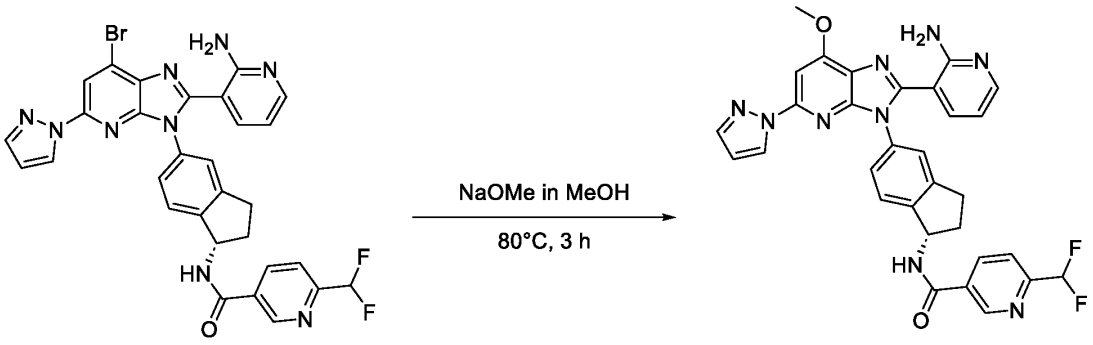
- 6.34 (m, 1H), 3.23 - 3.31 (m, 1H), 2.98 - 3.11 (m, 1H), 2.69 - 2.83 (m, 1H), 2.63 (s, 3H), 2.36 - 2.45 (m, 1H).

[00455] Example 71: (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-methoxy-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 122); (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-cyano-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 123); (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-fluoro-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 165); and (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-(difluoromethyl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide



Compound 122

[00456] Synthetic Route:



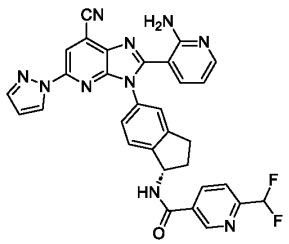
Intermediate 122-2 **Compound 122**

[00457] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-methoxy-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 122)

[00458] To a solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Intermediate 122-2**) (100 mg, 0.156 mmol) in MeOH (5 mL) was added CH_3ONa (42.0 mg, 0.780 mmol) and the resulting mixture was stirred for 3 h at 80°C. The reaction was quenched

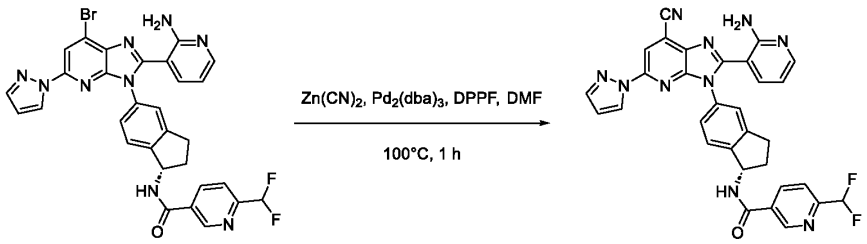
by the addition of H_2O (5 ml) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 30 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05 mmol/L formic acid) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-methoxy-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Compound 122**) (5 mg, 5% yield) as an off-white solid. MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O_2$, 593.21 m/z, found 594.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.13 (s, 1H), 8.42 - 8.50 (m, 1H), 8.32 - 8.40 (m, 1H), 7.95 - 8.05 (m, 1H), 7.80 - 7.90 (m, 2H), 7.50 (s, 1H), 7.40 - 7.45 (m, 1H), 7.30 - 7.40 (m, 1H), 7.22 - 7.30 (m, 2H), 6.85 - 7.20 (m, 1H), 6.55 - 6.60 (m, 1H), 6.40 - 6.52 (m, 1H), 5.60 - 5.70 (m, 1H), 4.18 (s, 3H), 3.00 - 3.15 (m, 1H), 2.85 - 3.00 (m, 1H), 2.58 - 2.63 (m, 1H), 2.00 - 2.20 (m, 1H). ^{19}F NMR (300 MHz, DMSO-d_6) δ (ppm): -116.05. (formic acid salt)

[00459] (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-cyano-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 123)



Compound 123

[00460] Synthetic Route:



Intermediate 122-2 Compound 123

[00461] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-cyano-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Example 123)

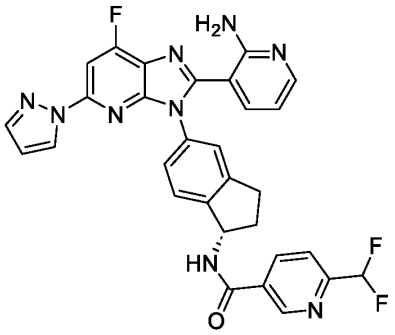
[00462] A mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Intermediate 122-2**) (80 mg, 0.125 mmol), $Zn(CN)_2$ (29.2 mg, 0.250 mmol), DPPF (14 mg, 0.025 mmol) and $Pd_2(dba)_3$ (23 mg, 0.025 mmol) in DMF (2 mL) was stirred for 1 h at 100°C. The resulting mixture was diluted with water (30 mL). The mixture was extracted with ethyl acetate (3 x 50 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a XBridge Prep Shield RP OBD C_{18} Column using a gradient of acetonitrile in water to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-cyano-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (21.2 mg, 28% yield) as a yellow solid. MS (ESI) calcd. for $C_{31}H_{22}F_2N_{10}O$, 588.19 m/z, found 589.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.28 - 9.34 (m, 1H), 9.12 - 9.21 (m, 1H), 8.43 - 8.52 (m, 1H), 8.33 - 8.42 (m, 1H), 8.28 - 8.32 (m, 1H), 8.05 - 8.11 (m, 1H), 7.82 - 7.93 (m, 2H), 7.33 - 7.54 (m, 4H), 6.88 - 7.22 (m, 1H), 6.61 - 6.69 (m, 1H), 6.50 - 6.58 (m, 1H), 5.64 - 5.73 (m, 1H), 2.91 - 3.12 (m, 2H), 2.57 - 2.63 (m, 1H), 2.08 - 2.20 (m, 1H).

[00463] The following compounds were prepared analogously to the synthetic preparation of Compound 123.

[00464] **Table 5B.** Characterization data of compounds prepared analogously to compound 325.

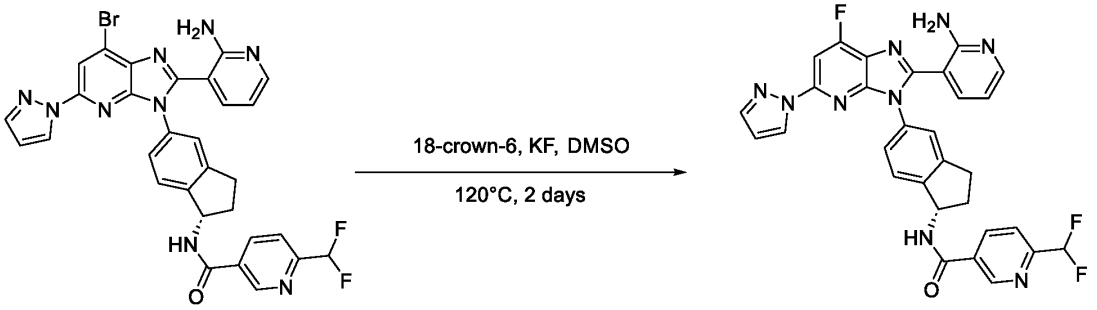
Cpd ID	Characterization Data
547	Observed mass (ESI): 554.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.89 - 8.94 (m, 1H), 8.42 - 8.45 (m, 1H), 8.12 - 8.18 (m, 3H), 8.02 - 8.05 (m, 1H), 7.37 - 7.44 (m, 3H), 7.30 - 7.37 (m, 2H), 6.46 - 6.54 (m, 1H), 5.56 - 5.67 (m, 1H), 2.96 - 3.07 (m, 1H), 2.82 - 2.96 (m, 1H), 2.54 - 2.59 (m, 1H), 2.51 (s, 3H), 2.00 - 2.13 (m, 1H).
548	Observed mass (ESI): 590.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 9.11 - 9.16 (m, 1H), 8.42 - 8.47 (m, 2H), 8.17 (s, 2H), 8.01 - 8.07 (m, 1H), 7.80 - 7.85 (m, 1H), 7.41 - 7.46 (m, 2H), 7.32 - 7.41 (m, 2H), 6.85 - 7.18 (m, 1H), 6.47 - 6.54 (m, 1H), 5.59 - 5.69 (m, 1H), 2.97 - 3.08 (m, 1H), 2.83 - 2.97 (m, 1H), 2.55 - 2.62 (m, 1H), 2.01 - 2.14 (m, 1H).

[00465] **(S)-N-(5-(2-(2-aminopyridin-3-yl)-7-fluoro-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 165)**



Compound 165

[00466] Synthetic Route:



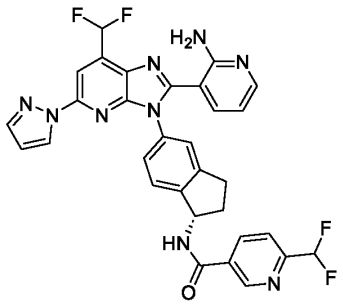
Intermediate 122-2 **Compound 165**

[00467] **Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-fluoro-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide**

[00468] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Intermediate 122-2**) (150 mg, 0.233 mmol) in DMSO (3 mL) was treated with 18-crown-6 (61.7 mg, 0.233 mmol) and KF (135.6 mg, 2.330 mmol) at room temperature. The resulting mixture was stirred for 2 days at 120°C under N_2 atmosphere. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3). The product was further purified by Prep-HPLC on a Xselect CSH Prep Fluoro-Phenyl Column using a gradient of acetonitrile in water (+ 10 mmol/L ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-fluoro-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Compound 165**) (11.4 mg, 8% yield) as an off-white solid. MS (ESI) calcd. for $C_{30}H_{22}F_3N_9O$, 581.19 m/z, found 582.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 9.14 (s, 1H), 8.40 - 8.50 (m, 1H), 8.32 - 8.40 (m, 1H), 8.00 - 8.10 (m, 1H), 7.82 - 7.85 (m, 2H), 7.75 - 7.80 (m, 1H), 7.37 - 7.45 (m, 2H), 7.30 - 7.37 (m, 2H), 6.80 - 7.20 (m, 1H), 6.55 - 6.60 (m, 1H), 6.45 - 6.52

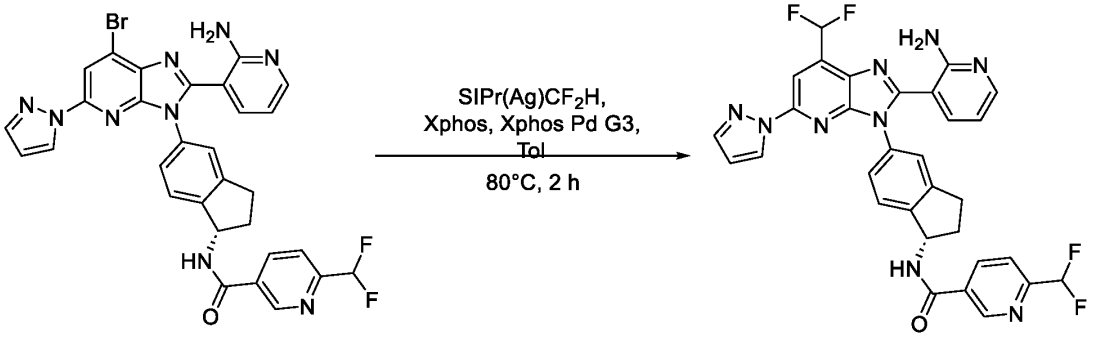
(m, 1H), 5.60 - 5.70 (m, 1H), 2.85 - 3.10 (m, 2H), 2.58 - 2.63 (m, 1H), 2.00 - 2.18 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm): -114.41, -116.05.

[00469] (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-(difluoromethyl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 177)



Compound 177

[00470] Synthetic Route:



Intermediate 122-2

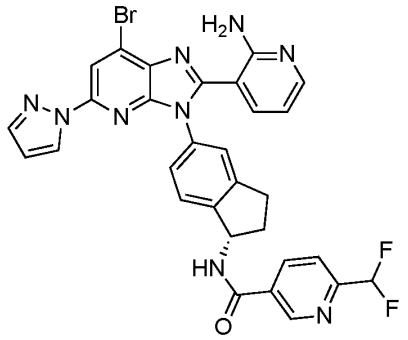
Compound 177

[00471] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-(difluoromethyl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 177)

[00472] A mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Intermediate 122-2**) (100 mg, 0.156 mmol, 1 equiv), XPhos (7.4 mg, 0.016 mmol, 0.1 equiv), XPhos Pd G3 (13 mg, 0.016 mmol, 0.1 equiv) and {1,3-bis[2,6-bis(propan-2-yl)phenyl]imidazolidin-2-ylidene}(difluoromethyl)silver (120 mg, 0.218 mmol, 1.4 equiv) in toluene (2 mL) was stirred for 2 h at 80°C under nitrogen atmosphere. The resulting mixture was diluted with water (20 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 50 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was

concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3). The product was further purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.1% formic acid) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-(difluoromethyl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (**Compound 177**, formic acid salt) (5.1 mg, 5% yield) as an off-white solid. MS (ESI) calcd. for $C_{31}H_{23}F_4N_9O$, 613.20 m/z, found 614.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 9.13 - 9.20 (m, 1H), 8.39 - 8.52 (m, 2H), 8.06 - 8.15 (m, 2H), 7.85 - 7.96 (m, 2H), 7.67 - 7.74 (m, 1H), 7.41 - 7.54 (m, 2H), 7.31 - 7.40 (m, 2H), 6.84 - 7.19 (m, 1H), 6.59 - 6.70 (m, 1H), 6.49 - 6.57 (m, 1H), 5.67 - 5.78 (m, 1H), 4.38 - 4.52 (m, 3H), 2.89 - 3.13 (m, 2H), 2.61 - 2.68 (m, 1H), 2.09 - 2.20 (m, 1H); ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm): -115.49, -116.04.

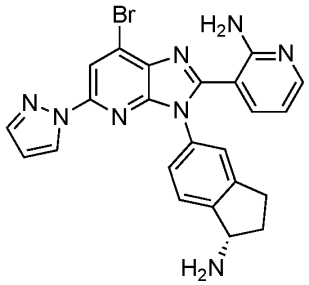
[00473] Intermediate 122-2: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-(difluoromethyl)nicotinamide



Intermediate 122-2

[00474] Intermediate 122-2 was prepared in a manner analogous to **Compound 3** using **Intermediate 122-1** in place of **Compound 2**, 6-(difluoromethyl)nicotinic acid in place of 3,4-difluoro-5-anisic acid and PyBOP in place of HATU. MS (ESI) calcd. for $C_{30}H_{22}BrF_2N_9O$: 641.11 m/z, found: 642.15 $[M+H]^+$. (formic acid salt)

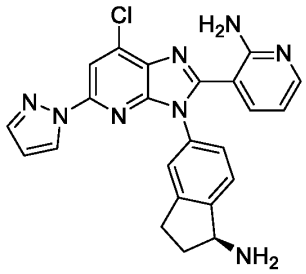
[00475] Intermediate 122-1: (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-7-bromo-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine



Intermediate 122-1

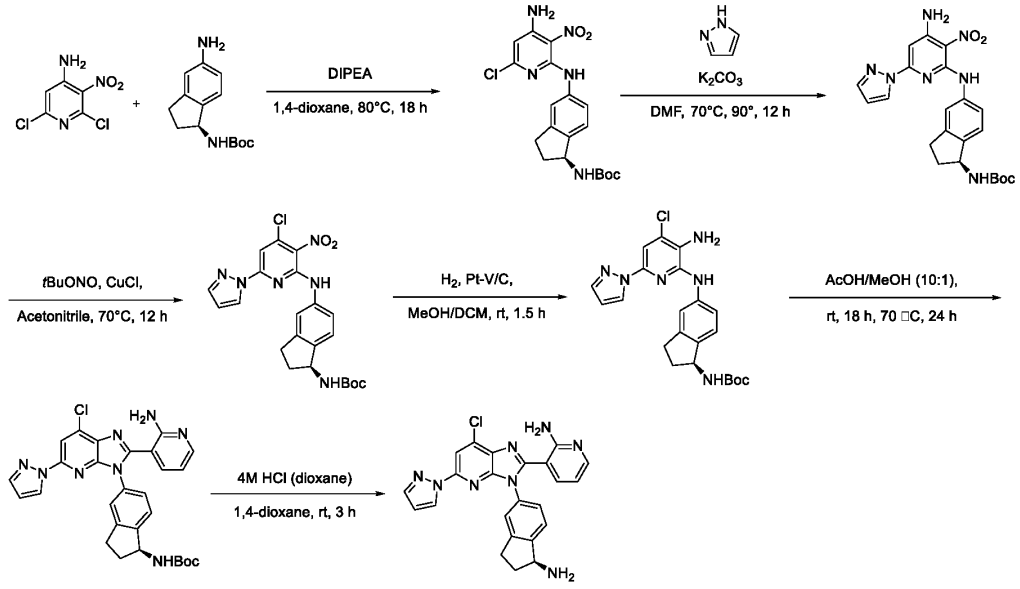
[00476] **Intermediate 122-1** was prepared in a manner analogous to **Intermediate 122-0** using copper (I) bromide in place of copper (I) chloride. MS (ESI) calculated for MS (ESI) calculated for $C_{23}H_{19}BrN_8$: 486.09, 488.09, found 487.11, 489.15 $[M+H]^+$.

[00477] **Intermediate 122-0: (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-7-chloro-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine**



Intermediate 122-0

[00478] Synthetic Route:



Intermediate 122-0

[00479] Step 1: Synthesis of (*S*)-*tert*-butyl (5-((4-amino-6-chloro-3-nitropyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate

[00480] To a solution of 2,6-dichloro-3-nitropyridin-4-amine (3.51 g, 16.4 mmol, 1.05 equiv) and (*S*)-*tert*-butyl (5-amino-2,3-dihydro-1*H*-inden-1-yl)carbamate (4.26 mg, 15.6 mmol, 1 equiv) in 1,4-dioxane (35 mL) was added N,N-diisopropylethylamine (8.23 mL, 46.8 mmol, 3 equiv) and the mixture was stirred at 80°C for 18 h. The reaction mixture was concentrated in vacuo and the residue was purified by silica gel column chromatography (0 – 15% methanol in dichloromethane) to obtain (*S*)-*tert*-butyl (5-((4-amino-6-chloro-3-nitropyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (6.25 g, 95 %) as an orange solid. MS (ESI) calculated for $C_{19}H_{22}ClN_5O_4$: 419.14 found 420.20 $[M+H]^+$.

[00481] Step 2: Synthesis of (*S*)-*tert*-butyl (5-((4-amino-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate

[00482] To a solution of (*S*)-*tert*-butyl (5-((4-amino-6-chloro-3-nitropyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (4.88 g, 11.6 mmol, 1 equiv) and pyrazole (1.67 g, 23.2 mmol, 2 equiv) in N,N-dimethylformamide (23 mL) was added potassium carbonate (4.92 g, 34.9 mmol, 3 equiv) and the resulting suspension was stirred at 70°C for 18 h and then at 90°C for 12 h. The reaction was allowed to cool to room temperature and was diluted with diethyl ether (20 mL) followed by water (50 mL) dropwise, during which an orange solid precipitated. The solid was filtered through a Buchner funnel. The crude solid was purified by silica gel column chromatography (5 - 15% methanol in dichloromethane) to obtain (*S*)-*tert*-butyl (5-((4-amino-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate

(3.18 g, 60%) as an orange solid. MS (ESI) calculated for $C_{22}H_{25}N_7O_4$: 451.20, found 452.26 $[M+H]^+$.

[00483] Step 3: Synthesis of (*S*)-*tert*-butyl (5-((4-chloro-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate

[00484] To a solution of (*S*)-*tert*-butyl (5-((4-amino-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (680 mg, 1.11 mmol, 1 equiv) in acetonitrile (4.1 mL) was added *tert*-butyl nitrite (172 mg, 1.67 mmol, 1.5 equiv) followed by copper (I) chloride (171 mg, 1.67 mmol, 1.5 equiv) and the resulting mixture was stirred at 70°C for 12 h. The reaction mixture was concentrated and purified by silica gel column chromatography (15 - 20% ethyl acetate in heptanes) to obtain (*S*)-*tert*-butyl (5-((4-chloro-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (177 mg, 34%) as a yellow solid. MS (ESI) calculated for $C_{22}H_{23}ClN_6O_4$: 470.15, found 471.16.

[00485] Step 4: Synthesis of (*S*)-*tert*-butyl (5-((3-amino-4-chloro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate

[00486] To a solution of (*S*)-*tert*-butyl (5-((4-chloro-3-nitro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (87 mg, 0.18 mmol, 1 equiv) in methanol (1.8 mL) and dichloromethane (1.8 mL) was added platinum on carbon (contains 1 wt% platinum, 2 wt% vanadium) (20 mg, 1.02 µmol, 0.5 mol%) and the mixture was stirred at room temperature for 1.5 h under hydrogen atmosphere. The reaction mixture was filtered through celite washing with dichloromethane (5 mL). The filtrate was concentrated *in vacuo* to obtain (*S*)-*tert*-butyl (5-((3-amino-4-chloro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (79.8 mg, 100%) as a pale-yellow oil, which was used without further purification in the next step. MS (ESI) calculated for $C_{22}H_{25}ClN_6O_2$: 440.17, found 441.24 $[M+H]^+$.

[00487] Step 5: Synthesis of (*S*)-*tert*-butyl (5-(2-(2-aminopyridin-3-yl)-7-chloro-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)carbamate

[00488] To a solution of (*S*)-*tert*-butyl (5-((3-amino-4-chloro-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)carbamate (79.8 mg, 0.181 mmol, 1 equiv) in acetic acid (650 µL) and methanol (65.0 µL) was added 2-aminopyridine-3-carboxaldehyde (24.8 mg, 0.199 mmol, 1.1 equiv) and the reaction was stirred at room temperature for 18 h, then at 70°C for 24 h. The reaction mixture was then cooled to 0°C and quenched with 2N aqueous sodium hydroxide (until pH ~9–10), then extracted with dichloromethane (3 x 5 mL). The organic layers were combined, washed with brine (3 mL), dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (60 - 70% ethyl acetate in heptanes) to obtain (*S*)-*tert*-butyl (5-(2-(2-aminopyridin-3-yl)-7-chloro-5-(1*H*-pyrazol-1-yl)-3*H*-

imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)carbamate (87 mg, 89%) as a pale-yellow solid. MS (ESI) calculated for $C_{28}H_{27}ClN_8O_2$: 542.19, found 543.22 $[M+H]^+$.

[00489] Step 6: Synthesis of (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine hydrochloride (Intermediate 122-0)

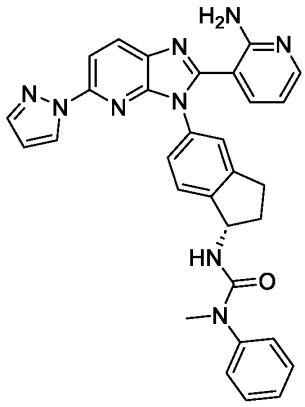
[00490] To a solution of (*S*)-*tert*-butyl (5-(2-(2-aminopyridin-3-yl)-7-chloro-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)carbamate (87 mg, 0.16 mmol) in 1,4-dioxane (1.0 mL) was added a 4N solution of hydrochloric acid in 1,4-dioxane (0.8 mL) and the mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated *in vacuo* co-evaporating with dichloromethane (3 x 5 mL) to obtain (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-7-chloro-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (**Intermediate 122-0**) (76.8 mg, 100%) as a beige solid, which was used in subsequent transformations without further purification. MS (ESI) calculated for $C_{23}H_{19}ClN_8$: 442.14, found 443.05 $[M+H]^+$.

[00491] Table 6. Characterization data of compounds prepared analogously to compounds 122, 123, 165, and 177.

Cpd ID	Characterization Data
124	MS (ESI) calcd. for $C_{31}H_{27}N_9O_2$, 557.23 m/z, found 558.25 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.50 - 8.56 (m, 1H), 8.29 - 8.36 (m, 1H), 7.98 - 8.06 (m, 1H), 7.74 -7.85 (m, 2H), 7.50 - 7.56 (m, 1H), 7.43 - 7.49 (m, 1H), 7.34 - 7.39 (m, 1H), 7.25 - 7.33 (m, 2H), 7.19 - 7.24 (m, 1H), 6.54 - 6.61 (m, 1H), 6.41 - 6.49 (m, 1H), 5.56 - 5.63 (m, 1H), 4.19 (s, 3H), 2.86 - 3.10 (m, 2H), 2.56 - 2.62 (m, 4H), 1.97 - 2.12 (m, 1H)
125	MS (ESI) calcd. for $C_{31}H_{24}N_{10}O$, 552.21 m/z, found 553.10 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.50 - 8.60 (m, 1H), 8.35 - 8.40 (m, 1H), 8.29 (s, 1H), 8.02 - 8.10 (m, 1H), 7.85 - 7.92 (m, 1H), 7.75 - 7.85 (m, 1H), 7.46 - 7.55 (m, 1H), 7.40 - 7.45 (m, 1H), 7.25 - 7.40 (m, 3H), 6.60 - 6.65 (m, 1H), 6.45 - 6.55 (m, 1H), 6.50 - 6.52 (m, 1H), 3.00 - 3.10 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.62 (m, 4H), 1.90 - 2.12 (m, 1H). (formic acid salt)
212	MS (ESI) calcd. for $C_{30}H_{24}FN_9O$: 545.21 m/z, found: 546.25 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ (ppm): 8.63 - 8.64 (m, 1H), 8.36 - 8.37 (m, 1H), 8.08 - 8.10 (m, 2H), 7.84 - 7.86 (m, 3H), 7.47 - 7.58 (m, 3H), 7.47 - 7.48 (m, 1H), 6.80 - 6.85 (m, 1H), 6.59 - 6.60 (m, 1H), 5.55 - 5.59 (m, 1H), 3.01 - 3.07 (m, 1H), 2.90 - 2.96 (m, 1H), 2.65 - 2.69 (m, 3H), 2.53 - 2.57 (m, 1H), 2.00 - 2.06 (m, 1H). (TFA salt)
213	MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$, 577.22 m/z, found 578.10 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 8.49 - 8.57 (m, 1H), 8.38 - 8.41 (m, 1H), 8.12 - 8.19 (m, 1H), 8.05 - 8.11 (m, 1H), 7.85 - 7.93 (m, 1H), 7.76 - 7.84 (m, 1H), 7.50 - 7.69 (m, 2H), 7.41 - 7.48 (m, 1H), 7.29 - 7.40 (m, 3H), 6.59 - 6.67 (m, 1H), 6.46 - 6.53 (m, 1H), 5.58 - 5.64 (m, 1H), 2.93 - 3.16 (m, 3H), 2.58 - 2.69 (m, 3H), 2.50 - 2.58 (m, 1H), 2.01 - 2.18 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm): -114.742, -115.521.

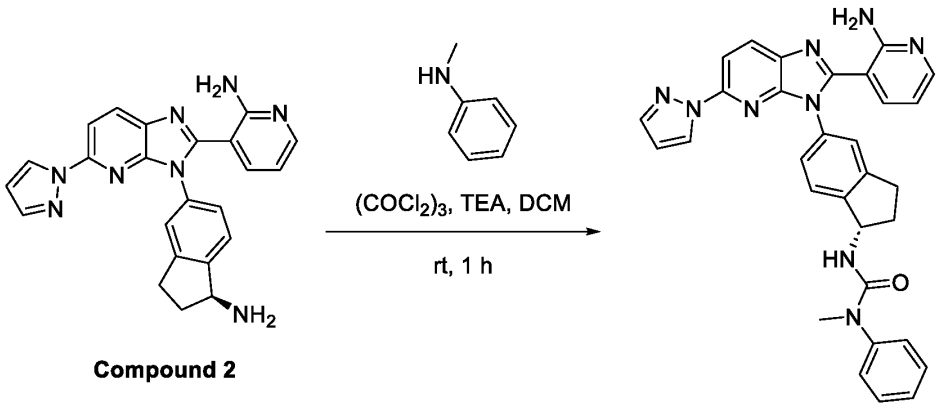
Cpd ID	Characterization Data
329	MS (ESI) calcd. for C31H21F3N10O, 606.19 m/z, found 607.10 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 9.10 - 9.18 (m, 1H), 8.39 - 8.49 (m, 1H), 8.27 - 8.35 (m, 1H), 8.09 - 8.14 (m, 1H), 8.02 - 8.08 (m, 1H), 7.81 - 7.88 (m, 1H), 7.28 - 7.48 (m, 4H), 6.83 - 7.17 (m, 1H), 6.48 - 6.56 (m, 1H), 6.34 - 6.44 (m, 1H), 5.56 - 5.70 (m, 1H), 3.00 - 3.10 (m, 1H), 2.86 - 2.99 (m, 1H), 2.57 - 2.62 (m, 1H), 2.02 - 2.17 (m, 1H). 19F NMR (376 MHz, DMSO-d6) δ (ppm): -116.06, -126.04.

[00492] **Example 72: (*S*)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-1-methyl-1-phenylurea (Compound 132)**



Compound 132

[00493] Synthetic Route:



Compound 2 **Compound 132**

[00494] **Step 1: Synthesis of (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1-phenylurea (Compound 132)**

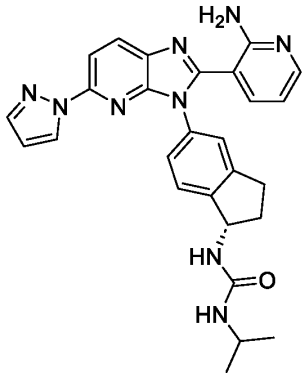
[00495] To a solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol) and triethylamine (74.3 mg, 0.735 mmol) in DCM (2.00 mL) was added triphosgene (24 mg, 0.081 mmol) and the mixture was stirred for 20 min at room temperature followed by addition of N-methylaniline (31.5 mg, 0.294 mmol). Stirring was continued for 1 h at room temperature. The resulting mixture was concentrated under reduced pressure and the residue was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.1% TFA) to afford (S)-3-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1-phenylurea (**Compound 132**) (2 mg, 1% yield) as a yellow solid. MS (ESI) calcd. for $C_{31}H_{27}N_9O$, 541.23 m/z, found 542.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.47 - 8.50 (m, 1H), 8.42 - 8.45 (m, 1H), 8.35 - 8.36 (m, 1H), 8.03 - 8.06 (m, 1H), 7.85 - 7.86 (m, 1H), 7.70 - 7.74 (m, 1H), 7.43 - 7.44 (m, 1H), 7.22 - 7.23 (m, 6H), 7.06 - 7.08 (m, 1H), 6.79 - 6.82 (m, 1H), 6.59 - 6.60 (m, 1H), 4.79 - 4.84 (m, 1H), 3.48 - 3.53 (m, 3H), 3.11 - 3.12 (m, 1H), 2.96 - 2.98 (m, 1H), 2.51 - 2.52 (m, 1H), 2.06 - 2.08 (m, 1H). (TFA salt)

[00496] The following compounds were prepared analogous to the synthetic preparation in Example 72 (Compound 132).

[00497] **Table 7.** Characterization data of compounds prepared analogously to compound 132.

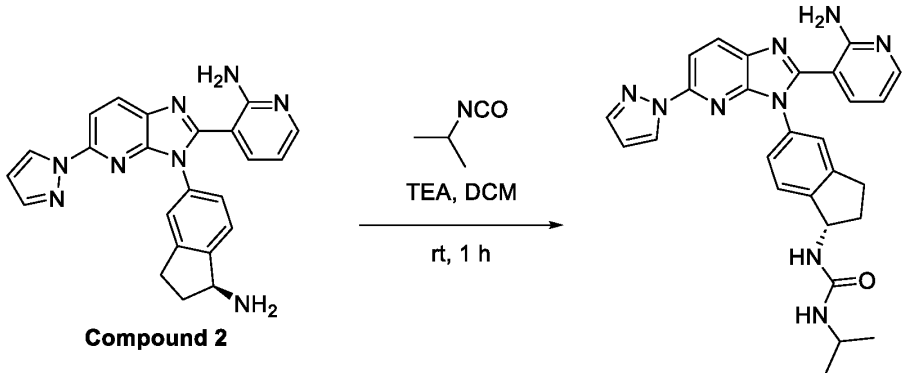
Cpd ID	Characterization Data
133	MS (ESI) calcd. for $C_{30}H_{25}N_9O$, 527.22 m/z, found 528.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.36 - 8.38 (m, 2H), 8.02 - 8.03 (m, 1H), 7.94 - 7.97 (m, 1H), 7.81 - 7.82 (m, 1H), 7.42 - 7.44 (m, 4H), 7.32 - 7.38 (m, 4H), 6.92 - 6.95 (m, 1H), 6.55 - 6.56 (m, 1H), 6.44 - 6.45 (m, 1H), 5.26 - 5.29 (m, 1H), 2.96 - 2.97 (m, 2H), 2.51 - 2.52 (m, 1H), 1.89 - 1.90 (m, 1H).

[00498] **Example 73: (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-isopropylurea (Compound 134)**



Compound 134

[00499] Synthetic Route:

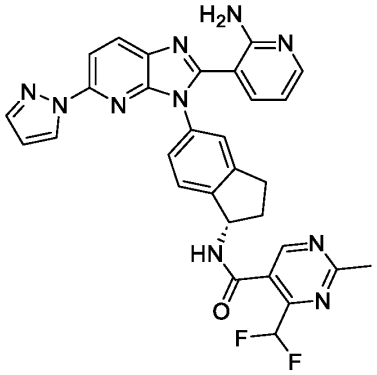


Compound 2 **Compound 134**

[00500] Step 1: Synthesis of (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-isopropylurea

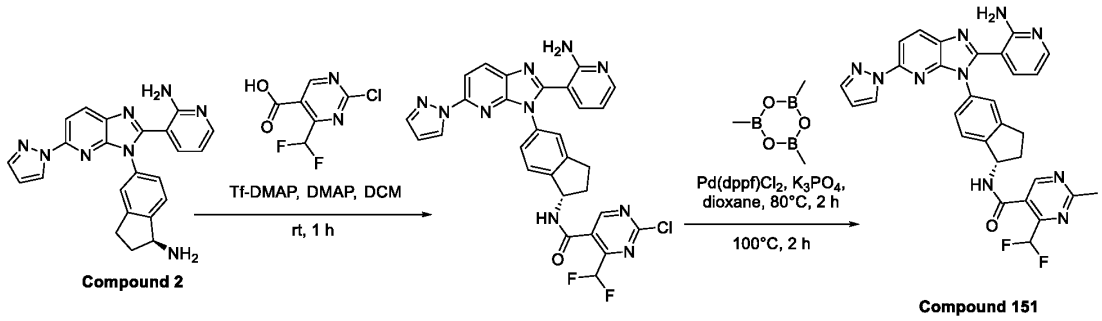
[00501] To a solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol) and triethylamine (74.3 mg, 0.735 mmol) in DCM (2.00 mL) was added 2-isocyanato-propane (20.8 mg, 0.245 mmol) and the mixture was stirred for 1 h at room temperature. The resulting mixture was concentrated under reduced pressure and the residue was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-isopropylurea (**Compound 134**) (25.3 mg, 17% yield) as an off-white solid. MS (ESI) calcd. for $C_{27}H_{27}N_9O$, 493.23 m/z, found 494.25 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.42 - 8.44 (m, 1H), 8.38 - 8.39 (m, 1H), 8.06 - 8.08 (m, 1H), 8.00 - 8.03 (m, 1H), 7.76 - 7.77 (m, 1H), 7.73 - 7.74 (m, 1H), 7.35 - 7.38 (m, 1H), 7.33 - 7.34 (m, 2H), 6.80 - 6.81 (m, 1H), 5.57 - 6.58 (m, 1H), 5.17 - 5.19 (m, 1H), 3.74 - 3.76 (m, 1H), 2.82 - 2.85 (m, 2H), 2.46 - 2.47 (m, 1H), 1.77 - 1.80 (m, 1H), 1.01 - 1.02 (m, 6H). (TFA salt)

[00502] Example 74: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-(difluoromethyl)-2-methylpyrimidine-5-carboxamide (Compound 151)



Compound 151

[00503] Synthetic Route:



Compound 2

Compound 151

[00504] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-chloro-4-(difluoromethyl)pyrimidine-5-carboxamide

[00505] A solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (200 mg, 0.490 mmol), 2-chloro-4-(difluoromethyl)pyrimidine-5-carboxylic acid (102 mg, 0.490 mmol) and DMAP (190 mg, 1.47 mmol) in DCM (10 mL) was treated with Tf-DMAP (107 mg, 0.490 mmol) at room temperature The resulting mixture was stirred for 1 h at room temperature. The reaction was quenched with water at room temperature and the resulting mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate in petroleum ether to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-chloro-4-(difluoromethyl)pyrimidine-5-carboxamide (100 mg, 34%

yield) as a yellow solid.: MS (ESI) calcd. for $C_{29}H_{21}ClF_2N_{10}O$, 598.16 m/z, found 599.15 $[M+H]^+$.

[00506] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-(difluoromethyl)-2-methylpyrimidine-5-carboxamide (Compound 151)

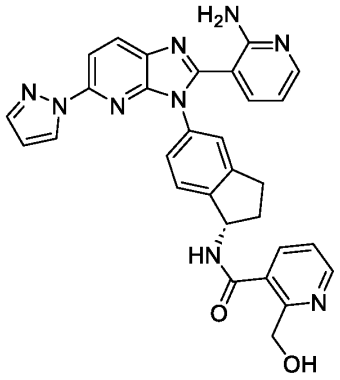
[00507] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-chloro-4-(difluoromethyl)pyrimidine-5-carboxamide (150 mg, 0.250 mmol), methylboronic acid (75 mg, 1.3 mmol) and K_3PO_4 (160 mg, 0.750 mmol) in 1,4-dioxane (5 mL) was added $Pd(dppf)Cl_2$ (36.7 mg, 0.050 mmol) at room temperature The resulting mixture was stirred for 3 h at 100°C under N_2 atmosphere. The reaction was quenched with water at room temperature The resulting mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.1% formic acid) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-(difluoromethyl)-2-methylpyrimidine-5-carboxamide (**Compound 151**, formic acid salt) (3.2 mg, 2% yield) as a yellow green solid.: MS (ESI) calcd. for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found 579.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.03 (m, 1H), 8.30 - 8.40 (m, 2H), 8.00 - 8.06 (m, 1H), 7.95 - 8.00 (m, 1H), 7.81 (s, 1H), 7.45 - 7.52 (m, 1H), 7.05 - 7.43 (m, 4H), 6.55 - 6.60 (m, 1H), 6.43 - 6.50 (m, 1H), 5.50 - 5.62 (m, 1H), 2.85 - 3.10 (m, 2H), 2.75 (s, 3H), 2.58 - 2.62 (m, 1H), 1.95 - 2.15 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -119.54.

[00508] The following compounds were prepared analogous to the synthetic preparation in Example 74 (Compound 151).

[00509] **Table 8.** Characterization data of compounds prepared analogously to compound 151.

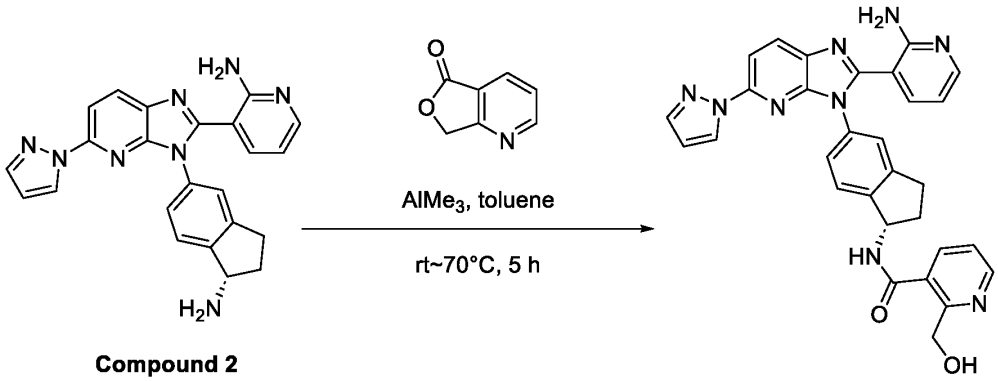
Cpd ID	Characterization Data
167	MS (ESI) calcd. for $C_{31}H_{25}F_2N_9O$, 577.22 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.38 (m, 2H), 7.95 - 8.05 (m, 1H), 7.88 - 7.95 (m, 2H), 7.74 - 7.81 (m, 1H), 7.46 - 7.53 (m, 2H), 7.00 - 7.41 (m, 4H), 6.50 - 6.57 (m, 1H), 6.39 - 6.50 (m, 1H), 5.47 - 5.59 (m, 1H), 2.82 - 3.08 (m, 2H), 2.50 - 2.61 (m, 4H), 1.95 - 2.08 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -115.13.

[00510] Example 75: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(hydroxymethyl)nicotinamide (Compound 152)



Compound 152

[00511] Synthetic Route:



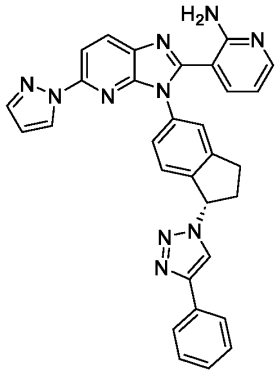
Compound 2 **Compound 152**

[00512] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(hydroxymethyl)nicotinamide (Compound 152)

[00513] To a solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (120 mg, 0.294 mmol) and 7H-furo[3,4-b]pyridin-5-one (79.4 mg, 0.588 mmol) in toluene (3 mL) was added $AlMe_3$ (0.44 mL, 0.882 mmol, 2M in Toluene) at 0°C under N_2 atmosphere. The resulting mixture was stirred for 5 h at 70°C. The reaction was quenched by the addition of water (100 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse phase column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-

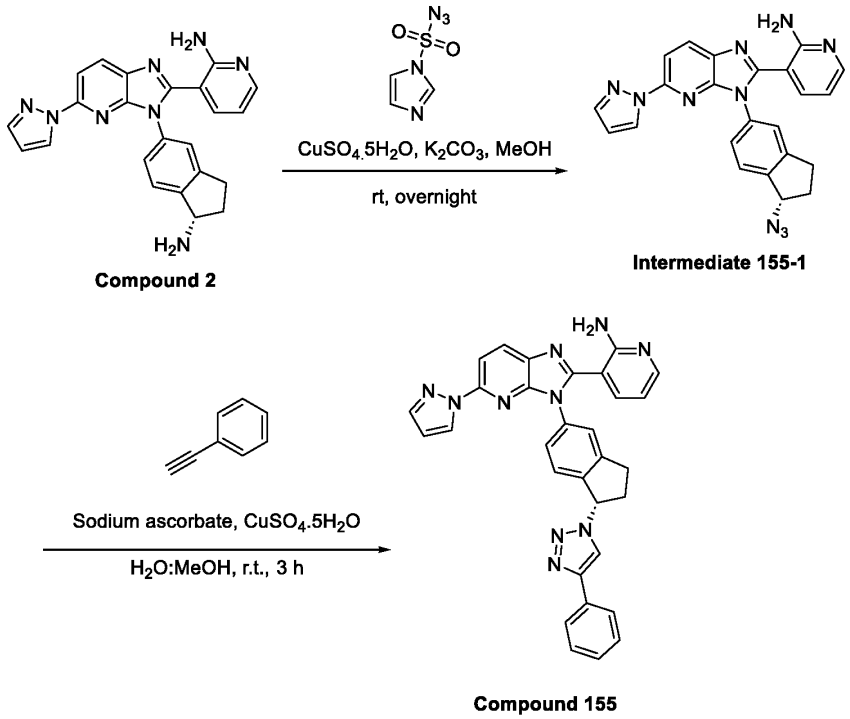
1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(hydroxymethyl)nicotinamide (**Compound 152** – TFA salt) (38.2 mg, 23% yield) as a brown solid.: MS (ESI) calcd. for $C_{30}H_{25}N_9O_2$: 543.21 m/z, found, 544.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-*d*$_6$) δ (ppm); 8.68 - 8.78 (m, 1H), 8.41 - 8.48 (m, 2H), 8.31 - 8.40 (m, 1H), 8.05 - 8.10 (m, 1H), 8.01 - 8.05 (m, 1H), 7.75 - 7.88 (m, 3H), 7.50 - 7.56 (m, 1H), 7.44 - 7.50 (m, 1H), 7.35 - 7.40 (m, 1H), 6.82 - 6.88 (m, 1H), 6.56 - 6.60 (m, 1H), 5.56 - 5.62 (m, 1H), 4.95 (s, 2H), 2.90 - 3.11 (m, 2H), 2.55 - 2.62 (m, 1H), 2.00 - 2.11 (m, 1H).

[00514] Example 76: (S)-3-(3-(1-(4-phenyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 155)



Compound 155

[00515] Synthetic Route:



[00516] Step 1: Synthesis of (S)-3-(3-(1-(4-phenyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 155)

[00517] A mixture of 3-{3-[(1S)-1-azido-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 155-1**) (200 mg, 0.460 mmol), phenylacetylene (940.3 mg, 9.200 mmol), copper(II) sulfate pentahydrate (23 mg, 0.092 mmol) and sodium ascorbate (36.7 mg, 0.184 mmol) in MeOH (1 mL) and H_2O (1 mL) was stirred for 3h at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-(4-phenyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 155**, trifluoroacetic acid salt) (31.0 mg, 10% yield) as an off-white solid.: MS (ESI) calcd. for $C_{31}H_{24}N_{10}$, 536.22 m/z, found 537.15 [M+H]+. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.63 (s, 1H), 8.39 - 8.42 (m, 2H), 8.03 - 8.05 (m, 2H), 7.83 - 7.89 (m, 3H), 7.69 - 7.70 (m, 1H), 7.44 - 7.46 (m, 1H), 7.41 - 7.44 (m, 2H), 7.31 - 7.32 (m, 3H), 6.31 - 6.76 (m, 3H), 3.30 - 3.31 (m, 1H), 3.08 - 3.10 (m, 1H), 2.83 - 2.86 (m, 1H), 2.58 - 2.61 (m, 1H).

[00518] Intermediate 155-1: (*S*)-3-(3-(1-azido-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine

[00519] Step 1: (S)-3-(3-(1-azido-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Intermediate 155-1)

[00520] A solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (300 mg, 0.734 mmol), imidazole-1-sulfonyl azide (153 mg, 0.881 mmol), potassium carbonate (409mg, 2.94 mmol) and $CuSO_4.5H_2O$ (9.2 mg, 0.037 mmol) in MeOH (5 mL) was stirred overnight at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-azido-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Intermediate 155-1**) (200 mg, 63% yield) as a yellow solid.: MS (ESI) calcd. for $C_{23}H_{18}N_{10}$, 434.17 m/z, found 435.15 $[M+H]^+$.

[00521] The following compounds were prepared analogous to the synthetic preparation in Example 76 (Compound 155).

[00522] **Table 9.** Characterization data of compounds prepared analogously to compound 155.

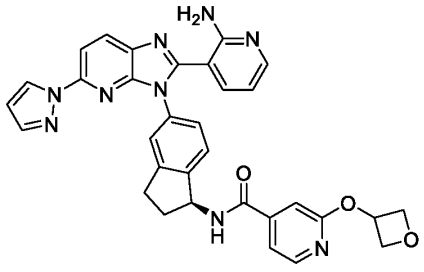
Cpd ID	Characterization Data
156	MS (ESI) calcd. for $C_{32}H_{26}N_{10}$, 550.23 m/z, found 551.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.39 - 8.42 (m, 2H), 8.03 - 8.04 (m, 2H), 7.90 - 7.98 (m, 1H), 7.70 - 7.81 (m, 1H), 7.67 - 7.70 (m, 1H), 7.55 - 7.56 (m, 1H), 7.16 - 7.28 (m, 7H), 6.73 - 6.75 (m, 1H), 6.54 - 6.55 (m, 1H), 6.20 - 6.23 (m, 1H), 3.98 - 3.99 (m, 2H), 3.19 - 3.21 (m, 1H), 3.02 - 3.04 (m, 1H), 2.77 - 2.79 (m, 1H), 2.48 - 2.49 (m, 1H). (TFA salt)
188	MS (ESI) calcd. for $C_{25}H_{20}N_{10}$, 460.19 m/z, found 461.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.36 - 8.37 (m, 2H), 8.17 - 8.18 (m, 1H), 8.01 - 8.02 (m, 2H), 7.80 - 7.81 (m, 2H), 7.53 - 7.54 (m, 1H), 7.28 - 7.30 (m, 1H), 7.23 - 7.24 (m, 2H), 6.56 - 6.57 (m, 1H), 6.43 - 6.44 (m, 1H), 6.33 - 6.35 (m, 1H), 3.56 - 3.58 (m, 1H), 3.06 - 3.08 (m, 1H), 2.83 - 2.84 (m, 1H), 2.53 - 2.56 (m, 1H).
197	MS (ESI) calcd. for $C_{29}H_{24}N_{12}$, 540.22 m/z, found, 541.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.45 (m, 3H), 7.91 - 8.09 (m, 2H), 7.71 - 7.86 (m, 2H), 7.54 (s, 1H), 7.27 - 7.37 (m, 2H), 7.18 - 7.26 (m, 1H), 6.52 - 6.65 (m, 2H), 6.42 - 6.51 (m, 1H), 6.29 - 6.39 (m, 1H), 3.87 (s, 3H), 3.21 - 3.37 (m, 1H), 2.99 - 3.14 (m, 1H), 2.78 - 2.91 (m, 1H), 2.55 - 2.67 (m,1H).
198	MS (ESI) calcd. for $C_{30}H_{23}N_{11}$, 537.21 m/z, found, 538.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.90 (s, 1H), 8.63 - 8.65 (m, 2H), 8.36 - 8.40 (m, 2H), 8.01 - 8.03 (m, 1H), 7.96 - 7.98 (m, 1H), 7.81 - 7.86 (m, 3H), 7.57 (s, 1H), 7.29 - 7.35 (m, 2H), 7.24 - 7.27 (m, 1H), 6.55 - 6.56 (m, 1H), 6.38 - 6.47 (m, 2H), 3.27 - 3.38 (m, 1H), 3.04 - 3.17 (m, 1H), 2.80 - 2.96 (m, 1H), 2.56 - 2.67 (m, 1H).
199	MS (ESI) calcd. for $C_{30}H_{23}N_{11}$, 537.21 m/z, found, 538.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.04 - 9.12 (m, 1H), 8.79 (s, 1H), 8.52 - 8.58 (m, 1H), 8.36 (s, 2H), 8.20 - 8.30 (m, 1H), 7.96 - 8.05 (m, 1H), 7.90 - 7.96 (m, 1H), 7.79 - 7.83 (m, 1H), 7.57 (s, 1H), 7.45 - 7.56 (m, 1H), 7.28 - 7.35 (m, 2H), 7.22 - 7.28 (m, 1H), 6.53 - 6.59 (m, 1H), 6.38 - 6.47 (m, 2H), 3.28 - 3.38 (m, 1H), 3.01 - 3.19 (m, 1H), 2.78 - 2.97 (m, 1H), 2.56 - 2.69 (m, 1H).

Cpd ID	Characterization Data
200	MS (ESI) calcd. for $C_{30}H_{23}N_{11}$, 537.21 m/z, found, 538.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.53 - 8.71 (m, 2H), 8.31 - 8.45 (m, 2H), 7.87 - 8.16 (m, 4H), 7.78 - 7.85 (m, 1H), 7.53 - 7.61 (m, 1H), 7.18 - 7.45 (m, 4H), 6.54 - 6.63 (m, 1H), 6.33 - 6.52 (m, 2H), 3.21 - 3.41 (m, 1H), 2.99 - 3.19 (m, 1H), 2.78 - 2.97 (m, 1H), 2.85 - 2.71 (m, 1H).
218	MS (ESI) calcd. for $C_{28}H_{27}N_{11}$, 517.25 m/z, found 518.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6+D_2O) δ (ppm); 8.38 - 8.43 (m, 2H), 7.97 - 8.11 (m, 3H), 7.80 - 7.88 (m, 1H), 7.52 - 7.59 (m, 1H), 7.22 - 7.37 (m, 3H), 6.54 - 6.61 (m, 1H), 6.42 - 6.51 (m, 1H), 6.28 - 6.34 (m, 1H), 3.55 (s, 2H), 3.23 - 3.35 (m, 1H), 3.04 - 3.16 (m, 1H), 2.78 - 2.89 (m, 1H), 2.58 - 2.65 (m, 1H), 2.12 (s, 6H).
219	MS (ESI) calcd. for $C_{28}H_{26}N_{10}O$, 518.23 m/z, found, 519.15 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.32 (m, 2H), 7.90 - 8.00 (m, 2H), 7.78 - 7.82 (m, 1H), 7.69 - 7.77 (m, 1H), 7.44 (s, 1H), 7.17 - 7.20 (m, 3H), 6.44 - 6.55 (m, 2H), 6.16 - 6.19 (m, 1H), 3.04 - 3.15 (m, 1H), 2.99 - 3.02 (m, 1H), 2.71 - 2.76 (m, 1H), 2.43 - 2.49 (m, 1H), 1.45 (s, 6H).
220	MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$, 516.21 m/z, found, 517.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.34 - 8.59 (m, 2H), 8.02 - 8.15 (m, 1H), 7.96 - 8.01 (m, 2H), 7.73 - 7.95 (m, 2H), 7.42 - 7.71 (m, 1H), 7.13 - 7.41 (m, 2H), 6.73 - 6.97 (m, 1H), 6.45 - 6.72 (m, 1H), 6.12 - 6.42 (m, 1H), 4.83 - 5.11 (m, 2H), 4.59 - 4.82 (m, 2H), 4.26 - 4.58 (m, 1H), 3.22 - 3.45 (m, 1H), 3.00 - 3.21 (m, 1H), 2.69 -2.99 (m, 1H), 2.43 - 2.61 (m, 1H). (TFA salt)
221	MS (ESI) calcd. for $C_{28}H_{24}N_{10}$, 500.22 m/z, found, 501.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.29 - 8.55 (m, 2H), 7.79 - 8.15 (m, 2H), 7.68 - 7.78 (m, 1H), 7.47 - 7.67 (m, 1H), 7.30 - 7.46 (m, 1H), 7.12 - 7.29 (m, 1H), 6.70 - 6.95 (m, 1H), 6.48 - 6.69 (m, 1H), 6.05 - 6.33 (m, 1H), 3.16 - 3.42 (m, 1H), 2.94 - 3.15 (m, 1H), 2.66 - 2.93 (m, 1H), 2.41 - 2.52 (m, 1H), 2.29 - 2.34 (m, 1H), 1.81 - 2.12 (m, 1H), 0.85 -1.11 (m, 2H), 0.58 - 0.84 (m, 2H). (TFA salt)
227	MS (ESI) calcd. for $C_{25}H_{20}N_{10}$, 460.19 m/z, found 461.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.37 (m, 2H), 8.17 - 8.18 (m, 1H), 8.01 - 8.02 (m, 2H), 7.80 - 7.81 (m, 2H), 7.53 - 7.54 (m, 1H), 7.28 - 7.30 (m, 1H), 7.23 - 7.24 (m, 2H), 6.56 - 6.57 (m, 1H), 6.43 - 6.44 (m, 1H), 6.33 - 6.35 (m, 1H), 3.56 - 3.58 (m, 1H), 3.06 - 3.08 (m, 1H), 2.83 - 2.84 (m, 1H), 2.53 - 2.56 (m, 1H).
250	MS (ESI) calcd. for $C_{28}H_{25}N_{11}$, 515.23 m/z, found, 516.30 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.51 (m, 2H), 8.16 (s, 1H), 7.93 - 8.10 (m, 2H), 7.78 - 7.88 (m, 1H), 7.64 - 7.76 (m, 1H), 7.60 (s, 1H), 7.30 - 7.40 (m, 1H), 7.21 - 7.29 (m, 1H), 6.68 - 6.82 (m, 1H), 6.50 - 6.63 (m, 1H), 6.21 - 6.38 (m, 1H), 4.02 - 4.40 (m, 5H), 3.18 - 3.38 (m, 1H), 2.95 - 3.15 (m, 1H), 2.73 - 2.90 (m, 1H), 2.46 - 2.50 (m, 1H).
251	MS (ESI) calcd. for $C_{29}H_{27}N_{11}$, 529.25 m/z, found, 530.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.35 (m, 2H), 7.90 - 8.09 (m, 2H), 7.83 - 7.88 (m, 1H), 7.70 - 7.75 (m, 1H), 7.40 - 7.52 (m, 1H), 7.13 - 7.35 (m, 3H), 6.62 - 6.65 (m, 2H), 6.09 - 6.20 (m, 1H), 3.57 - 3.65 (m, 3H), 3.10 - 3.19 (m, 3H), 2.97 - 3.02 (m, 1H), 2.73 - 2.76 (m, 1H), 2.51 - 2.59 (m, 1H), 2.22 - 2.30 (m, 3H).

Cpd ID	Characterization Data
254	MS (ESI) calcd. for $C_{31}H_{25}N_{11}$, 551.23 m/z, found 552.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.76 - 8.81 (m, 1H), 8.66 - 8.67 (m, 1H), 8.64 - 8.65 (m, 1H), 8.45 - 8.46 (m, 1H), 8.41 - 8.42 (m, 1H), 8.08 - 8.09 (m, 1H), 8.06 - 8.07 (m, 1H), 7.83 - 7.84 (m, 1H), 7.72 - 7.77 (m, 2H), 7.69 - 7.70 (m, 1H), 7.36 - 7.40 (m, 2H), 6.76 - 6.78 (m, 1H), 6.56 - 6.57 (m, 1H), 6.41 - 6.43 (m, 1H), 3.31 - 3.33 (m, 1H), 3.12 - 3.15 (m, 1H), 2.88 - 2.91 (m, 1H), 2.64 - 2.66 (m, 3H), 2.51 - 2.52 (m, 1H). (TFA salt)
285	MS (ESI) calcd. for $C_{27}H_{24}N_{10}$, 488.22 m/z, found 489.15 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.38 (m, 2H), 8.01 - 8.03 (m, 1H), 7.97 (d, J = 8.6 Hz, 1H), 7.89 (s, 1H), 7.81 - 7.82 (m, 1H), 7.54 (d, J = 1.9 Hz, 1H), 7.29 - 7.32 (m, 1H), 7.21 - 7.25 (m, 2H), 6.92 (s, 2H), 6.55 - 6.56 (m, 1H), 6.42 - 6.45 (m, 1H), 6.25 - 6.28 (m, 1H), 3.21 - 3.29 (m, 1H), 3.01 - 3.09 (m, 1H), 2.75 - 2.84 (m, 1H), 2.65 (q, J = 7.6 Hz, 2H), 2.52 - 2.56 (m, 1H), 1.21 (t, J = 7.6 Hz, 3H).
287	MS (ESI) calcd. for $C_{29}H_{26}N_{10}$, 514.23 m/z, found 515.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.37 (m, 2H), 8.01 - 8.02 (m, 1H), 7.94 - 7.97 (m, 2H), 7.81 (s, 1H), 7.53 (s, 1H), 7.28 - 7.31 (m, 1H), 7.22 - 7.24 (m, 2H), 6.92 (s, 2H), 6.54 - 6.55 (m, 1H), 6.42 - 6.44 (m, 1H), 6.24 - 6.27 (m, 1H), 3.51 - 3.60 (m, 1H), 3.21 - 3.28 (m, 1H), 3.02 - 3.08 (m, 1H), 2.74 - 2.83 (m, 1H), 2.51 - 2.56 (m, 1H), 2.27 - 2.31 (m, 2H), 2.14 - 2.19 (m, 2H), 1.96 - 1.98 (m, 1H), 1.80 - 1.98 (m, 1H).
304	MS (ESI) calcd. for $C_{26}H_{22}N_{10}$: 474.20 m/z, found: 475.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.38 - 8.48 (m, 2H), 7.99 - 8.10 (m, 2H), 7.81 - 7.90 (m, 2H), 7.68 - 7.73 (m, 1H), 7.55 - 7.61 (m, 1H), 7.21 - 7.39 (m, 2H), 6.73 - 6.82 (m, 1H), 6.55 - 6.62 (m, 1H), 6.19 - 6.30 (m, 1H), 3.18 - 3.31 (m, 1H), 3.01 - 3.11 (m, 1H), 2.73 - 2.86 (m, 1H), 2.43 - 2.51 (m, 1H), 2.26 (s, 3H)
320	MS (ESI) calcd. for $C_{29}H_{28}N_{10}$, 516.25 m/z, found 517.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.38 (m, 2H), 8.01 - 8.02 (m, 1H), 7.96 (d, J = 8.6 Hz, 1H), 7.88 (s, 1H), 7.81 (d, J = 1.7 Hz, 1H), 7.54 (d, J = 2.0 Hz, 1H), 7.29 - 7.31 (m, 1H), 7.21 -7.23 (m, 2H), 6.94 (s, 2H), 6.54 (t, J = 2.1 Hz, 1H), 6.40 - 6.43 (m, 1H), 6.25 (t, J = 7.1 Hz, 1H), 3.21 - 3.29 (m, 1H), 3.00 - 3.08 (m, 1H), 2.74 - 2.83 (m, 1H), 2.53 - 2.57 (m, 1H), 1.29 (s, 9H).
326	MS (ESI) calcd. for $C_{26}H_{20}F_2N_{10}$: 510.18 m/z, found, 511.30 $[M+H]^+$. ^1H-NMR (300 MHz, DMSO-d_6) δ (ppm); 8.63 - 8.65 (m, 1H), 8.32 - 8.38 (m, 2H), 7.90 - 8.09 (m, 2H), 7.78 - 7.85 (m, 1H), 7.63 - 7.69 (m, 1H), 7.02 - 7.45 (m, 4H), 6.90 - 6.99 (m, 2H), 6.52 - 6.59 (m, 1H), 6.32 - 6.49 (m, 2H), 3.15 - 3.22 (m, 1H), 2.99 - 3.10 (m, 1H), 2.75 - 2.85 (m, 1H), 2.50 - 2.60 (m, 1H). ^{19}F-NMR (282 MHz, DMSO-d_6) δ (ppm); -111.74.
345	MS (ESI) calcd. for $C_{29}H_{22}N_{10}$, 510.20 m/z, found, 511.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.35 (m, 1H), 8.36 - 8.38 (m, 1H), 8.03 - 8.07 (m, 1H), 8.01 - 8.02 (m, 1H), 7.95 - 7.97 (m, 1H), 7.81 - 7.85 (m, 1H), 7.71 - 7.75 (m, 1H), 7.43 - 7.52 (m, 3H), 7.22 - 7.27 (m, 2H), 7.09 - 7.18 (m, 1H), 6.99 - 7.05 (m, 2H), 6.85 - 6.87 (m, 1H), 6.51 - 6.60 (m, 1H), 6.42 - 6.45 (m, 1H), 3.26 - 3.33 (m, 1H), 3.11 - 3.28 (m, 1H), 2.85 - 3.08 (m, 1H), 2.52 - 2.60 (m, 1H).

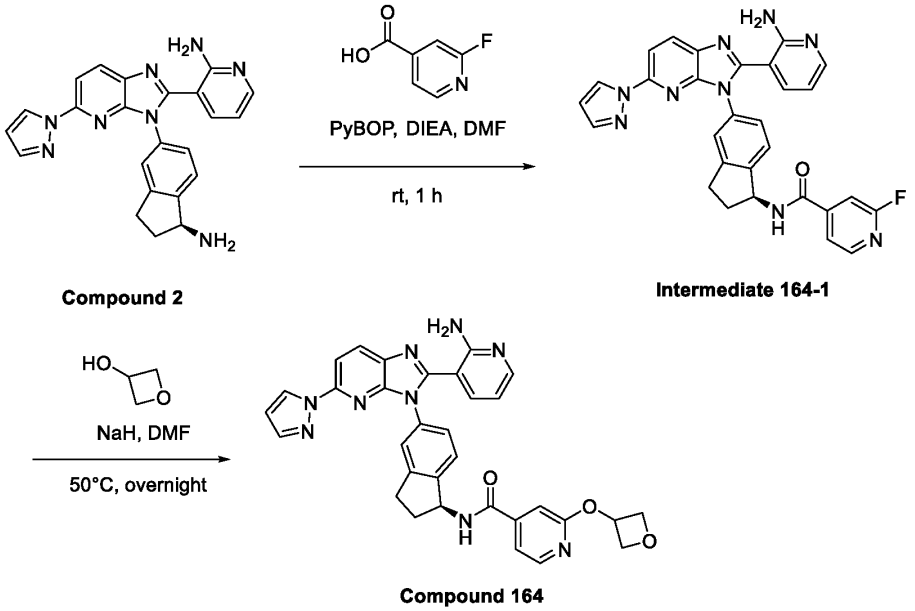
Cpd ID	Characterization Data
352	MS (ESI) calcd. for $C_{27}H_{23}N_{11}$, 501.21 m/z, found 502.15 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.44 (d, J = 8.5 Hz, 1H), 8.14 (s, 2H), 8.01 - 8.06 (m, 2H), 7.90 (s, 1H), 7.52 (d, J = 1.9 Hz, 1H), 7.31 - 7.35 (m, 1H), 7.21 - 7.25 (m, 2H), 6.92 (s, 2H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 6.23 (t, J = 7.2 Hz, 1H), 3.18 - 3.25 (m, 1H), 2.98 - 3.06 (m, 1H), 2.74 - 2.82 (m, 1H), 2.45 - 2.49 (m, 1H), 1.92 - 1.98 (m, 1H), 0.88 - 0.92 (m, 2H), 0.72 - 0.77 (m, 2H).
353	MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$, 516.21 m/z, found 517.35 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.40 (m, 2H), 8.32 (s, 1H), 8.02 (dd, J = 4.8, 1.8 Hz, 1H), 7.97 (d, J = 8.6 Hz, 1H), 7.81 - 7.82 (m, 1H), 7.55 (d, J = 1.8 Hz, 1H), 7.30 - 7.33 (m, 1H), 7.25 - 7.28 (m, 1H), 7.22 - 7.24 (m, 1H), 6.92 (s, 2H), 6.54 - 6.56 (m, 1H), 6.44 (dd, J = 7.7, 4.8 Hz, 1H), 6.31 - 6.36 (m, 1H), 5.80 (t, J = 7.6 Hz, 1H), 4.59 - 4.65 (m, 1H), 4.50 - 4.55 (m, 1H), 3.24 - 3.29 (m, 1H), 3.02 - 3.10 (m, 1H), 2.91 - 3.00 (m, 2H), 2.79 - 2.87 (m, 1H), 2.54 - 2.59 (m, 1H).
354	MS (ESI) calcd. for $C_{28}H_{24}N_{10}O$, 516.21 m/z, found 517.30 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.36 - 8.40 (m, 2H), 8.31 (s, 1H), 8.02 (dd, J = 4.9, 1.9 Hz, 1H), 7.97 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 1.6 Hz, 1H), 7.55 (d, J = 1.9 Hz, 1H), 7.29 - 7.34 (m, 1H), 7.26 - 7.28 (m, 1H), 7.24 - 7.25 (m, 1H), 6.92 (s, 2H), 6.54 - 6.57 (m, 1H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 6.31 - 6.36 (m, 1H), 5.80 (t, J = 7.5 Hz, 1H), 4.60 - 4.65 (m, 1H), 4.51 - 4.56 (m, 1H), 3.23 - 3.30 (m, 1H), 3.03 - 3.11 (m, 1H), 2.92 - 2.99 (m, 2H), 2.78 - 2.87 (m, 1H), 2.54 - 2.59 (m, 1H).
362	MS (ESI) calcd. for $C_{28}H_{22}F_2N_{10}$: 536.20 m/z, found, 537.30 $[M+H]^+$. ^{1} H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.44 (m, 2H), 8.10 (d, J = 8.8 Hz, 1H), 7.99 - 8.06 (m, 1H), 7.97 (d, J = 1.7 Hz, 1H), 7.81 - 7.83 (m, 1H), 7.54 (s, 1H), 7.29 - 7.37 (m, 1H), 7.18 - 7.28 (m, 2H), 6.93 (s, 2H), 6.50 - 6.58 (m, 1H), 6.37 - 6.48 (m, 1H), 6.31 (t, J = 7.0 Hz, 1H), 3.20 - 3.30 (m, 1H), 2.97 - 3.12 (m, 2H), 2.75 - 2.88 (m, 1H), 2.53 - 2.60 (m, 1H), 1.99 - 2.12 (m, 1H), 1.85 - 1.99 (m, 1H). ^{19} F-NMR (376 MHz, DMSO-d_6) δ (ppm); -127.24, -120.28.

[00523] Example 77: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(oxetan-3-yloxy)isonicotinamide (Compound 164)



Compound 164

[00524] Synthetic Route:



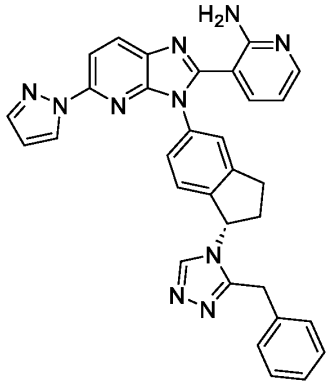
[00525] **Step 1: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(oxetan-3-yloxy)isonicotinamide (Compound 164)**To a solution of oxetan-3-ol (43.5 mg, 0.588 mmol) in DMF (4 mL) was added NaH (29.4 mg, 1.23 mmol, 60% purity) and the reaction mixture was stirred for 0.5 h at room temperature. To the mixture was added (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-fluoroisonicotinamide (**Intermediate 164-1**) (130 mg, 0.245 mmol). The resulting mixture was stirred at 50°C overnight. The reaction was quenched with H_2O (50 mL). The resulting mixture was extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated under vacuum. The resulting mixture was purified by Prep-HPLC on a XBridge Prep OBD C18 Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(oxetan-3-yloxy)isonicotinamide (**Compound 164**) (9.0 mg, 6% yield) as an off-white solid.: MS (ESI) calcd. for $C_{32}H_{27}N_9O_3$: 585.22 m/z, found, 586.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.43 (m, 2H), 8.19 - 8.30 (m, 1H), 8.01 - 8.06 (m, 1H), 7.91 - 8.00 (m, 1H), 7.75 - 7.85 (m, 1H), 7.17 - 7.55 (m, 6H), 6.52 - 6.59 (m, 1H), 6.42 - 6.51 (m,1H), 5.45 - 5.69 (m, 2H), 4.82 - 5.01 (m, 2H), 4.47 - 4.62 (m, 2H), 3.00 - 3.15 (m, 1H), 2.78 - 2.99 (m, 1H), 2.54 - 2.64 (m, 1H), 1.98 - 2.21 (m,1H). (TFA salt).

[00527] The following compounds were prepared analogous to the synthetic preparation in Example 77 (Compound 164).

[00528] **Table 10.** Characterization data of compounds prepared analogously to compound 164.

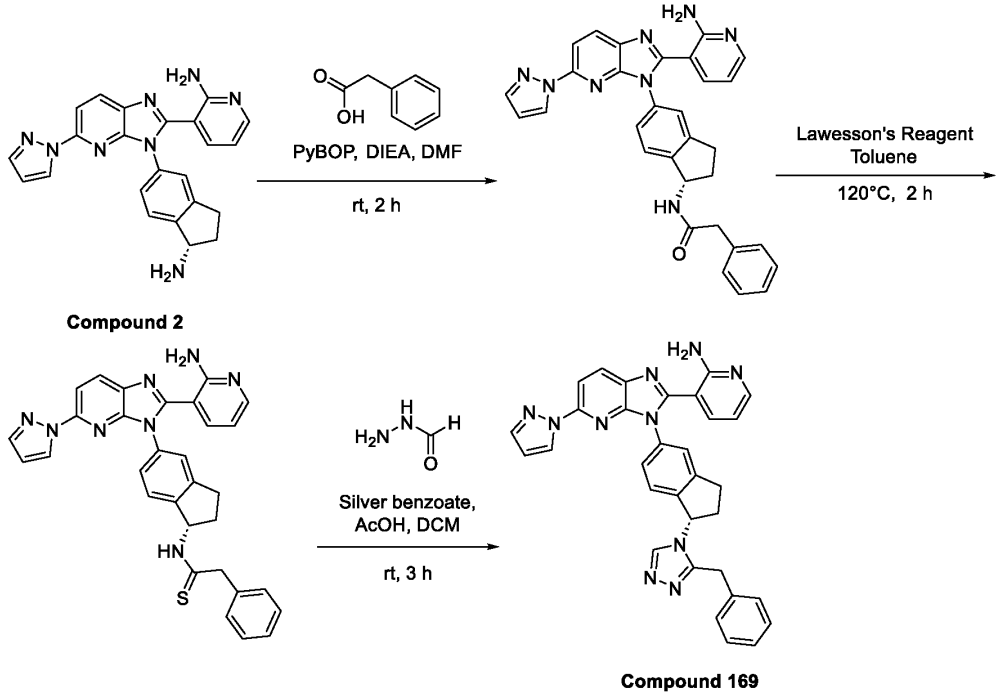
Cpd ID	Characterization Data
179	MS (ESI) calcd. for $C_{33}H_{30}N_{10}O_2$: 598.25 m/z, found, 599.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.09 - 8.40 (m, 3H), 7.87 - 8.01 (m, 1H), 7.76 - 7.86 (m, 1H), 7.68 - 7.77 (m, 1H), 7.23 - 7.41 (m, 4H), 7.09 - 7.22 (m, 2H), 6.43 - 6.57 (m, 2H), 5.38 - 5.56 (m,1H), 5.07 - 5.23 (m, 1H), 3.88 - 4.11 (m, 2H), 3.41 - 3.61 (m, 2H), 2.91 - 3.07 (m, 1H), 2.71 - 2.90 (m, 1H), 2.42 - 2.49 (m, 3H), 2.31 - 2.48(m,1H), 1.83 - 2.15 (m, 1H). (formic acid salt)

[00529] Example 78: (*S*)-3-(3-(1-(3-benzyl-4*H*-1,2,4-triazol-4-yl)-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (Compound 169)



Compound 169

[00530] Synthetic Route:



Compound 2

Compound 169

[00531] Step 1: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylacetamide

[00532] A solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (400 mg, 0.979 mmol), phenylacetic acid (160 mg, 1.18 mmol), PyBOP (611.5 mg, 1.175 mmol) and DIEA (316.4 mg, 2.447 mmol) in DMF (4 mL) was stirred for 2 h at room temperature. The reaction mixture was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylacetamide (300 mg, 58% yield) as a yellow solid.: MS (ESI) calcd. for $C_{31}H_{26}N_8O$, 526.22 m/z, found 527.30 $[M+H]^+$.

[00533] Step 2: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylethanethioamide

[00534] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylacetamide (400 mg, 0.760 mmol) and Lawesson's Reagent (338 mg, 0.836 mmol) in toluene (4 mL) was stirred for 2h at 120°C. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylethanethioamide (200 mg, 49% yield) as a yellow solid.: MS (ESI) calcd. for $C_{31}H_{26}N_8S$, 542.20 m/z, found 543.15 $[M+H]^+$.

[00535] Step 3: (S)-3-(3-(1-(3-benzyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 169)

[00536] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-phenylethanethioamide (500 mg, 0.921 mmol), N-formylhydrazine (66.4 mg, 1.11 mmol), silver benzoate (422 mg, 1.84 mmol) and AcOH (166 mg, 2.76 mmol) in DCM (5 mL) was stirred for 3 h at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a XSelect CSH OBD Column using a gradient of acetonitrile in water (+ 0.1% formic acid) to afford (S)-3-(3-(1-(3-benzyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 169**) (6.9 mg, 1.4% yield) as a white solid.: MS (ESI) calcd. for $C_{32}H_{26}N_{10}$, 550.23 m/z, found 551.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.34 (m, 3H), 7.97 - 7.99 (m, 2H), 7.78 - 7.79 (m, 1H), 7.46 - 7.47 (m, 1H), 7.15 - 7.30 (m, 7H), 6.76 - 6.79 (m, 1H), 6.52 - 6.53 (m, 1H), 6.40 -

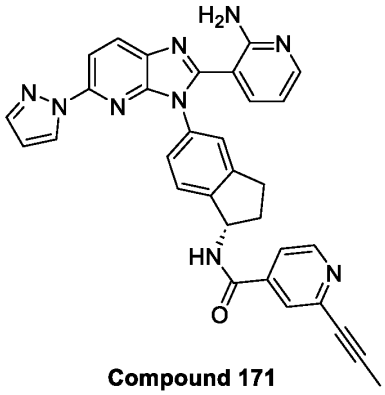
6.41 (m, 1H), 5.88 - 5.90 (m, 1H), 4.21 - 4.25 (m, 2H), 3.02 - 3.04 (m, 1H), 2.88 - 2.91 (m, 1H), 2.43 - 2.44 (m, 1H), 1.93 - 1.96 (m, 1H).

[00537] The following compounds were prepared analogous to the synthetic preparation in Example 78 (Compound 169).

Table 11. Characterization data of compounds prepared analogously to compound 169.

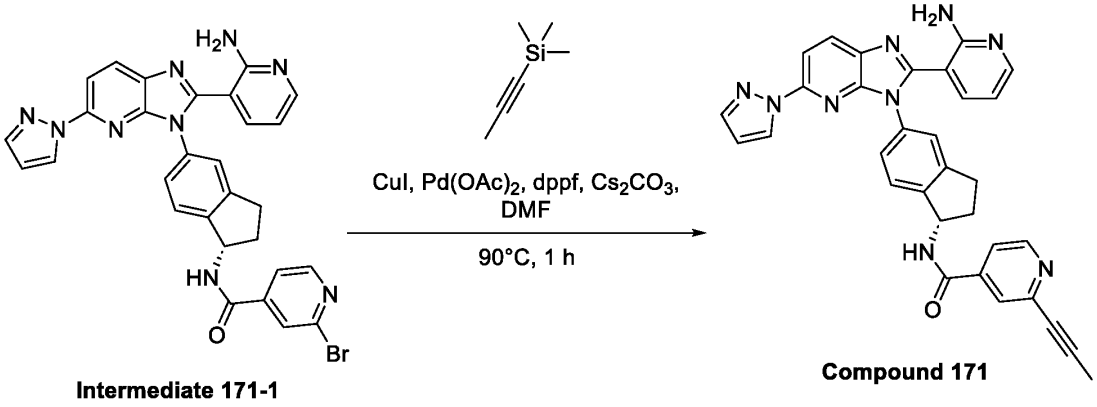
Cpd ID	Characterization Data
178	MS (ESI) calcd. for $C_{31}H_{24}N_{10}$, 536.22 m/z, found 537.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.52 - 8.53 (m, 1H), 8.39 - 8.40 (m, 2H), 7.98 - 8.00 (m, 2H), 7.81 - 7.82 (m, 1H), 7.68 - 7.69 (m, 2H), 7.59 - 7.65 (m, 3H), 7.57 - 7.58 (m, 1H), 7.23 - 7.32 (m, 3H), 6.56 - 6.57 (m, 1H), 6.46 - 6.47 (m, 1H), 5.89 - 5.92 (m, 1H), 3.03 - 3.05 (m, 2H), 2.77 - 2.80 (m, 1H), 2.51 - 2.52 (m, 1H). (formic acid salt)
222	MS (ESI) calcd. for $C_{30}H_{26}N_{12}$: 554.24 m/z, found, 555.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.58 (m, 2H), 8.27 - 8.34 (m, 1H), 8.00 - 8.12 (m, 1H), 7.87 - 8.00 (m, 1H), 7.76 - 7.85 (m, 1H), 7.54 - 7.59 (m, 1H), 7.27- 7.41 (m, 1H), 7.18 - 7.27 (m, 2H), 7.01 - 7.10 (m, 1H), 6.53 - 6.62 (m, 1H), 6.32 - 6.49 (m, 1H), 6.05 - 6.16 (m, 1H), 5.88 - 6.04 (m, 1H), 4.36 - 4.38 (m, 2H), 3.79 (s, 3H), 3.07 - 3.21 (m, 1H), 2.84 - 3.06 (m, 1H), 2.58 - 2.79 (m, 1H), 1.98 - 2.13 (m, 1H)
228	MS (ESI) calcd. for $C_{30}H_{26}N_{12}$: 554.24 m/z, found: 555.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.32 - 8.44 (m, 2H), 8.19 - 8.30 (m, 1H), 7.91 - 8.07 (m, 2H), 7.77 - 7.86 (m, 1H), 7.44 - 7.67 (m, 2H), 7.17 - 7.38 (m, 3H), 6.83- 7.04 (m, 2H), 6.56 - 6.62 (m,1H), 6.36 - 6.51 (m, 1H), 5.84 - 6.01 (m, 1H), 3.99 - 4.10 (m, 2H), 3.69 - 3.88 (m, 3H), 3.06 - 3.25 (m, 1H), 2.87 - 3.05 (m, 1H), 2.56 - 2.71 (m,1H), 1.95 - 2.21 (m, 1H)
384	MS (ESI) calcd. for $C_{29}H_{26}N_{10}$: 514.23 m/z, found, 515.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.58 - 8.65 (m, 1H), 8.38 - 8.49 (m, 2H), 7.99 - 8.16 (m, 1H), 7.89 - 7.98 (m, 1H), 7.72 - 7.88 (m, 1H), 7.64 - 7.71 (m, 1H), 7.57 - 7.63 (m, 1H), 7.46 - 7.56 (m, 1H), 7.35 - 7.46 (m, 1H), 7.25 - 7.34 (m, 1H), 6.51 - 7.01 (m, 2H), 5.93 - 6.16 (m, 1H), 3.13 - 3.33 (m, 1H), 2.94 - 3.12 (m, 1H), 2.67 - 2.93 (m, 3H), 2.18 - 2.38 (m, 1H), 1.05 - 1.29 (m, 1H), 0.49 - 0.68 (m, 2H), 0.25 - 0.36 (m, 2H). (TFA salt)

[00538] **Example 79: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(prop-1-yn-1-yl)isonicotinamide (Compound 171)**



Compound 171

[00539] Synthetic Route:



Intermediate 171-1

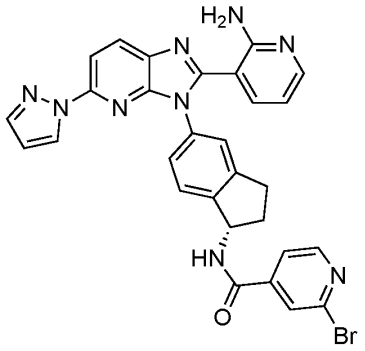
Compound 171

[00540] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(prop-1-yn-1-yl)isonicotinamide (Compound 171)

[00541] A mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-bromoisonicotinamide (**Intermediate 171-1**) (100 mg, 0.190 mmol), trimethyl(prop-1-yn-1-yl)silane (31.9 mg, 0.285 mmol), CuI (36.1 mg, 0.190 mmol), $Pd(OAc)_2$ (6.4 mg, 0.028 mmol), dppf (16 mg, 0.028 mmol) and Cs_2CO_3 (185 mg, 0.570 mmol) in DMF (3 mL) was stirred for 1 h at 90 °C under N_2. The reaction was quenched by the addition of water (100 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 50 mL) and the combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by Prep-HPLC on a XBridge Prep OBD C18 Column using a gradient of acetonitrile in water (+ 10 mmol/L TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-(prop-1-yn-1-yl)isonicotinamide (**Compound 171**, trifluoroacetic acid salt) (31.5 mg, 39% yield) as an off-white solid.: MS (ESI) calcd. for $C_{32}H_{25}N_9O$, 551.22 m/z, found, 552.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.65 - 8.69 (m, 1H), 8.38 - 8.45 (m, 1H), 8.33 - 8.38 (m, 1H), 7.95 - 8.05 (m,

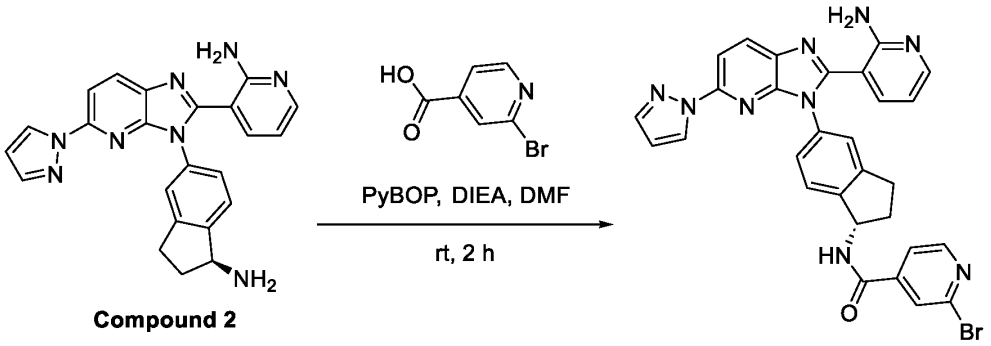
2H), 7.85 - 7.88 (m, 1H), 7.79 - 7.83 (m, 2H), 7.69 - 7.77 (m, 1H), 7.43 - 7.48 (m, 1H), 7.36 - 7.43 (m, 1H), 7.27 - 7.36 (m, 1H), 6.78 - 6.88 (m, 1H), 6.52 - 6.60 (m, 1H), 5.51 - 5.63 (m, 1H), 3.00 - 3.10 (m, 1H), 2.85 - 3.00 (m, 1H), 2.55 - 2.63 (m, 1H), 2.00 - 2.15 (m, 4H).

[00542] Intermediate 171-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-2-bromoisonicotinamide



Intermediate 171-1

[00543] Synthetic Route:



Compound 2

Intermediate 171-1

[00544] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-bromoisonicotinamide (Intermediate 171-1)

[00545] To a solution of 2-bromoisonicotinic acid (250 mg, 1.24 mmol), (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (505.5 mg, 1.238 mmol) and DIEA (479.9 mg, 3.714 mmol) in DMF (8 mL) was added PyBOP (644 mg, 1.238 mmol) at 0°C. The resulting mixture was stirred for 2 h at room temperature. The product was precipitated by the addition of water (80 mL). The precipitated solids were collected by filtration and washed with water (3 x 10 mL) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-2-bromoisonicotinamide (**Intermediate 171-1**) (600 mg, 82% yield) as a brown solid.: MS (ESI) calcd. for $C_{29}H_{22}BrN_9O$, 591.11 m/z, found, 592.20 $[M+H]^+$.

[00546] The following compounds were prepared analogous to the synthetic preparation in Example 79 (Compound 171).

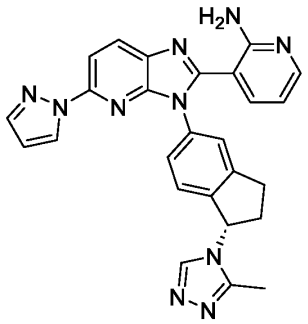
[00547] **Table 12.** Characterization data of compounds prepared analogously to compound 171.

Cpd ID	Characterization Data
180	MS (ESI) calcd. for $C_{32}H_{25}N_9O$, 551.22 m/z, found 552.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.85 - 8.93 (m, 1H), 8.32 - 8.40 (m, 2H), 8.18 - 8.30 (m, 1H), 8.00 - 8.08 (m, 1H), 7.95 - 8.00 (m, 1H), 7.80 - 7.83 (m, 1H), 7.50 - 7.60 (m, 1H), 7.49 (s, 1H), 7.20 - 7.30 (m, 3H), 7.05 - 7.20 (m, 2H), 6.55 - 6.58 (m, 1H), 6.40 - 6.48 (m, 1H), 6.20 - 6.40 (m, 1H), 3.10 - 3.25 (m, 2H), 2.55 - 2.65 (m, 1H), 2.30 - 2.45 (m, 4H). (formic acid salt).
181	MS (ESI) calcd. for $C_{35}H_{27}N_{11}O$, 617.24 m/z, found 618.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.08 - 9.19 (m, 1H), 8.63 - 8.72 (m, 1H), 8.30 - 8.47 (m, 2H), 7.89 - 8.06 (m, 3H), 7.80 - 7.88 (m, 1H), 7.69 - 7.78 (m, 1H), 7.57 - 7.67 (m, 1H), 7.49 - 7.56 (m, 1H), 7.41 - 7.48 (m, 1H), 7.09 - 7.26 (m, 2H), 6.88 - 7.06 (m, 2H), 6.38 - 6.54 (m, 3H), 5.58 - 5.60 (m, 1H), 3.78 (s, 3H), 2.83 - 3.12 (m, 2H), 2.53 - 2.66 (m, 1H), 1.97 - 2.14 (m, 1H). (formic acid salt)
182	.: MS (ESI) calcd. for $C_{35}H_{27}N_{11}O$, 617.24 m/z, found, 618.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.75-8.77 (m, 1H), 8.35- 8.38 (m, 2H), 8.08 - 8.09 (m, 1H), 8.01 - 8.02 (m, 2H), 7.81 - 7.97 (m, 3H), 7.41 - 7.43 (m, 2H), 7.26 - 7.32 (m, 2H), 6.44 - 6.62 (m, 3H), 5.61-5.66 (m, 1H), 3.89 (s, 3H), 2.95 - 3.15 (m, 2H), 2.49 - 2.58 (m, 1H), 2.05-2.19 (m, 1H).
209	MS (ESI) calcd. for $C_{37}H_{27}N_9O$, 613.23 m/z, found 614.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.81 - 8.89 (m, 1H), 8.51 - 8.58 (m, 1H), 8.42 - 8.50 (m, 1H), 8.11 - 8.19 (m, 1H), 8.01 - 8.10 (m, 2H), 7.83 - 7.94 (m, 3H), 7.62 - 7.71 (m, 3H), 7.51 - 7.60 (m, 4H), 7.45 - 7.50 (m, 1H), 7.36 - 7.44 (m, 1H), 6.88 - 6.97 (m, 1H), 6.56 - 6.63 (m, 1H), 5.68 - 5.75 (m, 1H), 3.07 - 3.20 (m, 1H), 2.91 - 3.06 (m, 1H), 2.58 - 2.69 (m, 1H), 2.07 - 2.20 (m, 1H). (TFA salt)
226	MS (ESI) calcd. for $C_{33}H_{27}F_2N_7O$, 575.22 m/z, found 576.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.14 - 9.15 (m, 1H), 8.43 - 8.44 (m, 1H), 8.00 - 8.39 (m, 2H), 7.82 - 7.85 (m, 1H), 7.67 - 7.70 (m, 1H), 7.41 - 7.49 (m, 3H), 7.27 - 7.29 (m, 1H), 6.84 - 7.21 (m, 1H), 6.50 - 6.79 (m, 1H), 5.64 - 5.66 (m, 1H), 3.31 - 3.34 (m, 1H), 2.90 - 3.04 (m, 2H), 2.51 - 2.52 (m, 1H), 2.31 - 2.34 (m, 2H), 2.00 - 2.19 (m, 3H), 1.89 - 1.99 (m, 2H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.08, -73.26. (TFA salt)
265	MS (ESI) calcd. for $C_{30}H_{25}N_7O$, 499.21 m/z, found 500.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.89 - 9.03 (m, 1H), 8.11 - 8.23 (m, 2H), 8.02 - 8.10 (m, 1H), 7.15 - 7.52 (m, 6H), 6.41 - 6.53 (m, 1H), 5.59 - 5.68 (m, 1H), 2.89- 3.18 (m, 2H), 2.56 - 2.64 (m, 1H), 2.45 - 2.51 (m, 3H), 2.01- 2.21 (m, 4H).
327	MS (ESI) calcd. for $C_{32}H_{28}N_8O_2$, 556.23 m/z, found 557.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.93 - 9.02 (m, 1H), 8.11 - 8.38 (m, 2H), 7.89 - 8.10 (m, 1H), 7.14 - 7.57 (m, 6H), 6.37 - 6.56 (m, 1H), 5.55 - 5.72 (m, 1H), 4.11 (s, 2H), 2.81 - 3.15 (m, 2H), 2.56 - 2.65 (m, 1H), 2.49 (s, 3H), 2.01 - 2.21 (m, 1H), 1.86 (s, 3H).

Cpd ID	Characterization Data
341	MS (ESI) calcd. for $C_{32}H_{24}N_8O_2$: 552.20 m/z, found, 553.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.91 - 9.15 (m, 1H), 8.32 - 8.48 (m, 2H), 8.25 - 8.27 (m, 1H), 8.04 - 8.19 (m, 1H), 7.81 - 7.92 (m, 2H), 7.61 - 7.72 (m, 2H), 7.41 - 7.51 (m, 3H), 7.31 - 7.36 (m, 1H), 6.79 - 6.89 (m, 1H), 5.62 - 5.72 (m, 1H), 3.03 - 3.16 (m, 1H), 2.82 - 2.99 (m, 1H), 2.63 - 2.69 (m, 4H), 2.03 - 2.18 (m, 1H).
404	MS (ESI) calcd. for $C_{29}H_{21}F_2N_7O$, 521.18 m/z, found, 522.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.12 - 9.16 (m, 1H), 8.44 - 8.47 (m, 1H), 8.26 - 8.28 (m, 1H), 8.03 - 8.07 (m, 1H), 7.82 - 7.85 (m, 1H), 7.74 - 7.76 (m, 1H), 7.61 - 7.63 (m, 1H), 7.44 - 7.47 (m, 2H), 7.29 - 7.31 (m, 1H), 6.84 - 7.19 (m, 1H), 6.74 - 6.78 (m, 1H), 5.61 - 5.69 (m, 1H), 4.32 (s, 1H), 3.01 - 3.12 (m, 1H), 2.86 - 2.99 (m, 1H), 2.57 - 2.61 (m, 1H), 2.02 - 2.13 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -74.06, -116.08. (TFA salt)
405	MS (ESI) calcd. for $C_{30}H_{23}F_2N_7O$, 535.19 m/z, found 536.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.25 - 9.35 (m, 1H), 9.14 (s, 1H), 8.42 - 8.50 (m, 1H), 8.10 - 8.20 (m, 1H), 8.00 - 8.06 (m, 1H), 7.83 - 7.90 (m, 1H), 7.40 - 7.50 (m, 2H), 7.35 - 7.40 (m, 1H), 7.25 - 7.35 (m, 1H), 7.20 - 7.35 (m, 1H), 6.90 - 7.20 (m, 1H), 6.40 - 6.50 (m, 1H), 5.60 - 5.75 (m, 1H), 3.00 - 3.15 (m,1H), 2.85 - 3.00 (m,1H), 2.55 - 2.65 (m,1H), 2.00 - 2.20 (m, 4H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.06. (formic acid salt)
406	MS (ESI) calcd. for $C_{32}H_{25}F_2N_7O$, 561.21 m/z, found 562.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.25 - 9.35 (m, 1H), 9.14 (s, 1H), 8.42 - 8.50 (m, 1H), 8.10 - 8.20 (m, 1H), 8.00 - 8.06 (m, 1H), 7.83 - 7.90 (m, 1H), 7.40 - 7.45 (m, 2H), 7.35 - 7.40 (m, 1H), 7.25 - 7.35 (m, 1H), 7.20 - 7.25 (m, 1H), 6.90 - 7.20 (m, 1H), 6.40 - 6.50 (m, 1H), 5.50 - 5.60 (m, 1H), 3.00 - 3.15 (m, 1H), 2.88 - 3.00 (m,1H), 2.55 - 2.65 (m, 1H), 2.00 - 2.15 (m, 1H), 1.50 - 1.60 (m, 1H), 0.85 - 0.93 (m, 2H), 0.73 - 0.80 (m, 2H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm);-116.07. (formic acid salt)
407	MS (ESI) calcd. for $C_{32}H_{28}F_2N_8O$, 578.24 m/z, found, 579.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.30 - 9.32 (m, 1H), 8.97 - 9.13 (m, 1H), 8.44 - 8.52 (m, 1H), 8.12 - 8.16 (m, 1H), 7.97 - 8.07 (m, 1H), 7.76 - 7.85 (m, 1H), 7.15 - 7.69 (m, 6H), 6.83 - 7.08 (m, 1H), 6.45 - 6.55 (m, 1H), 5.64 - 5.80 (m, 1H), 3.46 - 3.56 (m, 2H), 2.85 - 3.12 (m, 2H), 2.23 - 2.49 (m, 7H), 2.03 - 2.20 (m, 1H). ^{19}F-NMR (282 MHz, DMSO-d_6) δ (ppm); -116.04.
408	MS (ESI) calcd. for $C_{32}H_{25}F_2N_7O_2$, 577.20 m/z, found, 578.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.14 (s, 1H), 8.44 - 8.46 (m, 1H), 8.10 - 8.19 (m, 1H), 8.00 - 8.01 (m, 1H), 7.82 - 7.85 (m, 1H), 7.51 - 7.54 (m, 1H), 7.41 - 7.44 (m, 1H), 7.31 - 7.37 (m, 1H), 7.20 - 7.29 (m, 2H), 6.84 - 6.85 (m, 1H), 6.42 - 6.47 (m, 1H), 5.62 - 5.67 (m, 1H), 4.78 - 4.83 (m, 2H), 4.58 - 4.62 (m, 2H), 4.13 - 4.18 (m, 1H), 2.90 - 3.06 (m, 2H), 2.52 - 2.59 (m, 1H), 2.06 - 2.12 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6+D_2O) δ (ppm); -116.06.

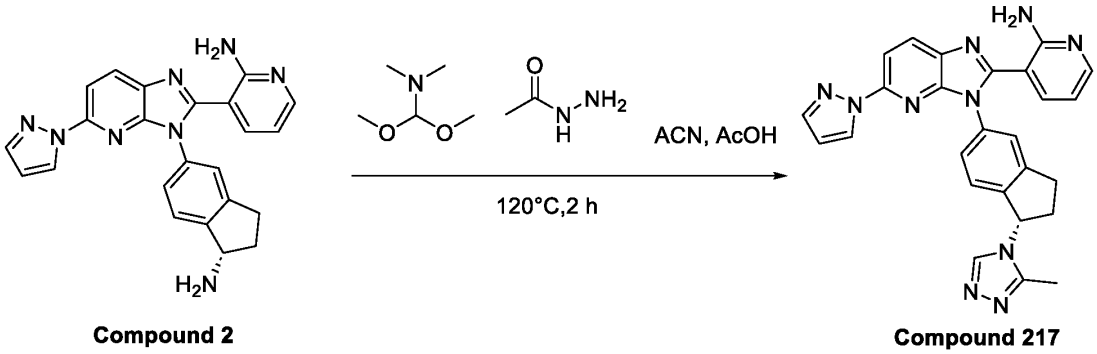
Cpd ID	Characterization Data
409	MS (ESI) calcd. for $C_{31}H_{25}F_2N_7O_2$: 565.20 m/z, found, 566.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.04 - 9.15 (m, 1H), 8.38 - 8.45 (m, 1H), 8.14 - 8.26 (m, 1H), 7.94 - 8.12 (m, 1H), 7.81 - 7.92 (m, 1H), 7.52 - 7.64 (m, 1H), 7.40 - 7.46 (m, 1H), 7.31 - 7.39 (m, 2H), 7.16 - 7.28 (m, 1H), 6.80 - 7.14 (m, 1H), 6.44 - 6.58 (m, 1H), 5.57 - 5.67 (m, 1H), 4.28 - 4.39 (m, 2H), 3.27 - 3.40 (m, 3H), 3.01 - 3.14 (m, 1H), 2.86 - 3.00 (m, 1H), 2.58 - 2.66 (m, 1H), 2.01 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.09.
412	MS (ESI) calcd. for $C_{31}H_{25}F_2N_7O$, 549.20 m/z, found, 550.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.26 - 9.33 (m, 1H), 9.12 - 9.18 (m, 1H), 8.41 - 8.47 (m, 1H), 7.88 - 8.22 (m, 2H), 7.79 - 7.87 (m, 1H), 7.35 - 7.48 (m, 3H), 7.22 - 7.33 (m, 2H), 6.84 - 7.03 (m, 1H), 6.20 - 6.51 (m, 1H), 5.59 - 5.79 (m, 1H), 2.99 - 3.12 (m, 1H), 2.83 - 2.98 (m, 1H), 2.59 - 2.62 (m, 1H), 2.37 - 2.47 (m, 2H), 2.01 - 2.16 (m, 1H), 1.08 - 2.25 (m, 3H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.07.
435	MS (ESI) calcd. for $C_{32}H_{27}N_7O$, 525.23 m/z, found 526.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.05 - 9.15 (m, 1H), 8.85 - 8.98 (m, 1H), 8.10 - 8.22 (m, 2H), 7.90 - 8.10 (m, 1H), 7.30 - 7.46 (m, 4H), 7.25 - 7.30 (m, 1H), 7.15 - 7.25 (m, 1H), 6.40 - 6.55 (m, 1H), 5.60 - 5.70 (m, 1H), 2.85 - 3.15 (m, 2H), 2.55 - 2.63 (m, 4H), 2.00 - 2.15 (m, 1H), 1.47 - 1.60 (m, 1H), 0.90 - 1.00 (m, 2H), 0.70 - 0.80 (m, 2H).
453	**MS (ESI)** calcd. for $C_{32}H_{25}F_2N_7O_2$: 577.20 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.02 - 9.20 (m, 1H), 8.37 - 8.54 (m, 1H), 8.11 - 8.29 (m, 1H), 7.95 - 8.08 (m, 1H), 7.77 - 7.91 (m, 1H), 7.51 - 7.65 (m, 1H), 7.40 - 7.50 (m, 1H), 7.30 - 7.39 (m, 2H), 7.18 - 7.28 (m, 1H), 6.80 - 7.17 (m, 1H), 6.40 - 6.60 (m, 1H), 5.60 - 5.75 (m, 1H), 5.49 - 5.59 (m, 1H), 4.46 - 4.70 (m, 2H), 2.86 - 3.15 (m, 3H), 2.70 - 2.85 (m, 1H), 2.61 - 2.68 (m, 1H), 2.02 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.07.
454	**MS (ESI)** calcd. for $C_{32}H_{25}F_2N_7O_2$: 577.20 m/z, found, 578.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.27 - 9.40 (m, 1H), 9.02 - 9.20 (m, 1H), 8.37 - 8.54 (m, 1H), 8.11 - 8.29 (m, 1H), 7.96 - 8.08 (m, 1H), 7.77 - 7.91 (m, 1H), 7.51 - 7.65 (m, 1H), 7.41 - 7.64 (m, 1H), 7.30 - 7.39 (m, 2H), 7.18 - 7.28 (m, 1H), 6.80 - 7.17 (m, 1H), 6.40 - 6.60 (m, 1H), 5.60 - 5.75 (m, 1H), 5.49 - 5.59 (m, 1H), 4.46 - 4.70 (m, 2H), 2.86 - 3.15 (m, 3H), 2.70 - 2.85 (m, 1H), 2.61 - 2.68 (m, 1H), 2.02 - 2.18 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.05.
459	MS (ESI) calcd. for $C_{32}H_{24}F_2N_6O$, 546.58 m/z, found, 547.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.19 - 8.22 (m, 1H), 7.94 - 8.05 (m, 2H), 7.81 - 7.84 (m, 1H), 7.73 - 7.76 (m, 1H), 7.47 - 7.59 (m, 2H), 7.36 - 7.42 (m, 2H), 7.22 - 7.24 (m, 1H), 6.73 - 6.81 (m, 1H), 5.55 - 5.62 (m, 1H), 3.02 - 3.11 (m, 1H), 2.82 - 2.95 (m, 1H), 2.55 - 2.57 (m, 1H), 2.01 - 2.11 (m, 1H), 1.51 - 1.59 (m, 1H), 0.91 - 0.94 (m, 2H), 0.72 - 0.75 (m, 2H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -73.88, -134.20, -137.77. (TFA salt)
460	MS (ESI) calcd. for $C_{34}H_{29}F_2N_7O$, 589.24 m/z, found 590.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.14 (s, 1H), 8.40 - 8.55 (m, 1H), 8.10 - 8.30 (m, 1H), 7.90 - 8.10 (m, 1H), 7.75 - 7.90 (m, 1H), 7.40 - 7.50 (m, 2H), 7.35 - 7.40 (m, 1H), 7.15 - 7.35 (m, 2H), 6.80 - 7.10 (m, 1H), 6.45 (s, 1H), 5.55 - 5.75 (m, 1H), 2.85 - 3.15 (m, 3H), 2.60 - 2.65 (m, 1H), 1.85 - 2.20 (m, 3H), 1.50 - 1.80 (m, 6H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.05.

[00548] Example 80: (S)-3-(3-(1-(3-methyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 217)



Compound 217

[00549] Synthetic Route:



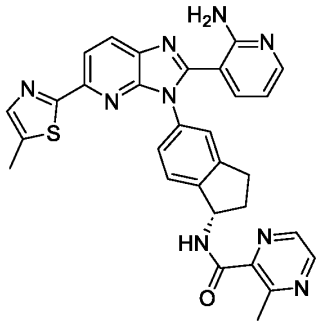
Compound 2 **Compound 217**

[00550] Step 1: (S)-3-(3-(1-(3-methyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine

[00551] To a solution of acetohydrazide (36.3 mg, 0.490 mmol, 2 equiv) in ACN (5 mL) was added (dimethoxymethyl)dimethylamine (58.4 mg, 0.490 mmol, 2 equiv). The resulting mixture was stirred for 2 h at 60°C. To the reaction mixture was added AcOH (29.4 mg, 0.490 mmol, 2 equiv) and 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (100 mg, 0.245 mmol, 1 equiv) and the reaction mixture was stirred at 120°C for 2 h. The reaction mixture was purified by Prep-HPLC on a Xselect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-(3-methyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 217**) (25.5 mg, 20.04%yield) as an off-white solid.: MS (ESI) calcd. for $C_{26}H_{22}N_{10}$: 474.20 m/z, found, 475.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 8.52 - 8.85 (m, 1H), 8.38 - 8.49 (m, 2H), 7.98 - 8.11 (m, 2H), 7.82 - 7.97 (m, 1H), 7.68 - 7.81 (m, 1H), 7.52 - 7.67 (m, 1H), 7.22 - 7.51 (m, 2H), 6.72 - 6.95 (m, 1H), 6.45 - 6.71 (m, 1H), 5.91 - 6.19 (m, 1H), 3.16 - 3.29 (m,

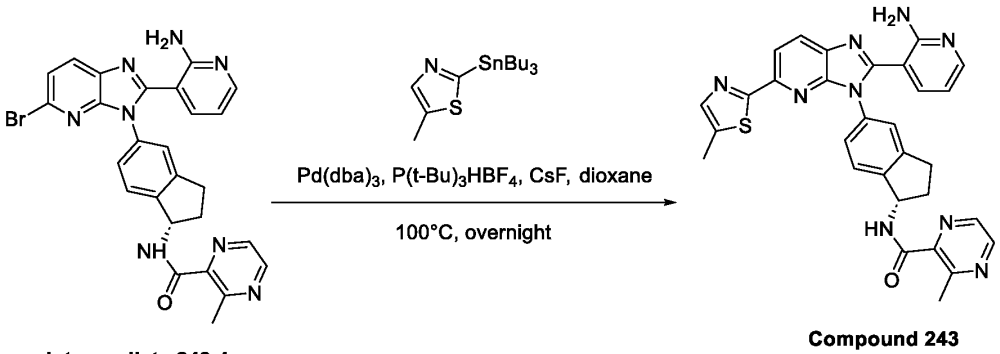
1H), 2.93 - 3.15 (m, 1H), 2.75 -2.89 (m, 1H), 2.52 - 2.53 (m, 3H), 2.19 - 2.39 (m, 1H). (TFA salt)

[00552] Example 81: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-methylpyrazine-2-carboxamide (Compound 243)



Compound 243

[00553] Synthetic Route:



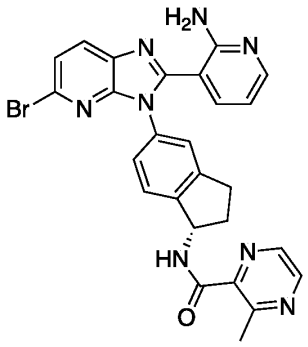
Intermediate 243-1 **Compound 243**

[00554] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-methylpyrazine-2-carboxamide (Compound 243)

[00555] A mixture of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-3-methylpyrazine-2-carboxamide (**Intermediate 243-1**) (100 mg, 0.185 mmol, 1 equiv), $Pd_2(dba)_3$ (16.9 mg, 0.018 mmol, 0.1 equiv) and CsF (140 mg, 0.925 mmol, 5 equiv) in dioxane (3 mL) was treated with 5-methyl-2-(tributylstannyl)-1,3-thiazole (143.4 mg, 0.370 mmol, 2 equiv) at room temperature under nitrogen atmosphere. The resulting mixture was stirred overnight at 100°C under nitrogen atmosphere. The reaction was quenched with water (50 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 50 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on

C18 silica gel using a gradient of acetonitrile in water (+ 10 mmol/L ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-3-methylpyrazine-2-carboxamide (**Compound 243**) (29.8 mg, 28% yield) as a light yellow solid.: MS (ESI) calcd. for $C_{30}H_{25}N_9OS$, 559.19 m/z, found 560.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.67 - 8.75 (m, 1H), 8.52 - 8.60 (m, 1H), 8.29 - 8.37 (m, 1H), 8.11 - 8.21 (m, 1H), 8.01 - 8.09 (m, 1H), 7.64 - 7.70 (m, 1H), 7.40 - 7.59 (m, 2H), 7.22 - 7.38 (m, 2H), 6.48 - 6.57 (m, 1H), 5.61 - 5.70 (m, 1H), 2.89 - 3.15 (m, 2H), 2.78 (s, 3H), 2.53 - 2.60 (m, 1H), 2.42- 2.50 (m, 3H), 2.12- 2.24 (m, 1H).

[00556] Intermediate 243-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin- 3-yl)-2,3-dihydro-1*H*-inden-1-yl)-3-methylpyrazine-2-carboxamide



Intermediate 243-1

[00557] Intermediate 243-1 was prepared in a manner analogous to **Compound 3** using PyBOP in place of HATU, **Intermediate 245-3** in place of **Compound 2** and 3-methylpyrazine-2-carboxylic acid in place of 3,4-difluoro-5-anisic acid.: MS (ESI) calcd. for $C_{26}H_{21}BrN_8O$, 540.10 m/z, found, 541.15 $[M+H]^+$.

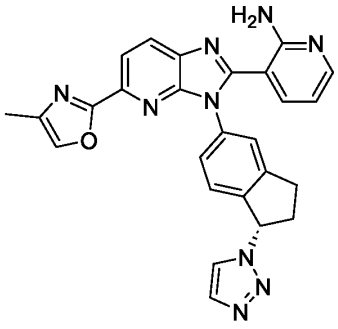
[00558] The following compounds were prepared analogous to the synthetic preparation in Example 81 (Compound 243).

[00559] Table 13A. Characterization data of compounds prepared analogously to compound 243.

Cpd ID	Characterization Data
300	MS(ESI) calcd. for $C_{31}H_{26}N_8OS$, 558.20 m/z, found 589.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 9.03 - 9.08 (m, 1H), 8.38 - 8.45 (m, 2H), 8.25 - 8.28 (m, 1H), 8.07 - 8.12 (m, 1H), 7.82 - 7.87 (m, 1H), 7.61 - 7.64 (m, 1H), 7.42 - 7.49. (m, 2H), 7.31 - 7.37 (m, 2H), 6.83 - 6.89 (m, 1H), 5.61 - 5.70 (m, 1H), 3.03 - 3.16 (m, 1H), 2.87 - 2.99 (m, 1H), 2.63 (s, 3H), 2.57 - 2.59 (m, 1H), 2.45 (s, 3H), 2.02- 2.19 (m, 1H). (TFA salt)

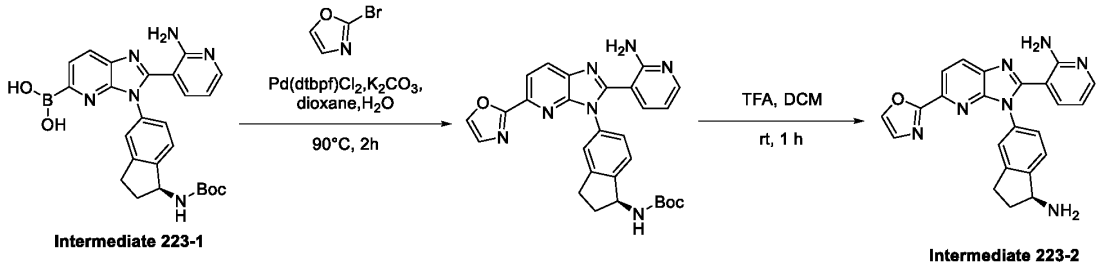
Cpd ID	Characterization Data
302	MS (ESI) calcd. for $C_{30}H_{25}N_9OS$, 559.19 m/z, found 560.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.68 - 8.71 (m, 1H), 8.52 - 8.59 (m, 1H), 8.33 - 8.39 (m, 1H), 8.17 - 8.23 (m, 1H), 8.06 - 8.11 (m, 1H), 7.69 - 7.72 (m, 1H), 7.31 - 7.49 (m, 4H), 6.72 - 6.83 (m, 1H), 5.55 - 5.67 (m, 1H), 2.83 - 3.09 (m, 2H), 2.75 (s, 3H), 2.55 - 2.61 (m, 1H), 2.44 (s, 3H), 2.03 - 2.29 (m, 1H). (TFA salt)
303	MS (ESI) calcd. for C26H21N9S, 491.16 m/z, found 492.20 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.20 - 8.40 (m, 2H), 8.05 - 8.20 (m, 2H), 7.90 - 8.05 (m, 1H), 7.70 - 7.82 (m, 1H), 7.61 (s, 1H), 7.35 - 7.50 (m, 1H), 7.05 - 7.30 (m, 3H), 6.40 - 6.58 (m, 1H), 6.20 - 6.40 (m, 1H), 3.15 - 3.30 (m, 1H), 2.95 - 3.15 (m, 1H), 2.65 - 2.90 (m, 1H), 2.35 - 2.45 (m, 4H)
314	MS (ESI) calcd. for $C_{31}H_{26}N_8OS$, 558.20 m/z, found 559.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.89 - 8.95 (m, 1H), 8.29 - 8.35 (m, 1H), 8.20 - 8.28 (m, 1H), 8.12 - 8.19 (m, 1H), 8.01 - 8.10 (m, 1H), 7.61 - 7.69 (m, 1H), 7.45 - 7.61 (m, 2H), 7.35 - 7.44 (m, 2H), 7.26 - 7.34 (m, 1H), 6.57 - 6.64 (m, 1H), 5.61 - 5.70 (m, 1H), 3.03 - 3.18 (m, 1H), 2.89 - 3.02 (m, 1H), 2.62 - 2.69 (m, 1H), 2.53 - 2.59 (m, 3H), 2.48 (s, 3H), 2.02 - 2.19 (m, 1H).
316	MS (ESI) calcd for $C_{26}H_{21}N_9S$: 491.16 m/z, found, 492.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.27 - 8.34 (m, 1H), 8.13 - 8.20 (m, 2H), 7.99 - 8.06 (m, 1H), 7.78 - 7.84 (m, 1H), 7.48 - 7.54 (m, 1H), 7.18 - 7.35 (m, 4H), 6.41 - 6.52 (m, 1H), 6.30 - 6.39 (m, 1H), 3.17 - 3.31 (m, 1H), 2.97 - 3.12 (m, 1H), 2.72 - 2.91 (m, 1H), 2.55 - 2.62 (m, 1H), 2.44 (s, 3H).
556	Observed mass (ESI): 572.45 [M+H]+. 1H NMR (400 MHz, DMSO-d6+D2O) δ (ppm): 9.11 - 9.42 (m, 1H), 8.72 - 8.83 (m, 1H), 8.56 - 8.71 (m, 1H), 8.28 - 8.53 (m, 2H), 7.93 - 8.12 (m, 1H), 7.42 - 7.62 (m, 1H), 7.33 - 7.41 (m, 1H), 7.17 - 7.32 (m, 2H), 6.35 - 6.56 (m, 1H), 4.29 - 4.45 (m, 1H), 4.08 - 4.28 (m, 2H), 3.09 - 3.32 (m, 1H), 2.87 - 3.05 (m, 2H), 2.72 - 2.86 (m, 2H), 2.39 - 2.48 (m, 1H), 1.73 - 2.12 (m, 4H), 1.06 - 1.42 (m, 2H), 0.64 - 0.82 (m, 4H).
559	Observed mass (ESI): 625.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.30 (d, J = 8.3 Hz, 1H), 7.98 - 8.12 (m, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.30 - 7.40 (m, 2H), 7.25 (dd, J = 7.7, 1.9 Hz, 1H), 6.91 (s, 2H), 6.64 (s, 1H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 5.34 - 5.59 (m, 1H), 4.40 - 4.55 (m, 1H), 4.15 - 4.23 (m, 2H), 3.87 (s, 3H), 3.14 - 3.22 (m, 2H), 3.05 - 3.11 (m, 2H), 2.86 - 2.93 (m, 1H), 2.25 - 2.31 (m, 1H), 1.90 - 2.06 (m, 3H), 1.28 - 1.48 (m, 2H), 0.68 - 1.48 (m, 4H).

[00560] Example 82: (S)-3-(3-(1-(1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(4-methyloxazol-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 245)



Compound 245

[00561] Synthetic Route:

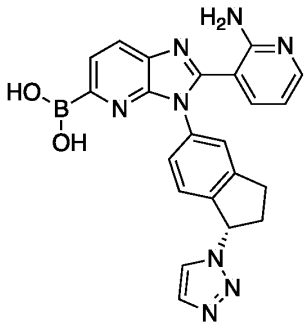


Intermediate 223-1

Intermediate 223-2

[00562] **Compound 245** was prepared by Suzuki coupling of **Intermediate 245-1** and 2-bromo-4-methyloxazole using a procedure analogous to Step 1 of **Intermediate 223-2**.: MS (ESI) calcd. for $C_{26}H_{21}N_9O$, 475.19 m/z, found 476.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.30 - 8.36 (m, 1H), 8.22 - 8.30 (m, 1H), 8.10 - 8.18 (m, 1H), 8.00 - 8.06 (m, 1H), 7.86 - 7.90 (m, 1H), 7.80 - 7.85 (m, 1H), 7.50 (s, 1H), 7.20 - 7.35 (m, 3H), 6.42 - 6.55 (m, 1H), 6.30 - 6.40 (m, 1H), 3.20 - 3.35 (m, 1H), 3.00 - 3.15 (m, 1H), 2.75 - 2.98 (m, 1H), 2.55 - 2.60 (m, 1H), 2.19 (s, 3H).

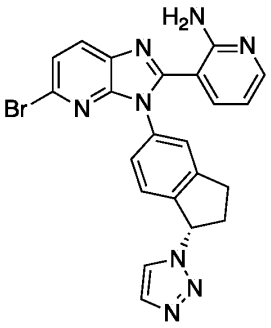
[00563] **Intermediate 245-1: (*S*)-(3-(1-(1*H*-1,2,3-triazol-1-yl)-2,3-dihydro-1*H*-inden-5-yl)-2-(2-aminopyridin-3-yl)-3*H*-imidazo[4,5-*b*]pyridin-5-yl)boronic acid**



Intermediate 245-1

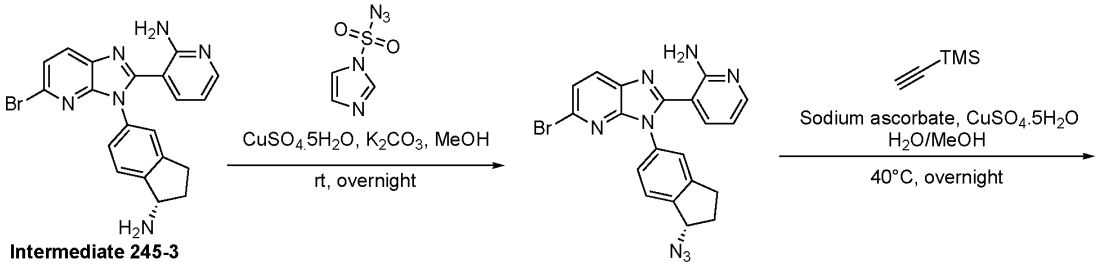
[00564] **Intermediate 245-1** was prepared in a manner analogous to **Intermediate 223-1** using **Intermediate 245-2** in place of **Intermediate 129-1.**: MS (ESI) calcd. for $C_{22}H_{19}BN_8O_2$, 438.17 m/z, found 439.10 $[M+H]^+$.

[00565] **Intermediate 245-2: (*S*)-3-(3-(1-(1*H*-1,2,3-triazol-1-yl)-2,3-dihydro-1*H*-inden-5-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine**



Intermediate 245-2

[00566] Synthetic Route:



[00567] **Step 1: Synthesis of (S)-3-(3-(1-azido-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine**

[00568] A mixture of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-bromoimidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 245-3**) (3 g, 7.12 mmol, 1 equiv), imidazole-1-sulfonyl azide (1.48 g, 8.55 mmol, 1.2 equiv), K_2CO_3 (3.94 g, 28.5 mmol, 4 equiv) and $CuSO_4.5H_2O$ (88.9 mg, 0.356 mmol, 0.05 equiv) in MeOH (30 mL) was stirred

overnight at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3) to afford (S)-3-(3-(1-azido-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (1.8 g, 57% yield) as a yellow solid.: MS (ESI) calcd. for $C_{20}H_{15}BrN_8$, 446.06 m/z, found 447.15 $[M+H]^+$.

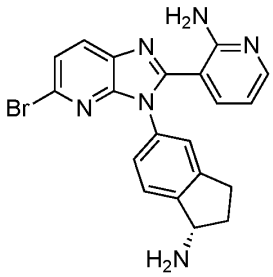
[00569] Step 2: Synthesis of (S)-3-(5-bromo-3-(1-(4-(trimethylsilyl)-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine

[00570] A mixture of (S)-3-(3-(1-azido-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (1.8 g, 4.0 mmol, 1 equiv), trimethylsilylacetylene (7.91 g, 80.5 mmol, 20 equiv), $CuSO_4.5H_2O$ (0.20 g, 0.81 mmol, 0.2 equiv) and sodium ascorbate (0.32 g, 1.6 mmol, 0.4 equiv) in MeOH (10 mL) and H_2O (10 mL) was stirred overnight at 40°C. The reaction was quenched by addition of water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 200 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated under vacuum to afford (S)-3-(5-bromo-3-(1-(4-(trimethylsilyl)-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (1.2 g, crude) as a yellow solid.: MS (ESI) calcd. for $C_{25}H_{25}BrN_8Si$, 544.12 m/z, found 545.10 $[M+H]^+$.

[00571] Step 3: Synthesis of (S)-3-(3-(1-(1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Intermediate 254-2)

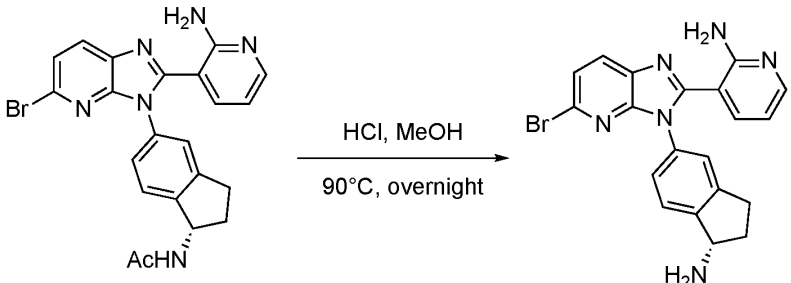
[00572] (S)-3-(5-bromo-3-(1-(4-(trimethylsilyl)-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (1.2 g, 2.2 mmol, 1 equiv) was dissolved in THF (12 mL) and $Et_3N.3HF$ (0.71 g, 4.4 mmol, 2 equiv) was added. The mixture was stirred for 2 h at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3) to afford (S)-3-(3-(1-(1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Intermediate 245-2**) (1 g, 96% yield) as a yellow solid.: MS (ESI) calcd. for $C_{22}H_{17}BrN_8$, 472.08 m/z, found 473.15 $[M+H]^+$.

[00573] Intermediate 245-3: (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine



Intermediate 245-3

[00574] Synthetic Route:

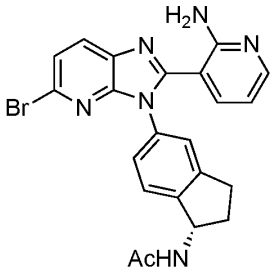


Intermediate 245-4 **Intermediate 245-3**

[00575] **Step 1: Synthesis of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Intermediate 245-3)**

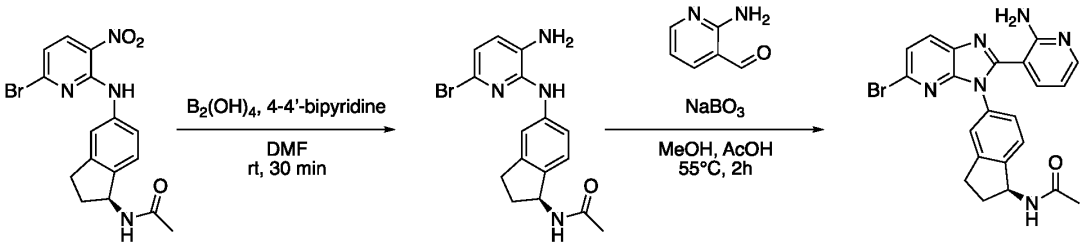
[00576] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]acetamide (**Intermediate 245-4**) (40 g, 86 mmol, 1 equiv) in methanol (200 mL) was added conc. HCl (200 mL) and the resulting mixture was stirred overnight at 90°C. The mixture was allowed to cool to room temperature. The resulting mixture was concentrated under reduced pressure. The residue was neutralized to pH 7~8 with saturated aqueous sodium bicarbonate. The precipitated solids were collected by filtration and washed with H_2O (3 x 100 mL). The resulting solid was air-dried to afford 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-bromoimidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 245-3**) (33 g, 91%) as a brown solid.: MS (ESI) calcd. for $C_{20}H_{17}BrN_6$, 421.07 m/z, found, 422.15 $[M+H]^+$.

[00577] **Intermediate 245-4: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)acetamide**



Intermediate 245-4

[00578] Synthetic Route:



Intermediate 245-5 **Intermediate 245-4**

[00579] **Step 1: Synthesis of (S)-N-(5-((3-amino-6-bromopyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide**

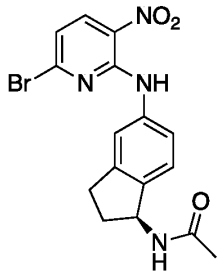
[00580] To a cooled (0°C) solution of N-[(1S)-5-[(6-bromo-3-nitropyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]acetamide (**Intermediate 245-5**) (25 g, 64 mmol, 1 equiv) in *N,N*-dimethylformamide (250 mL) was added 4,4'-bipyridine (0.5 g, 2 mmol, 3 mol%), followed by hypodiboric acid (17.3 g, 0.192 mol, 3 equiv). The resulting mixture was stirred at 0°C for 0.5 h. The reaction mixture was quenched by addition of 500 mL saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (3 x 250 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography, eluting with petroleum ether / dichloromethane / methanol (70:27:3) to afford N-[(1S)-5-[(3-amino-6-bromopyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]acetamide (16 g, 69%).: MS (ESI) calculated for $C_{16}H_{17}BrN_4O$, 360.06, found 361.00 $[M+H]^+$, 363.00 $[M+2+H]^+$.

[00581] **Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (Intermediate 245-4)**

[00582] A solution of N-[(1S)-5-[(3-amino-6-bromopyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]acetamide (15.5 g, 42.9 mmol, 1 equiv) in methanol (72 mL) and acetic acid (14 mL) was treated with 2-aminopyridine-3-carbaldehyde (6.29 g, 51.5 mmol, 1.2 equiv) followed by the addition of sodium perborate tetrahydrate (26.41 g, 172 mmol, 4 equiv) portion wise. The resulting mixture was stirred at 55°C for 2 h. The reaction mixture was concentrated under reduced pressure and then brought to pH 8 - 9 with saturated aqueous sodium bicarbonate. The

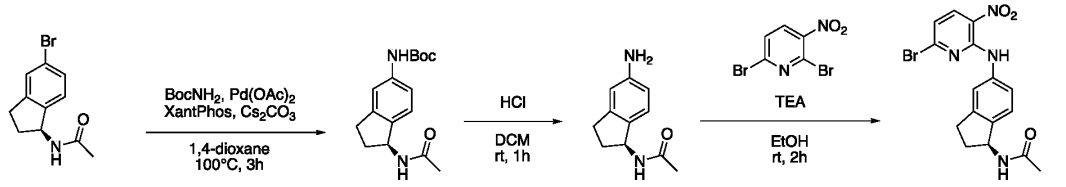
resulting precipitate was filtered. The filter cake was then washed with ethyl acetate (3 x 100 mL). The resulting filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography using a 0 to 20% gradient of ethyl acetate in petroleum ether followed by a 0 to 10% gradient of dichloromethane in methanol to provide (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (**Intermediate 245-4**) (4 g, 18% yield).: MS (ESI) calculated for $C_{22}H_{19}BrN_6O$, 462.08, found 463.00 $[M+H]^+$, 465.00 $[M+H+2]^+$.

[00583] Intermediate 245-5: (*S*)-*N*-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)acetamide



Intermediate 245-5

[00584] Synthetic Route:



Intermediate 245-6 **Intermediate 245-4**

[00585] Step 1: Synthesis of tert-butyl (S)-(1-acetamido-2,3-dihydro-1H-inden-5-yl)carbamate

[00586] To a mixture of N-[(1S)-5-bromo-2,3-dihydro-1H-inden-1-yl]acetamide (**Intermediate 245-6**) (40 g, 157 mmol, 1 equiv), *tert*-butyl carbamate (27.66 g, 236 mmol, 1.5 equiv), XantPhos (CAS: 161265-03-8) (9.11 g, 15.7 mmol, 10 mol%), $Pd(OAc)_2$ (3.54g, 15.7 mmol, 10 mol%), and cesium carbonate (154 g, 472 mmol, 10 mol%) was added 1,4-dioxane (300 mL) under nitrogen atmosphere. The resulting mixture was stirred for 3 h at 100°C. The reaction mixture was quenched by addition of water (50 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using an eluent of petroleum ether/dichloromethane/methanol (70:27:3) to afford tert-butyl N-[(1S)-1-acetamido-2,3-dihydro-1H-inden-5-yl]carbamate (43.1 g, 48% yield).: MS (ESI) calculated for $C_{16}H_{22}N_2O_3$: 290.16, found 289.05 $[M-H]^-$.

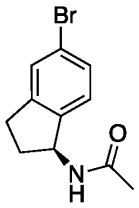
[00587] **Step 2: Synthesis of (S)-N-(5-amino-2,3-dihydro-1H-inden-1-yl)acetamide**

[00588] To a stirred solution of tert-butyl N-[(1S)-1-acetamido-2,3-dihydro-1H-inden-5-yl]carbamate (43.1 g, 148 mmol, 1 equiv) in dichloromethane (180 mL) was added 4N HCl in 1,4-dioxane (185 mL, 742 mmol, 5 equiv). The reaction mixture was stirred for 1h at room temperature. The reaction mixture was concentrated *in vacuo* and re-crystallized from ethyl acetate to afford N-[(1S)-5-amino-2,3-dihydro-1H-inden-1-yl]acetamide (hydrochloride salt) (23 g, 81% yield) as a white solid.: MS (ESI) calculated for $C_{11}H_{14}N_2O$, 190.11, found 191.15 $[M+H]^+$.

[00589] **Step 3: (S)-N-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (Intermediate 245-5)**

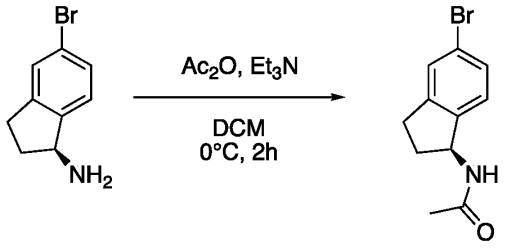
[00590] N-[(1S)-5-amino-2,3-dihydro-1H-inden-1-yl]acetamide (17 g, 89 mmol), 2,6-dibromo-3-nitropyridine (25.19 g, 89.36 mmol) was dissolved in triethylamine (45.21 g, 446.8 mmol, 5 equiv) and ethanol (200 mL). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with 400 mL water and the precipitate was rinsed with 1:1 ethanol/water (800 mL:800 mL) to afford N-[(1S)-5-[(6-bromo-3-nitropyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]acetamide (**Intermediate 245-5**) (26 g, 74% yield) as an orange solid.: MS (ESI) calculated for $C_{16}H_{15}BrN_4O_3$: 390.03, found 413.00 $[M+Na]^+$, 415.00 [M+ Na+2]$^+$.

[00591] **Intermediate 245-6: (*S*)-*N*-(5-bromo-2,3-dihydro-1*H*-inden-1-yl)acetamide**



Intermediate 245-6

[00592] Synthetic route:



Intermediate 245-6

[00593] **Step 1: Synthesis of (*S*)-*N*-(5-bromo-2,3-dihydro-1*H*-inden-1-yl)acetamide (Intermediate 245-6)**

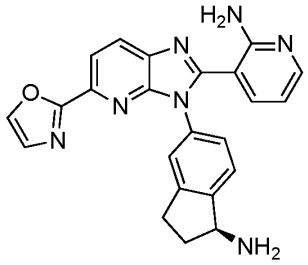
[00594] To a mixture of (S)-5-bromo-2,3-dihydro-1H-inden-1-amine (74 g, 350 mmol, 1 equiv) and triethylamine (106 g, 1.05 mol, 3 equiv) in dichloromethane (1.5 L) was added acetic anhydride (55.2 g, 526 mmol, 1.5 equiv) at 0°C and the mixture was stirred at 0°C for 2 h. The reaction mixture was quenched by addition of water (500 mL) and extracted with ethyl acetate (3 × 500 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was re-crystallized from petroleum ether to afford (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)acetamide (**Intermediate 245-6**) (90 g, 83% yield) as a white solid.: MS (ESI) calculated for $C_{11}H_{12}BrNO$, 253.01, found 254.00 $[M+H]^+$, 256.00 $[M+H+2]^+$.

[00595] The following compounds were prepared analogously to the synthetic preparation of Compound 245.

[00596] **Table 13B.** Characterization data of compounds prepared analogously to compound 245.

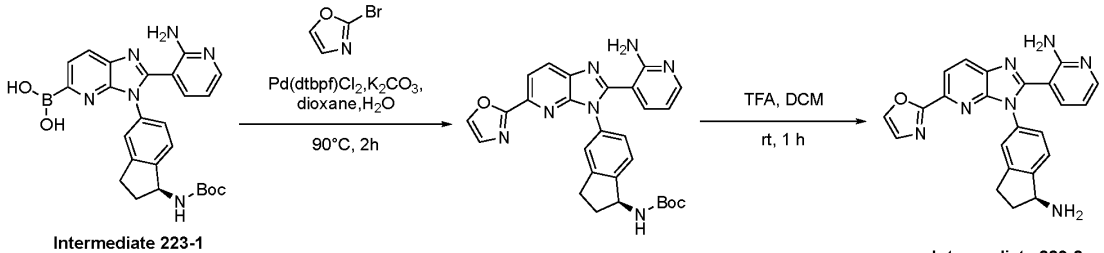
Cpd ID	Characterization Data
570	Observed mass (ESI): 657.37 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.18 - 8.23 (m, 1H), 7.99 - 8.02 (m, 1H), 7.91 - 8.01 (m, 1H), 7.81 - 7.89 (m, 1H), 7.47 - 7.53 (m, 1H), 7.29 - 7.38 (m, 1H), 7.18 - 7.22 (m, 2H), 6.61 - 6.71 (m, 1H), 6.37 - 6.45 (m,1H), 4.35 - 4.45 (m,1H), 4.25 - 4.31 (m,3H), 3.17 - 3.37 (m, 1H), 2.89 - 2.99 (m, 2H), 2.81 - 2.97 (m, 2H), 2.70 - 2.71 (m, 2H), 2.41 - 2.60 (m, 1H), 2.16 - 2.37 (m, 3H), 1.91 - 2.18 (m, 9H), 1.77 - 1.91 (m, 1H), 1.24 - 1.38 (m, 1H), 1.15 - 1.24 (m, 1H), 0.65 - 0.79 (m, 4H).
576	Observed mass (ESI): 616.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O) δ (ppm): 8.21 - 8.24 (m, 1H), 8.05 - 8.06 (m, 2H), 7.93 - 8.01 (m, 1H), 7.51 - 7.52 (m, 1H), 7.34 - 7.35 (m, 1H), 7.23 - 7.25 (m, 2H), 6.69 - 6.70 (m, 1H), 6.44 - 6.45 (m, 1H), 5.63 - 5.64 (m, 1H), 4.95 - 4.97 (m, 4H), 4.41 - 4.52 (m, 1H), 4.23 - 4.24 (m, 2H), 3.21 - 3.22 (m, 1H), 2.96 - 2.97 (m, 2H), 2.75 - 2.79 (m, 2H), 1.98 - 2.10 (m, 4H), 1.23 - 1.83 (m, 3H), 0.72 - 0.82 (m, 4H).
577	Observed mass (ESI): 602.35 [M+H]+. 1H NMR (500 MHz, DMSO-d6) δ (ppm): 8.83 (s, 1H), 8.34 - 8.43 (m, 1H), 8.26 - 8.34 (m, 1H), 8.24 (s, 1H), 7.93 - 8.03 (m, 1H), 7.44 - 7.58 (m, 1H), 7.30 (s, 1H), 7.20 - 7.27 (m, 2H), 6.37 - 6.50 (m, 1H), 4.23 - 4.44 (m, 1H), 4.11 - 4.27 (m, 2H), 4.02 (s, 3H), 3.07 - 3.23 (m, 1H), 2.82 - 3.00 (m, 2H), 2.59 - 2.82 (m, 2H), 2.35 - 2.47 (m, 1H), 1.61 - 2.09 (m, 4H), 1.08 - 1.38 (m, 2H), 0.60 - 0.76 (m, 4H).

[00597] **Intermediate 223-2: 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(1,3-oxazol-2-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine**



Intermediate 223-2

[00598] Synthetic Route:



Intermediate 223-1

Intermediate 223-2

[00599] **Step 1: Synthesis of tert-butyl N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(1,3-oxazol-2-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]carbamate**

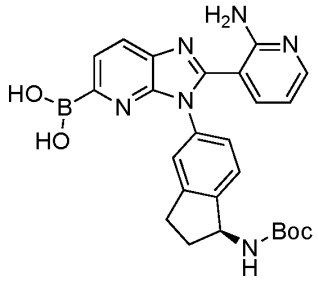
[00600] To a stirred mixture of 2-(2-aminopyridin-3-yl)-3-[(1S)-1-[(tert-butoxycarbonyl)amino]-2,3-dihydro-1H-inden-5-yl]imidazo[4,5-b]pyridin-5-ylboronic acid (Intermediate 223-1) (300 mg, 0.617 mmol, 1 equiv) in dioxane (6 mL) was added 2-bromo-1,3-oxazole (109.5 mg, 0.740 mmol, 1.2 equiv), Pd(dtbpf)Cl_2 (40 mg, 0.062 mmol, 0.1 equiv), K_2CO_3 (170.5 mg, 1.234 mmol, 2 equiv) and H_2O (1.5 mL). The resulting mixture was stirred at 90°C for 2 h under a nitrogen atmosphere. The mixture was purified by reverse phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% NH_4HCO_3) to afford tert-butyl N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(1,3-oxazol-2-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]carbamate (230 mg, 73%) as a yellow solid. MS (ESI) calcd. for $C_{28}H_{27}N_7O_3$: 509.22 m/z, found: 510.20 $[M+H]^+$.

[00601] Step 2: Synthesis of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(1,3-oxazol-2-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Intermediate 223-2)

[00602] To a solution of tert-butyl N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(1,3-oxazol-2-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]carbamate (220 mg, 0.432 mmol, 1 equiv) in DCM (6 mL) was added TFA (2 mL) and the resulting mixture was stirred at r.t for 1 h. The mixture was basified to pH 8 with aq. NaOH (2 mol/L). The resulting mixture was extracted with ethyl acetate (2 x 20 ml). The combined organic layers were concentrated under reduced pressure to afford 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(1,3-oxazol-2-

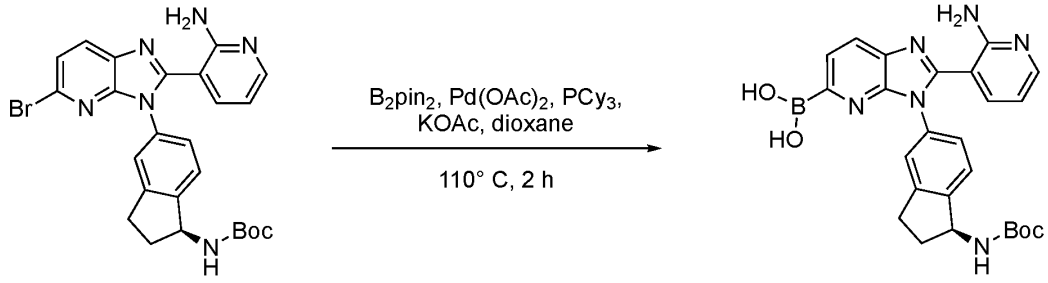
yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Intermediate 223-2) (200 mg, crude) as a yellow solid. MS (ESI) calcd. for $C_{23}H_{19}N_7O$: 409.17 m/z, found: 410.20 $[M+H]^+$.

[00603] Intermediate 223-1: (*S*)-(2-(2-aminopyridin-3-yl)-3-(1-((*tert*-butoxycarbonyl)amino)-2,3-dihydro-1*H*-inden-5-yl)-3*H*-imidazo[4,5-*b*]pyridin-5-yl)boronic acid



Intermediate 223-1

[00604] Synthetic Route:



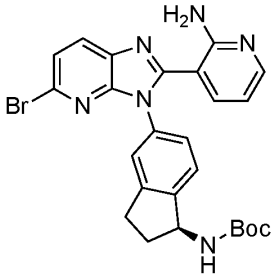
Intermediate 129-1 **Intermediate 223-1**

[00605] Step 1: Synthesis of (S)-(2-(2-aminopyridin-3-yl)-3-(1-((tert-butoxycarbonyl)amino)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-5-yl)boronic acid (Intermediate 223-1)

[00606] To a solution of tert-butyl (S)-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)carbamate (**Intermediate 129-1**) (3 g, 5.8 mmol) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (1.753 g, 6.905 mmol) in dioxane (30 mL) were added $Pd(OAc)_2$ (77.5 mg, 0.345 mmol), PCy_3 (193.6 mg, 0.690 mmol) and KOAc (1.412 g, 14.39 mmol) and the mixture was stirred for 2 h at 110 °C under a nitrogen atmosphere. After cooling to room temperature, the mixture was quenched with water (200 mL). The resulting mixture was extracted with ethyl acetate (3×200 mL). The organic layers were combined, dried over anhydrous sodium sulfate, filtered and concentrated. The crude product was purified by silica gel flash column chromatography (0-15%, MeOH/DCM) to afford (S)-(2-(2-aminopyridin-3-yl)-3-(1-((tert-butoxycarbonyl)amino)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-5-yl)boronic

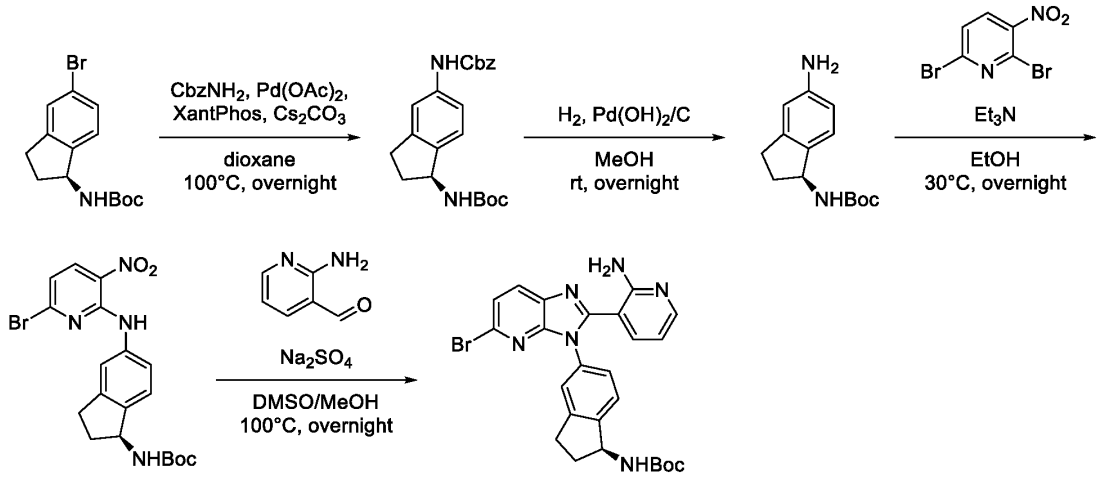
acid (**Intermediate 223-1**) (1.7 g, 61% yield) as a white solid. MS (ESI) calcd. for $C_{25}H_{27}N_6BO_4$: 486.21 m/z, found 487.25 $[M+H]^+$.

[00607] Intermediate 129-1: *tert*-butyl (*S*)-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)carbamate



Intermediate 129-1

[00608] Synthetic Route:



Intermediate 129-1

[00609] Step 1: Synthesis of benzyl N-[(1S)-1-[(tert-butoxycarbonyl)amino]-2,3-dihydro-1H-inden-5-yl]carbamate

[00610] To a solution of tert-butyl N-[(1S)-5-bromo-2,3-dihydro-1H-inden-1-yl]carbamate (60.00 g, 192.2 mmol, 1 equiv), benzyl carbamate (34.63 g, 230.6 mmol, 1.2 equiv) and XantPhos (22.24 g, 38.44 mmol, 0.2 equiv) in 1,4-dioxane (1.2 L) were added Cs_2CO_3 (125.23 g, 384.36 mmol, 2 equiv) and $Pd(OAc)_2$ (4.31 g, 19.2 mmol, 0.1 equiv). After stirring overnight at 100°C under nitrogen atmosphere the mixture was cooled to room temperature and the product was precipitated by the addition of H_2O. The precipitated solids were collected by filtration and washed with H_2O (3x400 ml). The solids were suspended in ethyl acetate and filtered, washing with ethyl acetate. The filtrate was concentrated under reduced pressure to afford benzyl N-[(1S)-1-[(tert-butoxycarbonyl)amino]-2,3-dihydro-1H-

inden-5-yl]carbamate (50 g, 46%) as a grey solid. MS (ESI) calcd. for $C_{22}H_{26}N_2O_4$, 382.19 m/z, found: 381.10 $[M-H]^-$.

[00611] Step 2: Synthesis of tert-butyl N-[(1S)-5-amino-2,3-dihydro-1H-inden-1-yl]carbamate

[00612] To a solution of benzyl N-[(1S)-1-[(tert-butoxycarbonyl)amino]-2,3-dihydro-1H-inden-5-yl]carbamate (50.00 g, 130.7 mmol, 1 equiv) in 500 ml CH_3OH was added 10% $Pd(OH)_2/C$ (5.00 g, 35.6 mmol, 0.27 equiv) in a pressure tank. The mixture was hydrogenated at room temperature under 30 psi of hydrogen overnight then filtered through a Celite pad and concentrated under reduced pressure to afford tert-butyl N-[(1S)-5-amino-2,3-dihydro-1H-inden-1-yl]carbamate (40 g, 73%) as a brown solid. MS (ESI) calcd. for $C_{14}H_{20}N_2O_2$, 248.15 m/z, found: 249.15 $[M+H]^+$.

[00613] Step 3: Synthesis of tert-butyl N-[(1S)-5-[(6-bromo-3-nitropyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]carbamate

[00614] A mixture of tert-butyl N-[(1S)-5-amino-2,3-dihydro-1H-inden-1-yl]carbamate (40.0 g, 161 mmol, 1 equiv) and triethylamine (48.90 g, 483.2 mmol, 3 equiv) in EtOH (800 mL) was stirred at room temperature until dissolved. 2,6-dibromo-3-nitropyridine (54.49 g, 193.3 mmol, 1.2 equiv) was added and the mixture was stirred at 30°C overnight. The mixture was allowed to cool to room temperature and the precipitated solids were collected by filtration and washed with EtOH (3 x 100 mL) to afford tert-butyl N-[(1S)-5-[(6-bromo-3-nitropyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]carbamate (30 g, 27%) as a red solid. MS (ESI) calcd. for $C_{19}H_{21}BrN_4O_4$, 448.07 m/z, found: 447.00 $[M-H]^-$.

[00615] Step 4: Synthesis of tert-butyl N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]carbamate (Intermediate 129-1)

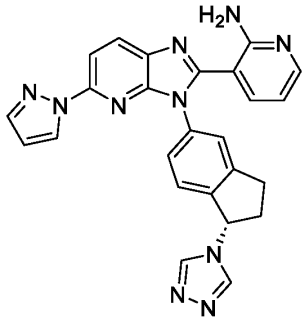
[00616] To a solution of tert-butyl N-[(1S)-5-[(6-bromo-3-nitropyridin-2-yl)amino]-2,3-dihydro-1H-inden-1-yl]carbamate (30.0 g, 66.8 mmol, 1 equiv) in DMSO (600 mL) and MeOH (100 mL) was added 2-aminopyridine-3-carbaldehyde (8.97 g, 73.4 mmol, 1.1 equiv) and the mixture was stirred until the solids were dissolved. $Na_2S_2O_4$ (25.57 g, 146.9 mmol, 2.2 equiv) was added and the mixture was stirred at 100°C overnight. The product was precipitated by the addition of H_2O. The precipitated solids were collected by filtration and washed with H_2O (3 x 500 ml). The residue was purified by silica gel column chromatography eluting with CH_2Cl_2 / MeOH (10:1) to afford tert-butyl N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]carbamate (Intermediate 129-1) (15 g, 36%) as a yellow solid. MS (ESI) calcd. for $C_{25}H_{25}BrN_6O_2$, 520.12 m/z, found: 521.20 $[M+H]^+$.

[00617] The following compounds were prepared analogous to the synthetic preparation in Example 82 (Compound 245).

[00618] **Table 14A.** Characterization data of compounds prepared analogously to compound 245.

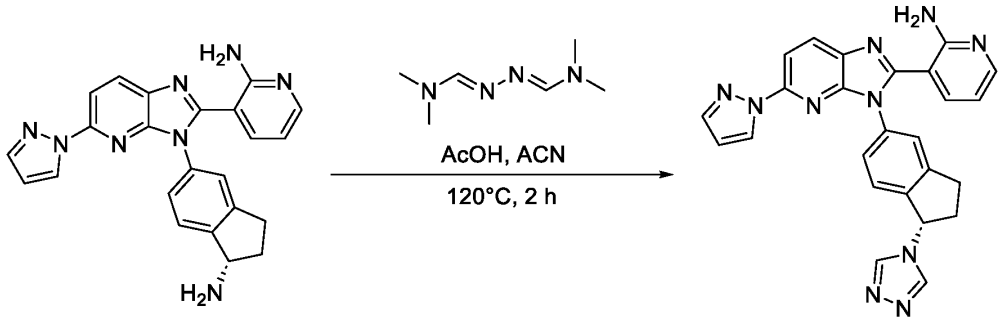
Cpd ID	Characterization Data
246	MS (ESI) calcd. for $C_{25}H_{19}N_9O$, 461.17 m/z, found 462.20 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.38 (m, 1H), 8.19 - 8.26 (m, 2H), 8.13 - 8.19 (m, 1H), 7.98 - 8.05 (m, 1H), 7.77 - 7.83 (m, 1H), 7.49 - 7.54 (m, 1H), 7.39 - 7.45 (m, 1H), 7.28 - 7.36 (m, 1H), 7.19 - 7.27 (m, 2H), 6.32 - 6.47 (m, 2H), 3.17 - 3.33 (m, 1H), 2.97 - 3.12 (m, 1H), 2.72 - 2.90 (m, 1H), 2.54 - 2.64 (m, 1H).
247	MS (ESI) calcd. for $C_{25}H_{21}N_{11}$, 475.20 m/z, found 476.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.26 - 8.28 (m, 1H), 8.17 - 8.18 (m, 1H), 8.07 - 8.08 (m, 1H), 7.93 - 7.95 (m, 2H), 7.80 - 7.81 (m, 1H), 7.52 - 7.53 (m, 1H), 7.20 - 7.28 (m, 3H), 6.44 - 6.45 (m, 1H), 6.41 - 6.43 (m, 1H), 4.21 - 4.22 (m, 3H), 3.21 - 3.24 (m, 1H), 3.09 - 3.11 (m, 1H), 2.85 - 2.88 (m, 1H), 2.56 - 2.59 (m ,1H).
315	MS (ESI) calcd for $C_{26}H_{20}F_2N_{10}$: 510.18 m/z, found, 511.10 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.24 - 8.35 (m, 2H), 8.13 - 8.20 (m, 1H), 7.97 - 8.09 (m, 2H), 7.66 – 7.97 (m, 2H), 7.47 - 7.56 (m, 1H), 7.15 - 7.39 (m, 3H), 6.87 - 6.98 (m, 1H), 6.42 - 6.51 (m, 1H), 6.30 - 6.39 (m, 1H), 3.19 - 3.31 (m, 1H), 3.00 - 3.13 (m, 1H), 2.76 - 2.88 (m, 1H), 2.57 - 2.67 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -94.20. (formic acid salt).

[00619] **Example 83: (S)-3-(3-(1-(4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 248)**



Compound 248

[00620] Synthetic Route:



Compound 2 **Compound 248**

[00621] Step 1: Synthesis of (S)-3-(3-(1-(4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 248)

[00622] A mixture of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (80 mg, 0.196 mmol, 1 equiv), AcOH (0.1 mL) and (E)-N'-((E)-(dimethylamino)methylene)-N,N-dimethylformohydrazonamide (111 mg, 0.784 mmol, 4 equiv) in ACN (2 mL) was stirred for 2 h at 120°C. The resulting mixture was diluted with water (20 mL). The mixture was extracted with ethyl acetate (3 x 50 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC on a XBridge Prep Shield RP OBD C_{18} Column using a gradient of acetonitrile in water (+ 10 mmol/L NH_4HCO_3) to afford (S)-3-(3-(1-(4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 248**) (31.8 mg, 40% yield) as a white solid.: MS (ESI) calcd. for $C_{25}H_{20}N_{10}$, 460.19 m/z, found 461.10 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.63 (s, 2H), 8.39 - 8.47 (m, 2H), 8.02 - 8.10 (m, 1H), 7.96 - 8.01 (m, 1H), 7.78 - 7.86 (m, 1H), 7.51 - 7.59 (m, 1H), 7.23 - 7.39 (m, 3H), 6.57 - 6.63 (m, 1H), 6.43 - 6.54 (m, 1H), 5.97 - 6.09 (m, 1H), 3.20- 3.36 (m, 1H), 2.98 - 3.13 (m, 1H), 2.77 - 2.89 (m, 1H), 2.31- 2.44 (m, 1H).

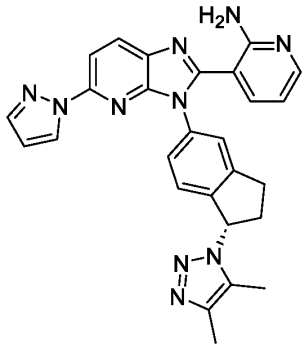
[00623] The following compounds were prepared analogously to the synthetic preparation of Compound 248.

[00624] Table 14B. Characterization data of compounds prepared analogously to compound 248.

Cpd ID	Characterization Data
528	Observed mass (ESI): 459.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.62 - 8.71 (m, 2H), 8.08 - 8.18 (m, 1H), 7.90 - 8.01 (m, 1H), 7.58 - 7.62 (m, 1H), 7.35 - 7.49 (m, 1H), 7.15 - 7.25 (m, 3H), 6.89 - 7.08 (m, 2H), 6.32 - 6.45 (m, 1H), 5.92 - 6.10 (m, 1H), 3.15 - 3.28 (m, 1H), 2.89 - 3.19 (m, 1H), 2.69 - 2.82 (m, 1H), 2.25 - 2.49 (m, 1H), 1.49 - 1.62 (m, 1H), 0.85 - 0.95 (m, 2H), 0.69 - 0.79 (m, 2H).

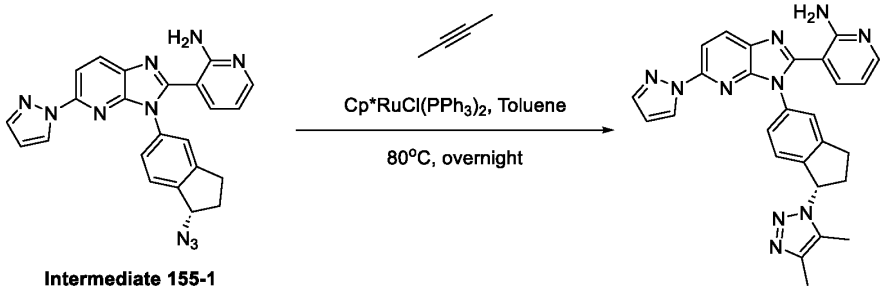
Cpd ID	Characterization Data
529	Observed mass (ESI): 463.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.46 - 8.78 (m, 2H), 8.25 - 8.45 (m, 2H), 7.91 - 8.14 (m, 1H), 7.77 - 7.90 (m, 1H), 7.62 - 7.76 (m, 1H), 7.51 - 7.61 (m, 1H), 7.43 - 7.61 (m, 1H), 7.29 - 7.42 (m, 1H), 7.03 - 7.28 (m, 3H), 6.42 - 6.71 (m, 1H), 5.83 - 6.14 (m, 1H), 3.12 - 3.27 (m, 1H), 2.89 - 3.04 (m, 1H), 2.64 - 2.82 (m, 1H), 2.24 - 2.44 (m, 1H).

[00625] Example 84: (S)-3-(3-(1-(4,5-dimethyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 249)



Compound 249

[00626] Synthetic Route:



Intermediate 155-1

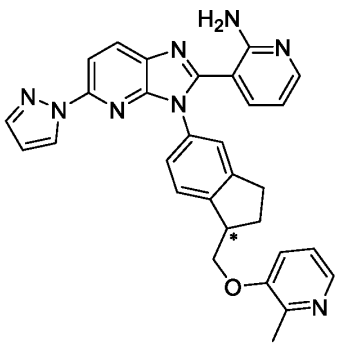
Compound 249

[00627] Step 1: Synthesis of (S)-3-(3-(1-(4,5-dimethyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 249)

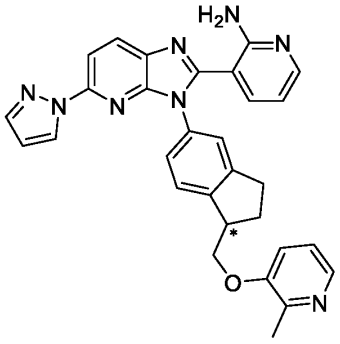
[00628] To a solution of 3-{3-[(1S)-1-azido-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 155-1**) (80 mg, 0.18 mmol, 1 equiv) and Cp*RuCl(PPh3)2 (220 mg, 0.276 mmol, 1.5 equiv) in toluene (5 mL) was added but-2-yne (99.5 mg, 1.84 mmol, 10 equiv) under N_2 atmosphere. The resulting mixture was stirred overnight at 80°C. The reaction was quenched with H_2O (50 mL) at room temperature. The

resulting mixture was extracted with ethyl acetate (100 mL x 3) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-(4,5-dimethyl-1H-1,2,3-triazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (4.2 mg, 5 % yield) as a white solid.: MS (ESI) calcd. for $C_{27}H_{24}N_{10}$, 488.21 m/z, found 489.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.39 - 8.51 (m, 2H), 7.95 - 8.11 (m, 2H), 7.79 - 7.91 (m, 2H), 7.52 - 7.63 (m, 1H), 7.31 - 7.42 (m, 1H), 7.16 - 7.21 (m, 1H), 6.77 - 6.91 (m, 1H), 6.55 - 6.62 (m, 1H), 6.13 - 6.25 (m, 1H), 3.20 - 3.41 (m, 1H), 2.99 - 3.19 (m, 1H), 2.71 - 2.91 (m, 1H), 2.35 - 2.51 (m, 1H), 2.15 - 2.29 (m, 6H). (TFA salt)

Example 85: (*)-3-(3-(1-(((2-methylpyridin-3-yl)oxy)methyl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 252) and **(*)-3-(3-(1-(((2-methylpyridin-3-yl)oxy)methyl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 253)**

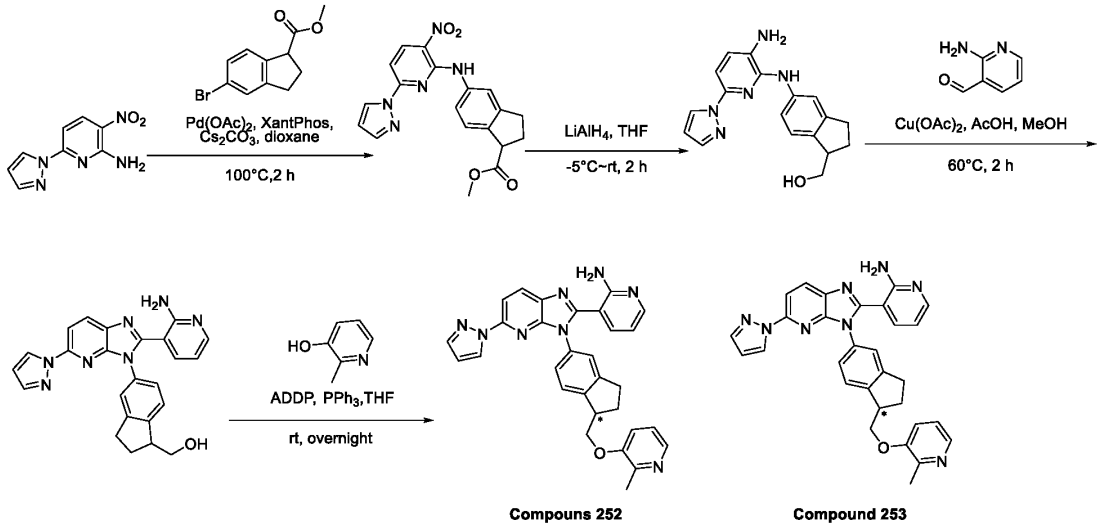


Compouns 252



Compound 253

[00629] Synthetic Route:



Step 1: Synthesis of methyl 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-indene-1-carboxylate

[00631] To a solution of methyl 5-bromo-2,3-dihydro-1H-indene-1-carboxylate (2.86 g, 11.2 mmol, 1 equiv) in dioxane (50 mL) was added Cs_2CO_3 (10.96 g, 33.63 mmol, 3 equiv), $Pd(OAc)_2$ (251.7 mg, 1.121 mmol, 0.1 equiv), XantPhos (648.7 mg, 1.121 mmol, 0.1 equiv) and 3-nitro-6-(pyrazol-1-yl)pyridin-2-amine (2.53 g, 12.3 mmol, 1.1 equiv) and the resulting mixture was stirred at 100°C for 2 h under nitrogen atmosphere. The resulting mixture was quenched with HCl (1M, 100 mL) and extracted with DCM (3 x 200 mL). The organic layers were combined, dried over Na_2SO_4 and concentrated under vacuum to afford methyl 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-indene-1-carboxylate (2 g, 47%yield).: MS (ESI) calcd. for $C_{19}H_{17}N_5O_4$: 379.13 m/z, found, 380.15 $[M+H]^+$.

[00632] **Step 2: Synthesis of (5-((3-amino-6-(1*H*-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1*H*-inden-1-yl)methanol**

[00633] To a solution of methyl 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-indene-1-carboxylate (2.0 g, 5.3 mmol, 1 equiv) in THF (50 mL) was added $LiAlH_4$ (1.00 g, 26.4 mmol, 5 equiv) in portions at 0°C. The resulting mixture was stirred at room temperature for 2 h. The resulting mixture was diluted with ethyl acetate (500 mL) and then poured into (1:1) ice / saturated NH_4Cl solution (500 mL). The resulting mixture was extracted with ethyl acetate (3 x 500 mL). The separated organic layers were combined, dried over sodium sulfate, filtered and concentrated under vacuum. The crude product was purified by silica gel flash chromatography (0-10% MeOH/DCM) to afford (5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)methanol (1.4 g, 74% yield) as a purple solid.: MS (ESI) calcd. for $C_{18}H_{19}N_5O$, 321.16 m/z, found, 322.10 $[M+H]^+$.

[00634] Step 3: Synthesis of (5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)methanol

[00635] To a solution of (5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)methanol (1.4 g, 4.36 mmol, 1 equiv) in AcOH (32 mL) and MeOH (8 mL) was added 2-aminopyridine-3-carbaldehyde (0.80 g, 6.53 mmol, 1.5 equiv) and $Cu(OAc)_2$ (0.79 g, 4.36 mmol, 1 equiv). The resulting mixture was stirred at 60°C for 2 h. The reaction was then quenched by addition of water (200 mL). The resulting mixture was extracted with ethyl acetate (3 x 200 mL). The organic layers were combined, dried over sodium sulfate, filtered and concentrated under a vacuum. The residue obtained was purified by silica gel chromatography (0-100% ethyl acetate in petroleum ether) to afford (5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)methanol (380 mg, 19% yield) as a purple solid.: MS (ESI) calcd. for $C_{24}H_{21}N_7O$, 423.18 m/z, found, 424.15 $[M+H]^+$.

[00636] Step 4: Synthesis of 3-(3-(1-(((2-methylpyridin-3-yl)oxy)methyl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compounds 252 and 253)

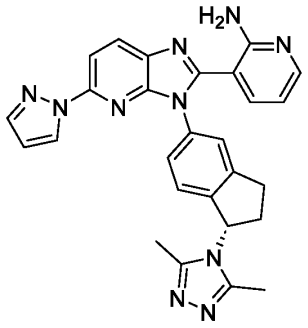
[00637] A solution of (5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)methanol (100 mg, 0.223 mmol, 1 equiv) in THF (5 mL) was treated with 2-methylpyridin-3-ol (51.5 mg, 0.472 mmol, 2 equiv) and PPh_3 (186 mg, 0.708 mmol, 3 equiv) and the resulting mixture was stirred for 5 min at room temperature under nitrogen atmosphere followed by the addition of a solution of 1,1-(azodicarbonyl)dipiperidine (177 mg, 0.708 mmol, 3 equiv) in THF dropwise at -5°C. The resulting mixture was stirred overnight at room temperature. The residue was quenched with H_2O (100 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by chiral Prep-HPLC on a CHIRALPAK ID-3 column using a mixture of [Hexanes/DCM 3:1 + 0.1% diethylamine] and ethanol to afford (*)-3-(3-(1-(((2-methylpyridin-3-yl)oxy)methyl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 252**) (24 mg, 20% yield) as an off-white solid (eluting first) and (*)-3-(3-(1-(((2-methylpyridin-3-yl)oxy)methyl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 253**) (25.0 mg, 21% yield) as an off-white solid (eluting second). *Denotes a stereocenter with undetermined absolute stereochemistry of a single diastereomer.

[00638] Compound 252: MS (ESI) calcd. for $C_{30}H_{26}N_8O$, 514.22 m/z, found, 515.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.25 - 8.43 (m, 2H), 7.88 - 8.06 (m, 3H), 7.73 - 7.85 (m, 1H), 7.45 - 7.59 (m, 1H), 7.31 - 7.44 (m, 2H), 7.11 - 7.30 (m, 3H), 6.46 - 6.59 (m,

1H), 6.31 - 6.45 (m, 1H), 4.24 - 4.37 (m, 1H), 4.11 - 4.23 (m, 1H), 3.59 - 3.79 (m, 1H), 2.79 - 3.15 (m, 2H), 2.35 - 2.44 (m, 1H), 2.21 - 2.33 (m, 3H), 1.91 - 2.16 (m, 1H).

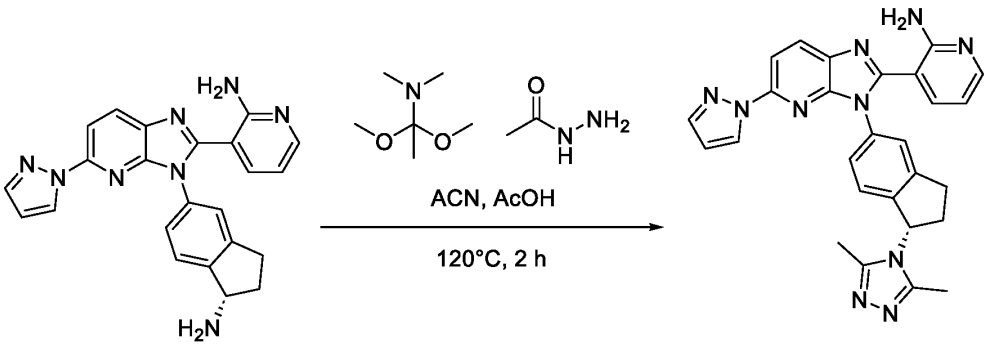
[00639] **Compound 253**:: MS (ESI) calcd. for $C_{30}H_{26}N_8O$, 514.22 m/z, found, 515.15 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.24 - 8.44 (m, 2H), 7.89 - 8.08 (m, 3H), 7.75 - 7.87 (m, 1H), 7.34 - 7.62 (m, 3H), 7.17 - 7.31 (m, 3H), 6.51 - 6.62 (m, 1H), 6.35 - 6.45 (m, 1H), 4.11 - 4.44 (m, 2H), 3.63 - 3.82 (m, 1H), 2.78 - 3.18 (m, 2H), 2.35 - 2.47 (m, 1H), 2.22 - 2.34 (m, 3H), 1.92 - 2.17 (m, 1H).

[00640] **Example 86: (S)-3-(3-(1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 272)**



Compound 272

[00641] Synthetic Route:



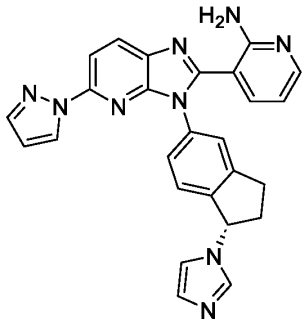
Compound 2 **Compound 272**

[00642] **Step 1: Synthesis of (S)-3-(3-(1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 272)**

[00643] A solution of (1,1-dimethoxyethyl)dimethylamine (48.9 mg, 0.367 mmol, 1.5 equiv) and acetohydrazide (27.2 mg, 0.367 mmol, 1.5 equiv) in ACN (1 mL) was stirred for 2 h at 60°C. 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-

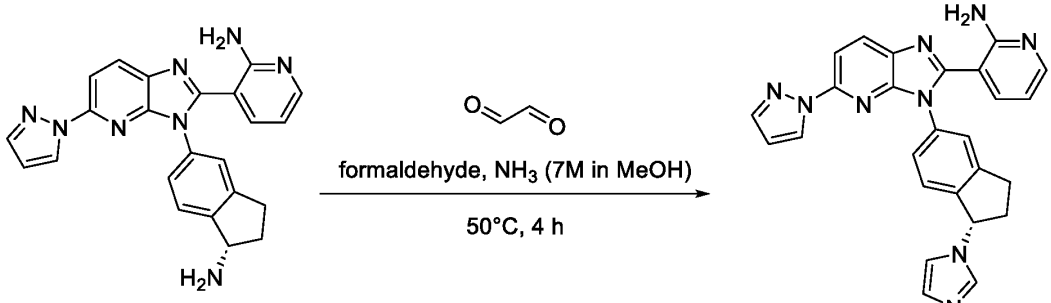
2-yl}pyridin-2-amine (Compound 2) (100 mg, 0.245 mmol, 1 equiv) was added and the mixture was stirred for 2 h at 120°C. The reaction mixture was purified by Prep-HPLC on a XSelect CSH F-Phenyl OBD Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-3-(3-(1-(3,5-dimethyl-4H-1,2,4-triazol-4-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (31 mg, 25% yield) as a white solid.: MS (ESI) calcd. for $C_{27}H_{24}N_{10}$, 488.22 m/z, found 489.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm); 8.42 - 8.52 (m, 1H), 8.37 - 8.41 (m, 1H), 8.01 - 8.11(m, 2H), 7.84 - 7.87 (m, 1H), 7.71 - 7.81 (m, 1H), 7.57 - 7.63 (m, 1H), 7.39 - 7.49 (m, 2H), 6.72 - 6.81 (m, 1H), 6.57 - 6.62 (m, 1H), 6.18 - 6.29 (m, 1H), 3.02 - 3.31 (m, 2H), 2.81 - 3.01 (m, 1H), 2.57 -2.58 (m, 1H), 2.19 - 2.49 (m, 6H). (TFA salt)

[00644] Example 87: (S)-3-(3-(1-(1H-imidazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 273)



Compound 273

[00645] Synthetic Route:



Compound 2 **Compound 273**

[00646] Step 1: Synthesis of (S)-3-(3-(1-(1H-imidazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine

[00647] To a stirred solution of glyoxal (42.6 mg, 0.735 mmol, 3 equiv) and formaldehyde (7.4 mg, 0.245 mmol, 1 equiv) were added 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Compound 2) (100 mg, 0.245 mmol, 1 equiv) and NH_3 in MeOH (2 mL, 7M) in portions. The resulting mixture was

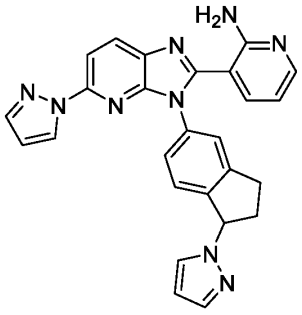
stirred for 4 h at 50°C. The resulting mixture was concentrated under reduced pressure. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 10 mmol/L NH_4HCO_3) to (S)-3-(3-(1-(1H-imidazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 273) (37.6 mg, 33% yield) as an off-white solid.: MS (ESI) calcd. for $C_{26}H_{21}N_9$, 459.19 m/z, found, 458.15 $[M-H]^-$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.25 (s, 1H), 8.42 - 8.46 (m, 2H), 8.03 - 8.09 (m, 2H), 7.84 - 7.85 (m, 1H), 7.64 - 7.72 (m, 4H), 7.40 - 7.42 (m, 2H), 6.78 - 6.81 (m, 1H), 6.58 - 6.62 (m, 1H), 6.18 - 6.21 (m, 1H), 3.32 - 3.40 (m, 1H), 2.99 - 3.12 (m, 1H), 2.83 - 3.00 (m, 1H), 2.45 - 2.61 (m, 1H). (TFA salt)

[00648] The following compounds were prepared analogously to the synthetic preparation in Example 87 (Compound 273).

[00649] **Table 14C.** Characterization data of compounds prepared analogously to compound 273.

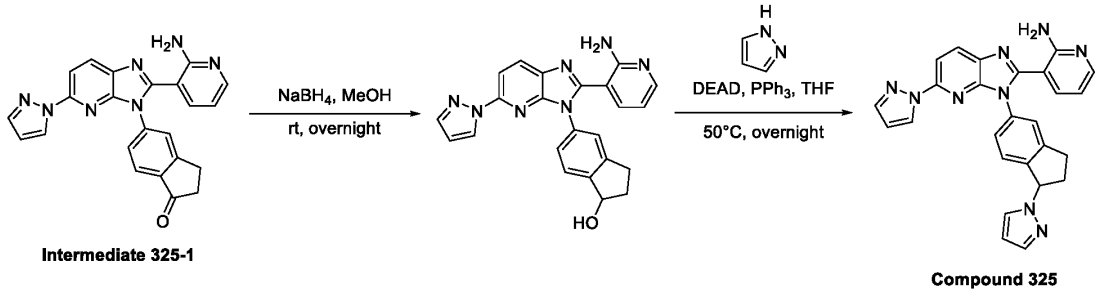
Cpd ID	Characterization Data
494	Observed mass (ESI): 512.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.60 - 8.72 (m, 2H), 8.40 - 8.50 (m, 2H), 8.00 - 8.15 (m, 2H), 7.80 - 7.90 (m, 2H), 7.55 - 7.70 (m, 3H), 7.45 - 7.52 (m, 1H), 6.70 - 6.80 (m, 1H), 6.57 - 6.63 (m, 1H), 5.25 - 5.35 (m, 1H), 4.70 - 4.96 (m, 4H), 3.20 - 3.35 (m, 1H), 2.90 - 3.10 (m, 1H), 2.60 - 2.65 (m, 1H), 2.40 - 2.50 (m, 1H). (TFA salt)

[00650] **Example 88: 3-(3-(1-(1H-pyrazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (compound 325)**



Compound 325

[00651] Synthetic Route:



Intermediate 325-1

Compound 325

[00652] Step 1: 5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-ol

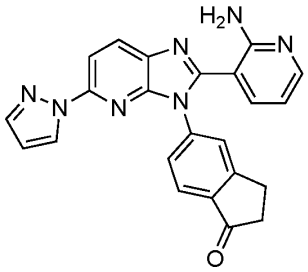
[00653] A solution of 5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-one (**Intermediate 325-1**) (500.0 mg, 1.225 mmol, 1 equiv) in MeOH (25 mL) was treated with $NaBH_4$ (139.3 mg, 3.675 mmol, 3 equiv) at 0°C. The resulting mixture was stirred overnight at rt. The reaction was quenched with water (30 mL) at rt. The resulting mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with MeOH/DCM (0~10%) to afford 5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-ol (300 mg, 60% yield) as a brown solid.: MS (ESI) calcd. for $C_{23}H_{19}N_7O$, 409.17 m/z, found 410.25 $[M+H]^+$.

[00654] **Step 2: 3-(3-(1-(1H-pyrazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 325)**

[00655] To a stirred solution of 5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-ol (100.0 mg, 0.244 mmol, 1.00 equiv), pyrazole (50.0 mg, 0.734 mmol, 3.00 equiv) and PPh_3 (192.8 mg, 0.734 mmol, 3.00 equiv) in THF (5.0 mL) was added DEAD (128.0 mg, 0.734 mmol, 3.00 equiv) in portions at 0°C under nitrogen atmosphere. The resulting mixture was stirred overnight at 50°C under nitrogen atmosphere. The reaction was quenched with water (30 mL) at rt. The resulting mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC on a XSelect CSH OBD Column using a gradient of acetonitrile in water (+ 0.1% formic acid) to afford 3-(3-(1-(1H-pyrazol-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 325**, formic acid salt) (7.4 mg, 6% yield) as a white solid.: MS (ESI) calcd for $C_{26}H_{21}N_9$: 459.19 m/z, found, 460.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.27 - 8.45 (m, 2H), 7.90 - 8.06 (m, 2H), 7.68 - 7.85 (m, 2H), 7.43 - 7.57 (m, 2H), 7.18 - 7.31 (m, 2H), 7.06 - 7.18 (m, 1H), 6.83 -

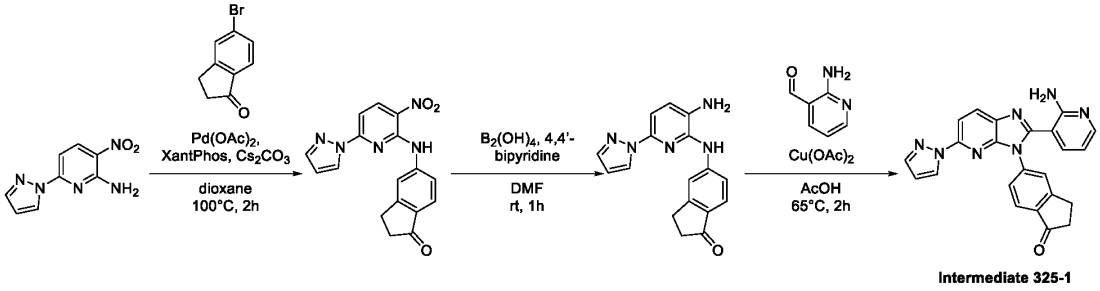
6.97 (m, 2H), 6.48 - 6.59 (m, 1H), 6.36 - 6.47 (m, 1H), 6.26 - 6.36 (m, 1H), 5.93 - 6.08 (m, 1H), 3.09 - 3.25 (m, 1H), 2.91 - 3.06 (m, 1H), 2.63 - 2.77 (m, 1H), 2.52 - 2.59 (m, 1H).

Intermediate 325-1: 5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-one



Intermediate 325-1

[00656] Synthetic Route:



[00657] **Step 1: Synthesis of 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one**

[00658] To a solution of 3-nitro-6-(pyrazol-1-yl)pyridin-2-amine (15.0 g, 73.1 mmol, 1 equiv) and 5-bromo-2,3-dihydroinden-1-one (15.43 g, 73.11 mmol, 1 equiv) in 1,4-dioxane (400 mL) were added $Pd(OAc)_2$ (1.64 g, 7.31 mmol, 0.1 equiv), XantPhos (4.23 g, 7.31 mmol, 0.1 equiv) and Cs_2CO_3 (71.46 g, 219.3 mmol, 3 equiv). The resulting mixture was maintained under nitrogen and stirred for 1 h at 100 °C. The mixture was allowed to cool to room temperature. Water was added and the precipitated solids were collected by filtration to afford 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one (37 g, 91%) as a black solid. MS (ESI) calcd. for $C_{17}H_{13}N_5O_3$: 335.10m/z, found: 336.00 $[M+H]^+$.

[00659] **Step 2: Synthesis of 5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one**

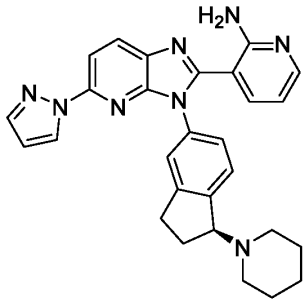
[00660] To a cooled (0°C) solution of 5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one (10.00 g, 29.82 mmol, 1 equiv) in DMF (100 mL) were added $B_2(OH)_4$ (8.02 g, 89.5 mmol, 3 equiv) and 4-(pyridin-4-yl)pyridine (232.9 mg, 1.491 mmol, 0.05 equiv). The resulting mixture was stirred for 1h at room temperature. Water was added and the precipitated solids were collected by filtration to afford 5-((3-amino-6-(1H-

pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one (8.5 g, 50%) as a black solid. MS (ESI) calcd. for $C_{17}H_{15}N_5O$: 305.13m/z, found: 306.15 $[M+H]^+$.

[00661] Step 3: Synthesis of 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydroinden-1-one (Intermediate 77-1)

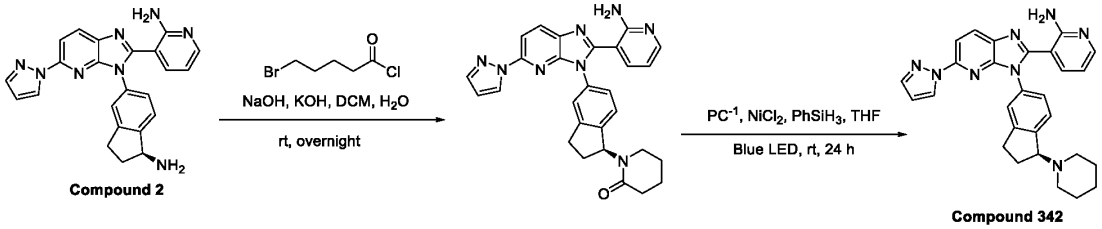
[00662] To a solution of 5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-one (8.5 g, 28 mmol, 1 equiv) in AcOH (400 mL) were added 2-aminopyridine-3-carbaldehyde (4.05 g, 33.2 mmol, 1.2 equiv) and $Cu(OAc)_2$ (1.00 g, 5.53 mmol, 0.2 equiv).The resulting mixture was stirred for 12 h at 65°C. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with MeOH/DCM (0~10%) to afford 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydroinden-1-one (Intermediate 325-1) (2.5 g, 16%) as a black solid. MS (ESI) calcd. for $C_{23}H_{17}N_7O$: 407.15m/z, found: 408.15 $[M+H]^+$.

[00663] Example 89: (S)-3-(3-(1-(piperidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 342)



Compound 342

[00664] Synthetic Route:



Compound 2 **Compound 342**

[00665] Step 1: Synthesis of (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)piperidin-2-one

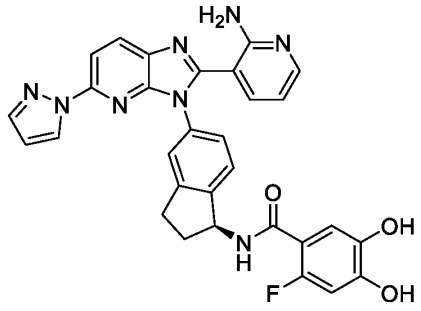
[00666] To a solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 2**) (200 mg, 0.490 mmol, 1 equiv) in DCM (50 mL) and H_2O (2 mL) was added a solution of NaOH (19.58 mg, 0.490 mmol, 1 equiv) in H_2O, TBAB (189.41 mg, 0.588 mmol, 1.2 equiv) and 5-bromopentanoyl

chloride (112.32 mg, 0.564 mmol, 1.15 equiv) in DCM (50 mL) dropwise at 0°C. The mixture was stirred for 1 h at 0~5°C. The reaction mixture was allowed to warm to room temperature and a solution of KOH (329.65 mg, 5.880 mmol, 12 equiv) in H_2O (0.01M) was added dropwise following by stirring overnight. The reaction was quenched with H_2O (100 mL). The resulting mixture was extracted with DCM (3 x 100 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)piperidin-2-one (trifluoroacetic acid salt) (28.4 mg, 11.54% yield) as an off-white solid.: MS (ESI) calcd. for $C_{28}H_{26}N_8O$, 490.22 m/z, found, 491.20 $[M+H]^+$.

[00667] Step 2: Synthesis of (S)-3-(3-(1-(piperidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Compound 342)

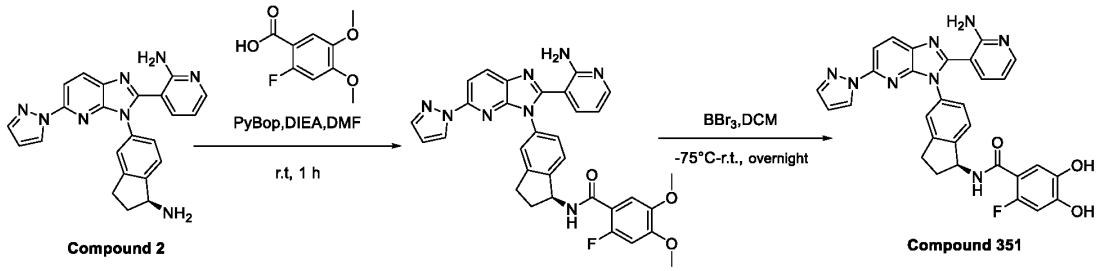
[00668] To a mixture of (S)-1-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)piperidin-2-one (100 mg, 0.204 mmol, 1 equiv) and $NiCl_2$ (7.92 mg, 0.061 mmol, 0.3 equiv) in THF (5 mL) was added phenylsilane (1.10 g, 10.200 mmol, 50 equiv) and 4,4'-di-tert-butyl-2,2'-bipyridine; bis[2-(pyridin-2-yl)phenyl]iridiumylium; hexafluorophosphate (55.89 mg, 0.061 mmol, 0.3 equiv) under nitrogen atmosphere. The resulting mixture was stirred overnight at room temperature under N_2 atmosphere and blue LED light (425 nm). The reaction was quenched with H_2O (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-3-(3-(1-(piperidin-1-yl)-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Compound 342**) (15.2 mg, 15.50% yield) as an off-white solid.: MS (ESI) calcd. for $C_{28}H_{28}N_8$: 476.20 m/z, found, 477.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.27 - 8.43 (m, 2H), 7.89 - 8.09 (m, 2H), 7.75 - 7.84 (m, 1H), 7.38 - 7.49 (m, 1H), 7.19 - 7.37 (m, 2H), 7.08 - 7.18 (m, 1H), 6.48 - 6.59 (m, 1H), 6.29 - 6.43 (m, 1H), 4.26 - 4.43 (m, 1H), 2.72 - 3.01 (m, 2H), 2.43 - 2.50 (m, 2H), 2.27 - 2.49 (m, 2H), 1.97 - 2.19 (m, 2H), 1.29 - 1.78 (m, 6H).

[00669] Example 90: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dihydroxybenzamide (Compound 351)



Compound 351

[00670] Synthetic Route:



[00671] **Step 1: Synthesis of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dimethoxybenzamide**

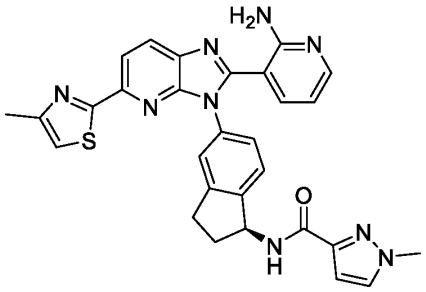
[00672] To a solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (150 mg, 0.367 mmol, 1 equiv) in DMF (3 mL) was added DIEA (142.39 mg, 1.101 mmol, 3 equiv), PyBOP (191.10mg, 0.367 mmol, 1 equiv) and 2-fluoro-4,5-dimethoxybenzoic acid (73.51 mg, 0.367 mmol, 1 equiv). The resulting mixture was stirred at room temperature for 1 h. The mixture was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA) to afford N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dimethoxybenzamide (163 mg, 75.3%) as a yellow solid.: MS (ESI) calcd. for $C_{32}H_{27}FN_8O_3$:590.22. found,591.25 $[M+H]^+$.

[00673] **Step 2: Synthesis of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dihydroxybenzamide (Compound 351)**

[00674] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dimethoxybenzamide (163 mg, 0.276 mmol, 1 equiv) in DCM (10 mL) under nitrogen atmosphere was added BBr_3 (345.69 mg, 1.380 mmol, 5 equiv) at -78°C . The mixture was stirred at r.t. overnight. The solvent was removed by distillation under vacuum. The residue was purified by reverse-phase flash chromatography on

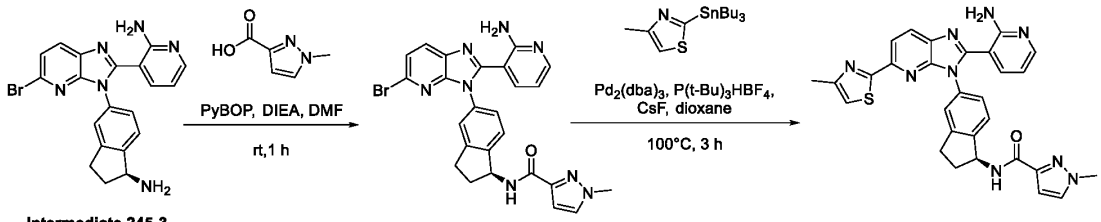
C18 silica gel using a gradient of acetonitrile in water (+ 0.05% TFA). The product was further purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.1% TFA) to afford N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-2-fluoro-4,5-dihydroxybenzamide (**Compound 351**) (7.1 mg, 4.50%) as a white solid.: MS (ESI) calcd. for $C_{30}H_{23}FN_8O_3$: 562.19. found, 585.25 $[M+Na]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ(ppm) 8.29 - 8.33 (m. 2H), 7.91 - 7.96 (m, 2H), 7.76 - 7.89 (m, 1H), 7.23 - 7.32 (m, 4H), 7.04 - 7.06 (m, 1H), 6.52 - 6.62 (m, 1H), 6.45 - 6.48 (m, 2H), 5.49 - 5.40 (m, 1H), 2.84 - 2.96 (m, 2H), 2.33 - 2.44 (m, 1H), 1.92 - 1.99 (m, 1H), 1.02 - 1.99 (m, 1H). F NMR δ (ppm) -122.24.

[00675] Example 91: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(4-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide (Compound 374)



Compound 374

[00676] Synthetic Route:



Intermediate 245-3 **Compound 374**

[00677] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide

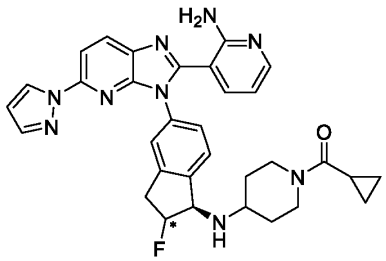
[00678] A solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-bromoimidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Intermediate 245-3) (600 mg, 1.424 mmol, 1 equiv), 1-methylpyrazole-3-carboxylic acid (179.61 mg, 1.424 mmol, 1 equiv), PyBOP (741.13 mg, 1.424 mmol, 1 equiv) and DIEA (552.20 mg, 4.272 mmol, 3 equiv) in DMF (5 mL) was stirred for 1h at room temperature. The reaction mixture was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium

bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide (600 mg, 71.62% yield) as a white solid.: MS (ESI) calcd. for $C_{25}H_{21}BrN_8O$, 528.10 m/z, found, 529.20 $[M+H]^+$.

[00679] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(4-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide (Compound 374)

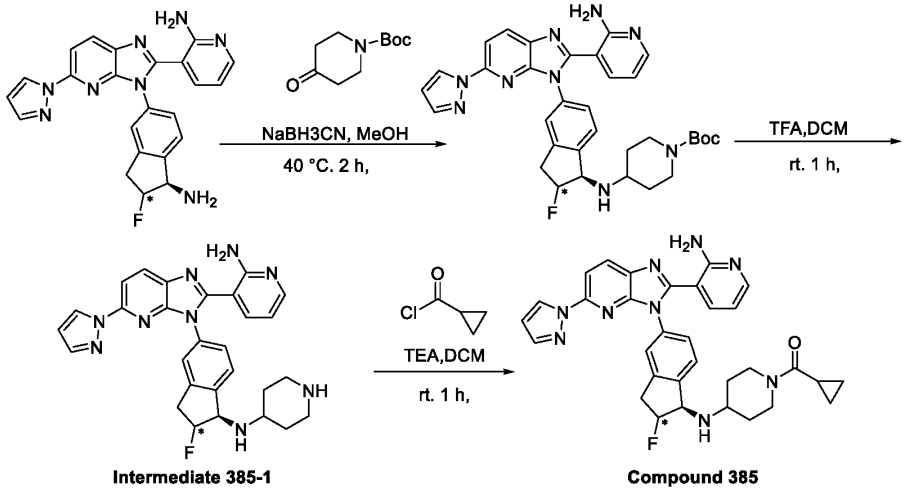
[00680] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-1-methylpyrazole-3-carboxamide (200 mg, 0.378 mmol, 1 equiv) in dioxane (3 mL) was added 4-methyl-2-(tributylstannyl)-1,3-thiazole (733.28 mg, 1.890 mmol, 5 equiv), $Pd_2(dba)_3$ (34.59 mg, 0.038 mmol, 0.1 equiv), $P(t\text{-}Bu)_3HBF_4$ (21.92 mg, 0.076 mmol, 0.2 equiv), and CsF (172.16 mg, 1.134 mmol, 3 equiv). The resulting mixture was maintained under nitrogen and stirred at 100 °C for 3 h. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(4-methylthiazol-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-1-methyl-1H-pyrazole-3-carboxamide (Compound 374) (19.6 mg, 9.27% yield) as a yellow solid.: MS (ESI) calcd. for $C_{29}H_{25}N_9OS$, 547.19 m/z, found, 548.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.21 - 8.35 (m, 1H), 8.10 - 8.20 (m, 1H), 7.90 - 8.08 (m, 1H), 7.68 - 7.85 (m, 1H), 7.10 - 7.51 (m, 5H), 6.62 - 6.81 (m, 1H), 6.35 - 6.55 (m, 1H), 5.43 - 5.70 (m, 1H), 3.78 - 4.00 (m, 3H), 2.73 - 3.15 (m, 2H), 2.35 - 2.50 (m, 4H), 2.00 - 2.30 (m, 1H).

[00681] Example 92: 3-{3-[(1R,2*)-1-[(1-cyclopropanecarbonylpiperidin-4-yl)amino]-2-fluoro-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Compound 385)



Compound 385

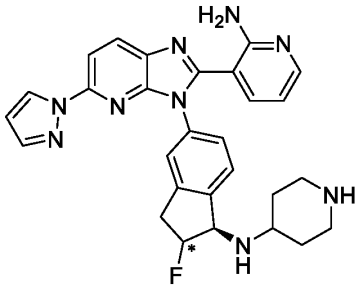
[00682] Synthetic Route:



[00683] Step 1: Synthesis of 3-{3-[(1R,2*)-1-[(1-cyclopropanecarbonylpiperidin-4-yl)amino]-2-fluoro-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Compound 385)

[00684] To a solution of 3-{3-[(1R,2R)-2-fluoro-1-(piperidin-4-ylamino)-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 385-1**) (50 mg, 0.098 mmol, 1 equiv) in DCM (4 mL) was added TEA (49.64 mg, 0.490 mmol, 5 equiv) and cyclopropanecarbonyl chloride (11.28 mg, 0.108 mmol, 1.1 equiv) and the mixture was stirred at rt for 1h. The solvent was removed under vacuum and the resulting crude was purified by Prep-HPLC on a XSelect CSH OBD Column using a gradient of acetonitrile in water (+ 0.1% FA) to 3-{3-[(1R,2*)-1-[(1-cyclopropanecarbonylpiperidin-4-yl)amino]-2-fluoro-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo [4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 385**) (14.9 mg, 25.70%) as white solid.: MS (ESI) calcd. for $C_{32}H_{32}FN_9O$, 577.27m/z, found 578.35 [M+H]+.^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.14 - 8.52 (m, 2H), 7.89 - 8.14 (m, 2H), 7.74 - 7.89 (m, 1H), 7.52 - 7.74 (m, 1H), 7.29 - 7.52 (m, 2H), 6.38 - 6.74 (m, 2H), 5.18 - 5.58 (m, 1H), 4.42 - 4.54 (m, 1H), 4.18 - 4.42 (m, 2H),4.11 - 4.18 (m, 1H),3.45 - 3.62 (m, 1H), 3.12 - 3.31 (m, 1H), 2.95 - 3.12 (m, 2H), 2.68 - 2.85 (m, 1H), 1.74 - 2.24 (m, 3H), 1.08 - 1.48 (m, 2H), 0.68 - 0.94 (m, 4H). (formic acid salt) *Denotes a stereocenter with undetermined absolute stereochemistry of a single diastereomer.

[00685] Intermediate 385-1: 3-(3-((1*R*,2*)-2-fluoro-1-(piperidin-4-ylamino)-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine

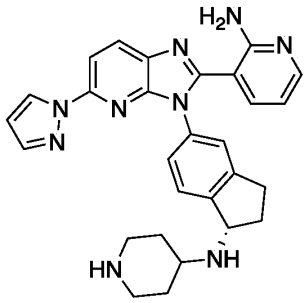


Intermediate 385-1

[00686] **Intermediate 385-1** was prepared in a manner analogous to **Intermediate 275-1** using **Intermediate 147-2** in place of **Example 2**. *Denotes a stereocenter with undetermined absolute stereochemistry of a single diastereomer. MS (ESI) calcd. for $C_{28}H_{28}FN_9$: 509.25 m/z, found: 510.15 $[M+H]^+$.

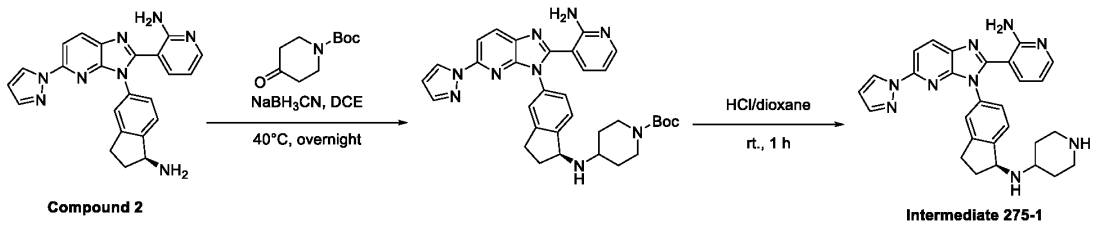
25 (m, 1H),3.23 - 3.09 (m, 2H), 2.92 – 2.80 (m, 2H), 2.43 -2.02 (m, 3H), 1.46 (m, 2H).

[00687] **Intermediate 275-1: (*S*)-3-(3-(1-(piperidin-4-ylamino)-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine**



Intermediate 275-1

[00688] Synthetic Route:



[00689] **Step 1: Synthesis of tert-butyl 4-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}piperidine-1-carboxylate**

[00690] To a solution of 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Compound 2**) (410 mg, 1.00 mmol) in DCE

(10 mL) was added *tert*-butyl 4-oxopiperidine-1-carboxylate (200 mg, 1.00 mmol). The resulting mixture was stirred at 40°C for 1h. To the above mixture was added $NaBH_3CN$ (252 mg, 4.02 mmol). The resulting mixture was stirred overnight at 40 °C. The mixture was filtered and the filter cake was washed with acetonitrile (3 x 5 mL). The filtrate was concentrated under reduced pressure. The resulting mixture was purified by reverse-phase flash column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl 4-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}piperidine-1-carboxylate (260 mg, 44% yield) as a yellow solid. MS (ESI) calcd. for $C_{33}H_{37}N_9O_2$: 591.31 m/z, found: 592.40 $[M+H]^+$.

[00691] Step 2: Synthesis of 3-{3-[(1S)-1-(piperidin-4-ylamino)-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Intermediate 275-1)

[00692] A solution of tert-butyl 4-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}piperidine-1-carboxylate (260 mg, 0.439 mmol) in 4N HCl in 1,4-dioxane (10 mL) was stirred at room temperature for 1h. The solvent was removed by distillation under vacuum to afford 3-{3-[(1S)-1-(piperidin-4-ylamino)-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine HCl (**Intermediate 275-1**) (220 mg) as a yellow solid, which was used directly in subsequent steps without further purification. MS (ESI) calcd. for $C_{28}H_{29}N_9$: 491.25 m/z, found: 492.25 $[M+H]^+$.

[00693] The following compounds were prepared analogous to the synthetic preparation in Compound 275-1's Buchwald intermediate.

[00694] Table 15A. Characterization data of compounds prepared analogously to Compound 275-1's Buchwald intermediate.

Cpd ID	Characterization Data
593	Observed mass (ESI): 600.15 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.34 - 8.37 (m, 2H), 7.99 - 8.01 (m, 2H), 7.88 (s, 1H), 7.49 - 7.80 (m, 1H), 7.47 (s, 1H), 7.22 - 7.46 (m, 2H), 6.88 - 6.94 (m, 3H), 6.54 (s, 1H), 6.42 - 6.44 (m, 1H), 4.37 (t, J = 6.9 Hz, 1H), 3.83 - 3.87 (m, 2H), 2.78 - 2.98 (m, 5H), 2.42 - 2.45 (m, 1H), 2.07 - 2.11 (m, 2H), 1.85 - 1.99 (m, 1H), 1.65 - 1.80 (m, 1H), 1.34 - 1.56 (m, 2H).

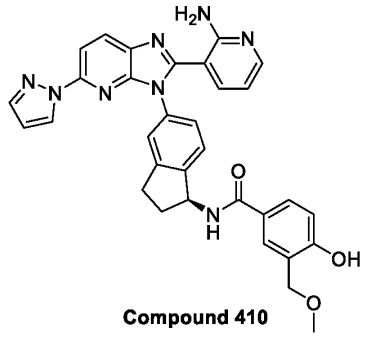
[00695] The following compounds were prepared analogous to the synthetic preparation in Example 92 (Compound 385).

[00696] Table 15B. Characterization data of compounds prepared analogously to compound 385.

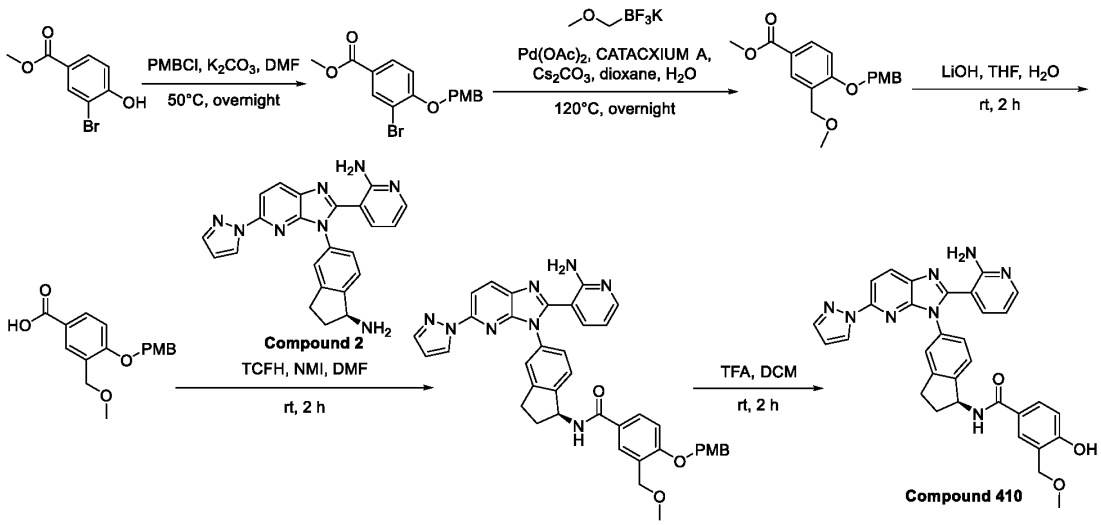
Cpd ID	Characterization Data

386	MS (ESI) calcd. for $C_{32}H_{32}FN_9O$,577.27m/z, found 577.90 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.18 - 8.52 (m, 2H), 7.89 - 8.18 (m, 2H), 7.72 - 7.89 (m, 1H), 7.47 - 7.72 (m, 1H), 7.12 - 7.42 (m, 3H), 6.36 - 6.74 (m, 2H), 5.34 - 5.69 (m, 1H), 4.42 - 4.62 (m, 1H), 4.18 - 4.36 (m, 2H),4.12 - 4.14 (m, 1H), 3.18 - 3.34 (m, 2H), 3.06 - 3.18 (m, 2H), 2.76 - 2.98 (m, 1H), 1.82 - 2.22 (m, 3H), 1.18 - 1.59 (m, 2H), 0.68 - 0.95 (m, 4H). (formic acid salt)
441	.: MS (ESI) calcd. for $C_{30}H_{29}N_9O$,531.25 m/z, found, 532.35 $[M+H]+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.35 - 8.37 (m, 2H), 8.00 - 8.01 (m, 1H), 7.95 - 7.97 (m, 1H), 7.81 - 7.82 (m, 1H), 7.50 - 7.53 (m, 1H), 7.34 - 7.35 (m, 1H), 7.23 - 7.27 (m, 2H), 6.55 - 6.56 (m, 1H), 6.47 - 6.49 (m, 1H), 4.39 - 4.41 (m, 1H), 4.20 - 4.21 (m, 1H), 3.86 - 3.99 (m, 2H), 3.77 - 3.80 (m, 1H), 3.50 - 3.63 (m, 1H), 2.94 - 3.00 (m, 1H), 2.79 - 2.81 (m, 1H), 2.28 - 2.41 (m, 1H), 1.53 - 1.54 (m, 1H), 1.51 - 1.52 (m, 1H), 0.70 - 0.74 (m, 4H).

[00697] Example 93: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-hydroxy-3-(methoxymethyl)benzamide (Compound 410)



[00698] Synthetic Route:



[00699] Step 1: Synthesis of methyl 3-bromo-4-((4-methoxybenzyl)oxy)benzoate

[00700] To a solution of methyl 3-bromo-4-hydroxybenzoate (1 g, 4.328 mmol, 1 equiv) and K_2CO_3 (0.90 g, 6.492 mmol, 1.5 equiv) in DMF (15 mL) was added PMBCl (1.01 g, 6.492 mmol, 1.5 equiv) at room temperature and the mixture was stirred at 50°C overnight. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting

mixture was extracted with ethyl acetate (3 x 150 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue obtained was purified by silica gel chromatography (0~20% ethyl acetate/petroleum ether) to afford methyl 3-bromo-4-[(4-methoxyphenyl)methoxy]benzoate (1.5 g, 90.79% yield) as a white solid. Structure confirmed by TLC (Rf = 0.3, PE:EA = 10:1) and NMR/MS of downstream derivatives.

[00701] Step 2: Synthesis of methyl 4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzoate

[00702] To a solution of methyl 3-bromo-4-[(4-methoxyphenyl)methoxy]benzoate (1 g, 2.847 mmol, 1 equiv) in dioxane (8 mL) and H_2O (2 mL) was added potassium trifluoro(methoxymethyl)borate (0.87 g, 5.694 mmol, 2 equiv), $Pd(OAc)_2$ (0.06 g, 0.285 mmol, 0.1 equiv), bis(adamantan-1-yl)(butyl)phosphane (0.20 g, 0.569 mmol, 0.2 equiv) and Cs_2CO_3 (2.78 g, 8.541 mmol, 3 equiv). The resulting mixture was maintained under nitrogen and stirred at 120°C overnight. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 150 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue obtained was purified by silica gel chromatography (0~20% ethyl acetate/petroleum ether) to afford methyl 4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzoate (400 mg, 41.30% yield) as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm); 7.86 - 7.92 (m, 2H), 7.38 - 7.41 (m, 2H), 7.19 - 7.22 (m, 1H), 6.94 - 6.97 (m, 2H), 5.14 (s, 2H), 4.43 (s, 2H), 3.81 - 3.89 (m, 6H), 3.31 - 3.34 (m, 3H).

[00703] Step 3: Synthesis of 3-(methoxymethyl)-4-[(4-methoxyphenyl)methoxy]benzoic acid

[00704] To a solution of methyl 4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzoate (600 mg, 1.897 mmol, 1 equiv) in THF (3 mL) was added LiOH (136.27 mg, 5.691 mmol, 3 equiv) in H_2O (3 mL). The resulting mixture was stirred at room temperature for 2 h. The resulting mixture was concentrated under reduced pressure to afford 3-(methoxymethyl)-4-[(4-methoxyphenyl)methoxy]benzoic acid (550 mg, crude) as a yellow solid.: MS (ESI) calcd. for $C_{17}H_{18}O_5$, 302.12 m/z, found, 301.10 $[M-H]^-$.

[00705] Step 4: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzamide

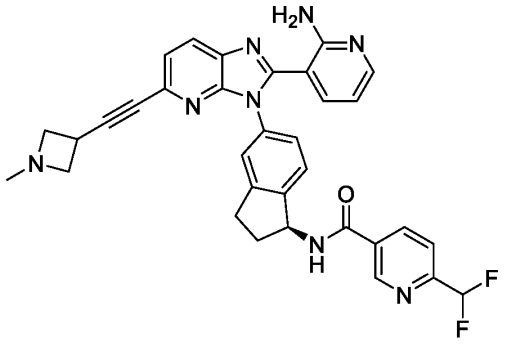
[00706] To a solution of 3-(methoxymethyl)-4-[(4-methoxyphenyl)methoxy]benzoic acid (300 mg, 0.992 mmol, 1 equiv) in DMF (5 mL) was added 3-{3-[(1S)-1-amino-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (Compound 2) (405.33 mg, 0.992 mmol, 1 equiv), TCFH (278.42 mg, 0.992 mmol, 1 equiv) and NMI (244.42 mg,

2.976 mmol, 3 equiv). The resulting mixture was maintained under nitrogen and stirred at room temperature for 2 h. the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 150 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzamide (450 mg, 58.91% yield) as a yellow solid.: MS (ESI) calcd. for $C_{40}H_{36}N_8O_4$, 692.29 m/z, found, 693.35 $[M+H]^+$.

[00707] Step 5: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-hydroxy-3-(methoxymethyl)benzamide (Compound 410)

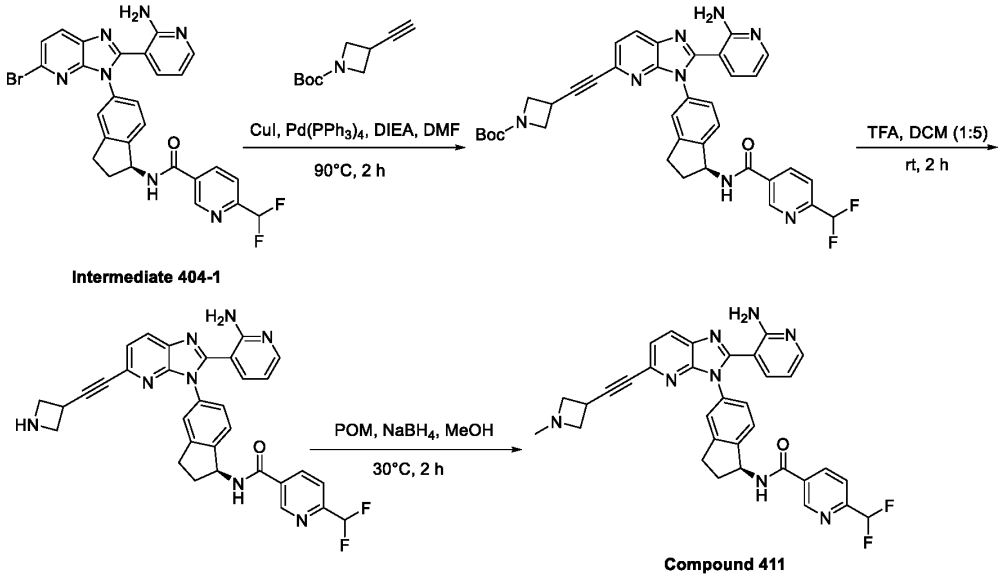
[00708] A solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-((4-methoxybenzyl)oxy)-3-(methoxymethyl)benzamide (250 mg, 0.361 mmol, 1 equiv) in TFA (4 mL) and DCM (12 mL) was stirred at room temperature for 2 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-4-hydroxy-3-(methoxymethyl)benzamide (Compound 410) (82.8 mg, 39.31% yield) as an off-white solid.: MS (ESI) calcd. for $C_{32}H_{28}N_8O_3$, 572.22 m/z, found, 573.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 10.06 - 10.20 (m, 1H), 8.57 - 8.80 (m, 1H), 8.20 - 8.46 (m, 2H), 7.98 - 8.08 (m, 1H), 7.90 - 7.97 (m, 1H), 7.85 - 7.89 (m, 1H), 7.81 - 7.84 (m, 1H), 7.66 - 7.80 (m, 1H), 7.18 - 7.45 (m, 4H), 6.72 - 7.01 (m, 3H), 6.48 - 6.60 (m, 1H), 6.35 - 6.47 (m, 1H), 5.48 - 5.72 (m, 1H), 4.40 (s, 2H), 3.32 - 3.36 (m, 3H), 2.80 - 3.15 (m, 2H), 2.41 - 2.50 (m, 1H), 1.98 - 2.23 (m, 1H).

[00709] Example 94: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-((1-methylazetidin-3-yl)ethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 411)



Compound 411

[00710] Synthetic Route:



[00711] **Step 1: Synthesis of tert-butyl (S)-3-((2-(2-aminopyridin-3-yl)-3-(1-(6-(difluoromethyl)nicotinamido)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-5-yl)ethynyl)azetidine-1-carboxylate**

[00712] To a stirred mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Intermediate 404-1) (150 mg, 0.260 mmol, 1 equiv), CuI (9.91 mg, 0.052 mmol, 0.20 equiv), $Pd(PPh_3)_4$ (60.14 mg, 0.052 mmol, 0.2 equiv) and DIEA (100.90 mg, 0.780 mmol, 3 equiv) in DMF (5 mL) was added tert-butyl 3-ethynylazetidine-1-carboxylate (70.75 mg, 0.390 mmol, 1.50 equiv) under N_2 atmosphere. The reaction mixture was stirred at 90°C for 2 h. After cooling to room temperature, the reaction was quenched with water (50 mL). The resulting mixture was extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl (S)-3-((2-(2-aminopyridin-3-yl)-3-(1-(6-

(difluoromethyl)nicotinamido)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-5-yl)ethynyl)azetidine-1-carboxylate (110 mg, 70.98% yield) as a yellow solid.: MS (ESI) calcd. for $C_{37}H_{34}F_2N_8O_3$: 676.27 m/z, found, 677.30 $[M+H]^+$.

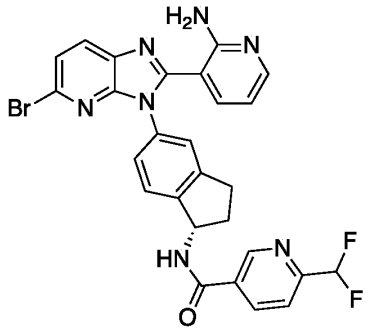
[00713] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(azetidin-3-ylethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide

[00714] A solution of tert-butyl (S)-3-((2-(2-aminopyridin-3-yl)-3-(1-(6-(difluoromethyl)nicotinamido)-2,3-dihydro-1H-inden-5-yl)-3H-imidazo[4,5-b]pyridin-5-yl)ethynyl)azetidine-1-carboxylate (100 mg, 0.147 mmol, 1 equiv) in TFA (1 mL) and DCM (5 mL) was stirred at room temperature for 2 h. The resulting mixture was concentrated to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(azetidin-3-ylethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (80 mg, crude) as a yellow solid.: MS (ESI) calcd. for $C_{32}H_{26}F_2N_8O$, 576.22 m/z, found, 577.35 $[M+H]^+$.

[00715] Step 3: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-((1-methylazetidin-3-yl)ethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 411)

[00716] A mixture of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(azetidin-3-ylethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (80 mg, 0.139 mmol, 1 equiv) and paraformaldehyde (37.49 mg, 0.417 mmol, 3 equiv) in MeOH (4 mL) was stirred for 2 h at 30°C. To the reaction mixture was added Sodium borohydride (15.75 mg, 0.417 mmol, 3.00 equiv). The reaction was quenched with water (50 mL). The resulting mixture was extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-((1-methylazetidin-3-yl)ethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide (Compound 411) (15.6 mg, 16.79% yield) as a white solid.: MS (ESI) calcd. for $C_{33}H_{28}F_2N_8O$, 590.24 m/z, found, 591.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.12 - 9.17 (m, 1H), 8.42 - 8.46 (m, 1H), 8.12 - 8.17 (m, 1H), 7.97 - 8.02 (m, 1H), 7.81 - 7.85 (m, 1H), 7.45 - 7.51 (m, 1H), 7.41 - 7.44 (m, 1H), 7.34 - 7.39 (m, 1H), 7.30 - 7.32 (m, 1H), 7.22 - 7.24 (m, 1H), 6.87 - 7.19 (m, 1H), 6.42 - 6.46 (m, 1H), 5.61 - 5.68 (m, 1H), 3.51 - 3.55 (m, 2H), 3.32 - 3.44 (m, 1H), 3.01 - 3.11 (m, 3H), 2.85 - 2.99 (m, 1H), 2.61 - 2.62 (m, 1H), 2.21 (s, 3H), 2.01 - 2.13 (m, 1H). ^{19}F NMR (282 MHz, DMSO-d_6) δ (ppm); -116.05.

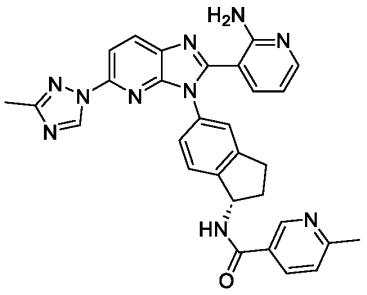
[00717] Intermediate 404-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-(difluoromethyl)nicotinamide



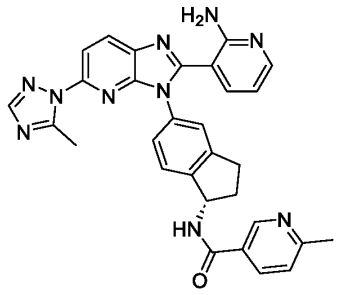
Intermediate 404-1

[00718] **Intermediate 404-1** was prepared in a manner analogous to **Example 3** using PyBOP in place of HATU, **Intermediate 245-3** in place of **Example 2** and 6-(difluoromethyl)nicotinic acid in place of 3,4-difluoro-5-anisic acid. MS data. MS (ESI) calcd. for $C_{27}H_{20}BrF_2N_7O$: 575.09 m/z, found: 576.30 $[M+H]^+$.

[00719] **Example 95: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 417) and (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 418)**

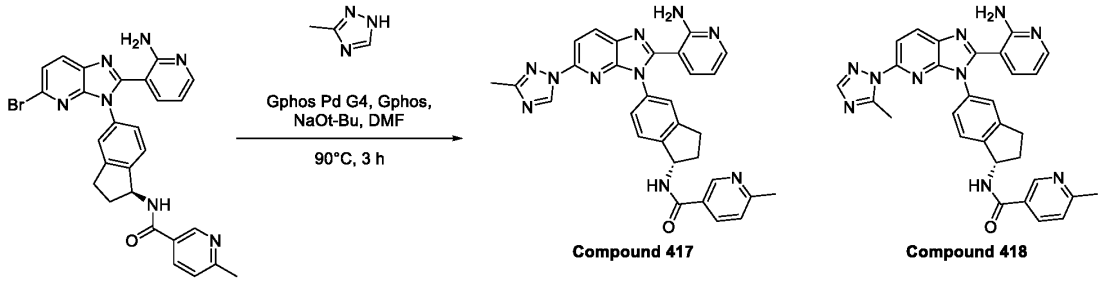


Compound 417



Compound 418

[00720] Synthetic Route:



Intermediate 265-1

Compound 417

Compound 418

[00721] **Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-**

methylnicotinamide (Compound 417) and (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 418)

[00722] To a stirred solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (**Intermediate 265-1**) (200 mg, 0.370 mmol, 1 equiv), 3-methyl-1H-1,2,4-triazole (61.50 mg, 0.740 mmol, 2 equiv), GPhos (39.73 mg, 0.074 mmol, 0.2 equiv) and GPhos Pd G4 (69.98 mg, 0.074 mmol, 0.2 equiv) in DMF (3 mL) was added sodium tert-butylate (1.5 M, 0.5 mL, 2 equiv) under N_2 atmosphere. The reaction mixture was stirred at 90°C for 3 h. After cooling to room temperature, the reaction was quenched with water (50 mL). The resulting mixture was extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated to afford crude product. The crude product was purified by Prep-HPLC on a XSelect CSH Fluoro Phenyl column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (**Compound 417**, TFA salt, 18.1 mg, 8.98% yield) as a white solid and (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(5-methyl-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (**Compound 418**, TFA salt, 8.1 mg, 3.52% yield) as a white solid.

[00723] **Compound 417**:: MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found, 543.30 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 9.26 - 9.33 (m, 1H), 9.12 - 9.18 (m, 1H), 8.41 - 8.47 (m, 1H), 7.88 - 8.22 (m, 2H), 7.79 - 7.87 (m, 1H), 7.35 - 7.48 (m, 3H), 7.22 - 7.33 (m, 2H), 6.84 - 7.03 (m, 1H), 6.20 - 6.51 (m, 1H), 5.59 - 5.79 (m, 1H), 2.99 - 3.12 (m, 1H), 2.83 - 2.98 (m, 1H), 2.59 - 2.62 (m, 1H), 2.37 - 2.47 (m, 2H), 2.01 - 2.16 (m, 1H), 1.08 - 2.25 (m, 3H).

[00724] **Compound 418:**: MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found, 543.30 $[M+H]^+$.^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.97 - 9.04 (m, 1H), 8.47 - 8.54 (m, 2H), 8.04 - 8.11 (m, 2H), 7.88 - 7.93 (m, 2H), 7.71 - 7.77 (m, 1H), 7.52 - 7.54 (m, 1H), 7.41 - 7.43 (m, 1H), 7.29 - 7.31 (m, 1H), 6.85 - 6.91 (m, 1H), 5.56 - 5.63 (m, 1H), 3.01 - 3.12 (m, 1H), 2.83 - 2.99 (m, 1H), 2.66 - 2.73 (m, 6H), 2.63 - 2.65 (m, 1H), 2.02 - 2.14 (m, 1H).

[00725] The following compounds were prepared analogously to the synthetic preparation of Compound 417 and 418.

[00726] **Table 15C.** Characterization data of compounds prepared analogously to compound 417 and 418.

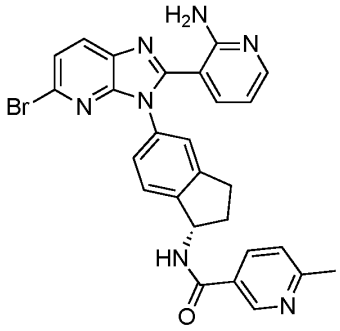
Cpd ID	Characterization Data
544	Observed mass (ESI): 663.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.27 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 2.7 Hz, 1H), 7.96- 8.03 (m, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.28 -7.38 (m, 2H), 7.25- 7.14 (m, 1H), 6.92 (s, 2H), 6.47- 6.35 (m, 1H), 6.16 (d, J = 2.8 Hz, 1H), 5.28- 5.59 (m, 1H), 4.33- 4.54 (m, 1H), 3.91- 4.31 (m, 2H), 3.65 -3.81 (m, 4H), 3.02- 3.29 (m, 8H), 2.81-2.98 (m, 1H), 2.11- 2.29 (m, 1H), 1.61- 2.08 (m, 3H), 1.16- 1.49 (m, 2H), 0.60- 0.81 (m, 4H).
546	Observed mass (ESI): 691.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.26 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 2.7 Hz, 1H), 7.99 (dd, J = 4.8, 1.8 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.26 - 7.39 (m, 2H), 7.18 - 7.21(m, 1H), 6.92 (s, 2H), 6.38 - 6.42 (m, 1H), 6.14 (d, J = 2.8 Hz, 1H), 5.31 - 5.46 (m, 1H), 4.32 - 4.45 (m, 1H), 4.19 - 4.25 (m, 2H), 3.52 - 3.63 (m, 2H), 3.32 - 3.35(m, 1H), 3.27 (s, 3H), 3.11 - 3.18 (m, 1H), 2.93 - 3.10 (m, 6H), 2.13 - 2.22 (m, 1H), 1.91 - 2.00 (m, 5H), 1.35 - 1.47 (m, 3H), 1.23 - 1.32 (m, 1H), 0.65 - 0.75 (m, 4H).
549	Observed mass (ESI): 656.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 8.33 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 2.7 Hz, 1H), 8.03 – 7.99 (m, 1H), 7.90 (d, J = 8.7 Hz, 1H), 7.48 (s, 1H), 7.41 (d, J = 2.1 Hz, 1H), 7.34 (s, 1H), 7.28 – 7.20 (m, 2H), 6.94 (s, 2H), 6.46 – 6.39 (m, 2H), 5.66 (d, J = 2.4 Hz, 1H), 4.38 (s, 1H), 3.93 (d, J = 11.4 Hz, 2H), 3.65 (s, 5H), 3.52 – 3.41 (m, 2H), 3.00 – 2.89 (m, 2H), 2.80 (d, J = 7.8 Hz, 2H), 2.65 (d, J = 12.3 Hz, 2H), 1.98 (s, 1H), 1.88 (d, J = 12.6 Hz, 3H), 1.78 – 1.65 (m, 3H), 1.42 (s, 2H), 1.24 (s, 1H).
550	Observed mass (ESI): 657.45 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.86 (s, 1H), 8.35 (d, J = 8.6 Hz, 1H), 8.17 (d, J = 2.7 Hz, 1H), 8.07 (d, J = 5.6, 1.8 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 1.9 Hz, 1H), 7.47 – 7.35 (m, 2H), 6.68 (d, J = 6.6 Hz, 1H), 6.21 (d, J = 2.8 Hz, 1H), 5.73 (d, J = 2.3 Hz, 1H), 5.02 (s, 1H), 3.87 – 3.56 (m, 9H), 3.44 (s, 1H), 3.30 – 3.10 (m, 5H), 3.02 – 2.88 (m, 1H), 2.76 (d, 2H), 2.59 (s, 1H), 2.28 – 1.93 (m, 3H), 1.71 (d, J = 11.0 Hz, 2H), 1.23 (s, 1H).
551	Observed mass (ESI): 646.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.32-8.30 (m, 1H), 8.17-8.16 (m, 1H), 8.00-7.99 (m, 1H), 7.76-7.74 (m, 1H), 7.46-7.41 (m, 2H), 7.32 (s, 1H), 7.31-7.22 (m, 2H), 6.94 (s, 2H), 6.43-6.40 (m, 1H), 6.07-6.06 (m, 1H), 5.66 (s, 1H), 4.34-4.32 (m, 3H), 3.68 – 3.64 (m, 7H), 3.34-3.31 (m, 3H), 3.31 (s, 1H), 2.76 (s, 2H), 2.67-2.66 (m, 2H), 2.50-2.49 (m, 1H), 2.00-1.98 (m, 2H), 1.98-1.84(m, 2H), 1.50-1.32 (m, 2H).
552	Observed mass (ESI): 675.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.25 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 2.7 Hz, 1H), 7.98 (dd, J = 4.9, 1.9 Hz, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.39 - 7.50 (m, 2H), 7.16 - 7.24 (m, 1H), 6.91 (s, 2H), 6.35 - 6.40 (m, 1H), 6.03 (d, J = 2.8 Hz, 1H), 5.34 - 5.58 (m, 1H), 4.63 - 4.70 (m, 2H), 4.38 - 4.54 (m, 1H), 4.10 - 4.27 (m, 2H), 3.48 - 3.65 (m, 4H), 2.98 - 3.25 (m, 5H), 2.78 - 2.96 (m, 1H), 1.81 - 2.29 (m, 5H), 1.25 - 1.47 (m, 2H), 0.62 - 0.77 (m, 4H).
553	Observed mass (ESI): 663.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.26 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 2.6 Hz, 1H), 7.99 (dd, J = 4.8, 1.9 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.28 - 7.36 (m, 2H), 7.20 (dd, J = 7.7, 1.9 Hz, 1H), 6.91 (s, 2H), 6.40 (dd, J = 7.7, 4.8 Hz, 1H), 5.89 (d, J = 2.7 Hz, 1H), 5.36 - 5.55 (m, 1H), 4.39 - 4.50 (m, 1H), 4.27 - 4.37 (m, 1H), 4.13 - 4.24 (m, 2H), 4.05 - 4.12 (m, 2H), 3.61 -3.75 (m, 2H), 3.23 (s, 3H), 3.19 - 3.22 (m, 1H), 3.14 - 3.16 (m, 1H), 3.02 - 3.11 (m, 3H), 2.84 - 2.93 (m, 1H), 1.83 - 2.06 (m, 3H), 1.22 - 1.43 (m, 2H), 0.65 - 0.77 (m, 4H). (formic acid salt)

Cpd ID	Characterization Data
554	Observed mass (ESI): 638.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.49 - 8.58 (m, 1H), 8.39. - 8.48 (m, 1H), 7.95 - 8.04 (m, 2H), 7.45 - 7.54 (m, 1H), 7.31 - 7.34 (m, 1H), 7.21 - 7.29 (m, 2H), 7.03 - 7.06 (m, 1H), 6.41 - 6.51 (m, 1H), 4.31 - 4.35 (m, 1H), 4.15 - 4.28 (m, 2H), 3.31 - 3.35 (m, 3H), 3.09 - 3.29 (m, 1H), 2.89 - 3.01 (m, 2H), 2.72 - 2.88 (m, 2H), 2.41 - 2.45 (m, 1H), 1.78 - 2.03 (m, 4H), 1.15 - 1.30 (m, 2H), 0.71 - 0.78 (m, 4H).
562	Observed mass (ESI): 615.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.25 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 2.7 Hz, 1H), 7.99 (dd, J = 4.8, 1.9 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.27 - 7.15 (m, 2H), 6.94 (s, 2H), 6.41 (dd, J = 7.7, 4.8 Hz, 1H), 5.85 (d, J = 2.7 Hz, 1H), 4.31 - 4.38 (m, 1H), 4.10 - 4.15 (m, 2H), 3.93 - 3.82 (m, 4H), 2.88 - 2.98 (m, 2H), 2.86 - 2.71 (m, 2H), 2.41 - 2.27 (m, 2H), 2.15 - 1.86 (m, 4H), 1.86 - 1.71 (m, 2H), 1.26 - 1.38 (m, 2H), 1.00 - 1.18 (m, 2H),0.67 - 0.71 (m, 3H).
563	Observed mass (ESI): 658.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ ppm: 8.26 (d, J = 8.6 Hz, 1H), 8.13 (d, J = 2.7 Hz, 1H), 7.92 - 8.05 (m, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.31 (s, 1H), 7.13 - 7.30 (m, 2H), 6.94 (s, 2H), 6.35 - 6.48 (m, 1H), 6.08 - 6.20 (m, 1H), 4.31 - 4.50 (m, 1H), 4.06 - 4.30 (m, 2H), 3.15 - 3.28 (m, 5H), 2.88 - 3.04 (m, 2H), 2.68 - 2.85 (m, 2H), 2.33 - 2.47 (m, 5H), 2.22 (s, 3H), 1.68 - 2.10 (m, 5H), 1.21 - 1.32 (m,1H), 1.08 - 1.19 (m,1H), 0.59 - 0.79 (m, 4H).
564	Observed mass (ESI): 673.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ ppm: 8.21 - 8.26 (m, 1H), 8.12 (d, J = 2.8 Hz,1H), 7.98 - 7.99 (m, 1H), 7.72 - 7.80 (m, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.30 - 7.31 (m, 1H), 7.15 - 7.26 (m, 2H), 6.95 (s, 2H), 6.36 - 6.46 (m, 1H), 6.14 (d, J = 2.7 Hz, 1H), 4.30 - 4.41 (m, 1H), 4.12 - 4.29 (m, 2H), 3.56 - 3.68 (m, 2H), 3.31 - 3.35 (m, 1H), 3.27 (s, 3H), 3.18 - 3.24 (m, 1H), 2.87 - 3.01 (m, 4H), 2.72 - 2.87 (m, 2H), 2.40 - 2.48 (m, 1H), 1.71 - 2.13 (m, 7H), 1.44 - 1.57 (m, 2H), 1.14 - 1.36 (m, 2H), 0.64 - 0.77 (m, 4H).
565	Observed mass (ESI): 693.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm) 8.28 (d, J = 8.7 Hz, 1H), 8.18 (d, J = 2.7 Hz, 1H), 8.00 (m, J = 4.9, 1.8 Hz, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 1.9 Hz, 1H), 7.16- 7.26 (m, 2H), 6.96 (s, 2H), 6.38- 6.45 (m, 1H), 6.28 (d, J = 2.8 Hz, 1H), 4.35 - 4.42 (m, 1H), 4.11 - 4.31 (m, 2H), 3.79- 3.92 (m, 5H), 3.11- 3.30 (m, 5H), 2.90- 3.04 (m, 2H), 2.70- 2.86 (m, 2H), 2.38- 2.48 (m, 1H), 1.74- 2.09 (m, 4H), 1.12- 1.41 (m, 2H), 0.61- 0.77 (m, 4H). (formic acid salt)
566	Observed mass (ESI): 645.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm) 8.31 (d, J = 8.6 Hz, 1H), 8.16 (d, J = 2.7 Hz, 1H), 7.95 - 8.05 (m, 1H), 7.74 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 1.9 Hz, 1H), 7.13 - 7.27 (m, 2H), 6.96 (s, 2H), 6.37 - 6.47 (m, 1H), 6.04 (d, J = 2.7 Hz, 1H), 4.89 -5.02 (m, 1H), 4.30 - 4.41 (m, 1H), 4.11 - 4.30 (m, 2H), 3.64 - 3.82 (m, 2H), 3.10 - 3.29 (m, 1H), 3.00 - 3.09 (m, 2H), 2.86 -2.95 (m, 2H), 2.65 - 2.85 (m, 2H), 2.39 - 2.49 (m, 1H), 2.30 (s, 3H), 1.86 - 2.13 (m, 3H), 1.62 - 1.83 (m, 2H), 1.10 -1.39 (m, 2H), 0.60 - 0.78 (m, 4H).
567	Observed mass (ESI): 632.3 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ ppm: 8.32 (d, J = 8.4 Hz, 1 H), 8.18 (s, 1H), 8.00 (d, J = 4.8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.24 (m, 2H), 6.96 (s, 2H), 6.42 (d, J = 8.0 Hz, 1H), 6.08 (s, 1H), 5.47 - 5.50 (m, 1H), 4.91 - 4.94 (m, 2H), 4.60 - 4.63 (m, 2H), 4.32 - 4.34 (m, 1H), 4.17 - 4.23 (m, 2H), 3.17 - 3.24 (m, 1H), 2.91 - 2.99 (m, 2H), 2.78 - 2.81 (m, 2H), 2.43 - 2.45 (m, 1H), 1.74 - 2.11 (m, 5H), 1.26 - 1.33 (m, 1H), 1.17 - 1.22 (m, 1H), 0.68 - 0.72 (m, 4H).

Cpd ID	Characterization Data
568	Observed mass (ESI): 653.3 [M+H]+. MS (ESI) calcd. for C37H36N10O2: 652.30 m/z, found: 653.30 [M+H]+/1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.54 - 8.62 (m, 1H), 8.43 (dd, J = 4.7, 1.3 Hz, 1H), 8.28 - 8.37 (m, 2H), 8.00 (dd, J = 4.8, 1.9 Hz, 1H), 7.69 - 7.80 (m, 2H), 7.43 - 7.54 (m, 2H), 7.33 (s, 1H), 7.18 - 7.30 (m, 2H), 6.95 (s, 2H), 6.37 - 6.47 (m, 1H), 6.27 (d, J = 2.7 Hz, 1H), 4.29 - 4.40 (m, 1H), 4.15 - 4.20 (m, 2H), 3.16 - 3.24(m, 1H), 2.88 - 2.97 (m, 2H), 2.72 - 2.86 (m, 2H), 2.40 - 2.47 (m, 1H), 1.70 - 2.06 (m, 5H), 1.27 - 1.37(m, 1H), 1.10 - 1.21(m, 1H), 0.67 - 0.71 (m, 4H).
569	Observed mass (ESI): 618.45 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ ppm: 8.33 (d, J = 8.6 Hz, 1H), 8.21 (d, J = 2.5 Hz, 1H), 7.96 - 8.02 (m, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.29 - 7.35 (m, 1H), 7.18 - 7.28 (m, 2H), 6.94 (s, 2H), 6.51 (d, J = 2.6 Hz, 1H), 6.34 - 6.46 (m, 1H), 5.11 (s, 1H), 4.31 - 4.41 (m, 1H), 4.11 - 4.29 (m, 2H), 3.12 - 3.27 (m, 2H), 2.87 - 3.00 (m, 2H), 2.73 - 2.83 (m, 2H), 1.76 - 2.12 (m, 5H), 1.50 (s, 6H), 1.15 - 1.34 (m, 2H), 0.65 - 0.76 (m, 4H).
571	Observed mass (ESI): 514.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32 (d, J = 8.7 Hz, 1H), 8.21 (d, J = 2.7 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.65 - 7.76 (m, 1H), 7.49 - 7.62 (m, 1H), 7.44 (d, J = 7.9 Hz, 1H), 7.19 - 7.40 (m, 4H), 6.19 (d, J = 2.8 Hz, 1H), 5.06 - 5.30 (m, 1H), 4.22 - 4.35 (m, 1H), 3.68 - 3.77 (m, 4H), 3.19 - 3.28 (m, 4H), 3.08 - 3.10 (m, 1H), 2.98 - 3.07 (m, 1H), 2.01 - 2.30 (m, 2H).
572	Observed mass (ESI): 665.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.32 (d, J = 8.6 Hz, 1H), 8.17 - 8.25 (m, 1H), 7.80 (d, J = 8.6 Hz, 1H), 7.66 - 7.76 (m, 1H), 7.49 - 7.63 (m, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.29 - 7.33 (m, 1H), 7.20 - 7.28 (m, 2H), 6.19 (d, J = 2.8 Hz, 1H), 5.29 - 5.55 (m, 1H), 4.33 - 4.48 (m, 1H), 4.11 - 4.24 (m, 2H), 3.68 - 3.77 (m, 4H), 3.21 - 3.26 (m, 5H), 3.12 - 3.18 (m, 1H), 2.96 - 3.08 (m, 3H), 2.79 - 2.93 (m, 1H), 1.74 - 2.09 (m, 3H), 1.16 - 1.45 (m, 2H), 0.62 - 0.78 (m, 4H).
573	Observed mass (ESI): 656.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.31 - 8.42(m, 2H), 7.97 (d, J = 4.9,1H), 7.85 - 7.93 (m, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 7.22 (dd, J = 7.7, 2.1 Hz, 2H), 6.77 (d, J = 2.7 Hz, 1H), 6.42 (dd, J = 7.7, 4.9 Hz, 1H), 5.40 (d, J = 3.5 Hz, 1H), 4.29 - 4.38 (m, 1H), 4.15 - 4.20 (m, 2H), 3.46 (s, 3H), 3.16 - 3.20 (m, 1H), 2.91 - 2.96 (m, 2H), 2.77 - 2.80 (m, 2H), 2.40 - 2.42 (m, 1H), 1.72 - 2.00 (m, 4H), 1.17 - 1.30 (m, 2H), 0.69 - 0.72 (m, 4H).
574	Observed mass (ESI): 653.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.34 - 8.45 (m, 2H), 8.13 - 8.20 (m, 1H), 7.93 - 8.05 (m, 2H), 7.43 - 7.60 (m, 2H), 7.35 (s, 1H), 7.19 - 7.31 (m, 2H), 7.02 (d, J = 2.7 Hz, 1H), 6.94 (s, 2H), 6.55 (d, J = 9.3 Hz, 1H), 6.36 - 6.47 (m, 2H), 4.29 - 4.44 (m, 1H), 4.08 - 4.29 (m, 2H), 3.14 - 3.29 (m, 1H), 2.87 - 3.03 (m, 2H), 2.67 - 2.87 (m, 2H), 2.39 - 2.42 (m, 1H), 1.68 - 2.25 (m, 5H), 1.10 - 1.41 (m, 2H), 0.60 - 0.79 (m, 4H).
575	Observed mass (ESI): 653.4 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.46 (d, J = 2.8 Hz, 1H), 8.36 - 8.44 (m, 3H), 8.02 (dd, J = 4.8, 1.8 Hz, 1H), 7.98 (d, J = 8.6 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 1.9 Hz, 1H), 7.21 - 7.31 (m, 2H), 6.98 (d, J = 2.8 Hz, 1H), 6.94 (s, 2H), 6.43 (dd, J = 7.7, 4.8 Hz, 1H), 6.27 - 6.32 (m, 2H), 4.30 - 4.41 (m, 1H), 4.12 - 4.27 (m, 2H), 3.12 - 3.29 (m, 1H), 2.87 - 3.04 (m, 2H), 2.71 - 2.85 (m, 2H), 2.40 - 2.46 (m, 1H), 1.90 - 2.18 (m, 3H), 1.71 - 1.87 (m, 2H), 1.10 - 1.39 (m, 2H), 0.65 - 0.76 (m, 4H).

Cpd ID	Characterization Data
582	Observed mass (ESI): 653.15 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.28 - 8.37 (m, 1H), 8.21 - 8.27 (m, 1H), 7.95 - 8.05 (m, 1H), 7.71 - 7.81 (m, 1H), 7.45 - 7.51 (m, 1H), 7.31 - 7.35 (m, 1H), 7.19 - 7.28 (m, 2H), 6.93 - 7.01 (m, 2H), 6.42 - 6.45 (m,1H), 6.22 - 6.25 (m, 1H), 4.33 - 4.40 (m,1H), 4.25 - 4.29 (m, 2H), 3.20 - 3.25 (m, 1H), 3.15 (s, 3H), 2.89 - 3.01 (m, 2H), 2.72 - 2.89 (m, 2H), 2.45 - 2.50 (m, 1H), 1.91 - 2.08 (m, 2H), 1.85 - 1.91 (m, 1H), 1.75 - 1.85 (m, 2H), 1.23 - 1.37 (m, 1H), 1.13 - 1.20 (m, 1H), 0.80 - 0.85 (m, 1H), 0.63 - 0.75 (m, 4H).
590	Observed mass (ESI): 604.45 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.30 - 8.36 (m, 2H), 8.01 (d, J = 1.5 Hz, 1H), 7.99 (d, J = 1.5 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.34 (s, 1H), 7.22 - 7.28 (m, 2H), 6.94 (s, 2H), 6.52 (s, 1H), 6.41 - 6.45 (m, 1H), 4.46 (s, 2H), 4.41 - 4.45 (m, 1H), 4.20 - 4.23 (m, 2H), 3.25 (s, 3H), 3.18 - 3.22 (m, 1H), 2.93 - 2.97 (m, 2H), 2.76 - 2.81 (m, 2H), 2.41 - 2.42 (m, 1H), 1.70 - 2.00 (m, 4H), 1.15 - 1.30 (m, 2H), 0.68 - 0.72 (m, 4H) (formic acid salt).
591	Observed mass (ESI): 631.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ(ppm): 8.31 - 8.50 (m, 2H), 8.01 (dd, J = 4.8, 1.9 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.32 - 7.38 (m, 1H), 7.22 - 7.30 (m, 2H), 6.95 (s, 2H), 6.80 (d, J = 2.6 Hz, 1H), 6.39 - 6.48 (m, 1H), 4.35 (t, J = 7.2 Hz, 1H), 4.11 - 4.27 (m, 2H), 3.28 - 3.33 (m, 3H), 3.16 - 3.27 (m, 1H), 2.97 - 3.09 (m, 3H), 2.87 - 2.96 (m, 2H), 2.72 - 2.86 (m, 2H), 2.41 - 2.49 (m, 1H), 1.70 - 2.14 (m, 5H), 1.11 - 1.37 (m, 2H), 0.64 - 0.75 (m, 4H).
597	Observed mass (ESI): 616.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.29 - 8.37 (m, 2H), 8.00 (dd, J = 4.8, 1.8 Hz, 1H), 7.92 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 1.9 Hz, 1H), 7.19 - 7.29 (m, 2H), 6.93 (s, 2H), 6.63 (d, J = 2.6 Hz, 1H), 6.38 - 6.46 (m, 1H), 4.92 (dd, J = 8.5, 5.7 Hz, 2H), 4.70 - 4.78 (m, 2H), 4.31 - 4.41 (m, 2H), 4.18 - 4.22 (m, 2H), 3.22 - 3.25 (m, 1H), 2.86 - 3.00 (m, 2H), 2.72 - 2.84 (m, 2H), 2.40 - 2.46 (m, 1H), 2.08 - 2.10 (m, 1H), 1.95 - 2.04 (m, 2H), 1.86 - 1.95 (m, 1H), 1.75 - 1.83 (m, 1H), 1.14 - 1.35 (m, 2H), 0.62 - 0.75 (m, 4H).
598	Observed mass (ESI): 670.45 [M+H]+. 1H NMR (300 MHz, DMSO-d6+D2O)δ(ppm): 8.24 - 8.27 (m, 1H), 8.13 - 8.14 (m, 1H), 7.99 - 8.00 (m, 1H), 7.97 - 7.98 (m, 1H), 7.75 - 7.78 (m, 1H), 7.50 - 7.69 (m, 1H), 7.40 - 7.47 (m, 1H), 7.20 - 7.30 (m, 2H), 6.40 - 6.45 (m, 1H), 6.13 - 6.14 (m, 1H), 5.66 - 5.67 (m, 1H), 4.35 - 4.37 (m, 1H), 4.14 - 4.32 (m, 4H), 3.58 - 3.64 (s, 3H), 3.23 - 3.25 (m, 4H), 2.91 - 2.99 (m, 1H), 2.64 - 2.80 (m, 4H), 2.43 - 2.53 (m, 4H), 2.21 (s, 3H), 1.92 - 1.97 (m, 1H), 1.72 - 1.80 (m, 2H), 1.31 - 1.35 (m, 2H),
599	Observed mass (ESI): 615.4 [M+H]+. 1H-NMR (400 MHz, DMSO-d6) δ (ppm): 8.30 - 8.40 (m, 1H), 8.00 - 8.08 (m, 1H), 7.81 - 7.90 (m, 1H), 7.41 - 7.60 (m, 3H), 7.32 - 7.40 (m, 1H), 7.20 - 7.32 (m, 2H), 7.00 - 7.15 (m, 2H), 6.32 - 6.50 (m, 1H), 5.61 (s, 1H), 4.30 - 4.45 (m, 1H), 4.10 - 4.30 (m, 2H), 3.10 - 3.30 (m, 2H), 2.90 - 3.10 (m, 2H), 2.73 - 2.90 (m, 2H), 2.22 - 2.36 (m, 1H), 1.90 - 2.05 (m, 3H), 1.70 - 1.90 (m, 2H), 1.25 - 1.40 (m, 2H), 0.60 - 0.80 (m, 6H), 0.23 (s, 2H).

[00727] Intermediate 265-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-methylnicotinamide



Intermediate 265-1

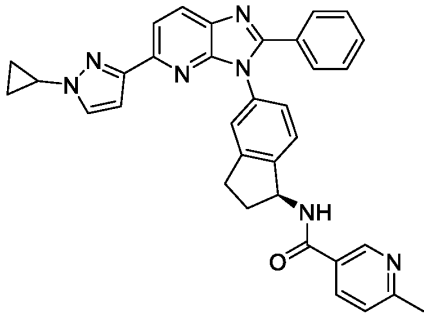
[00728] **Intermediate 265-1** was prepared in a manner analogous to **Example 3** using PyBOP in place of HATU, **Intermediate 245-3** in place of **Example 2** and 6-methylpyridine-3-carboxylic acid in place of 3,4-difluoro-5-anisic acid. MS (ESI) calcd. for $C_{27}H_{22}BrN_7O$: 539.11 m/z, found: 540.20 $[M+H]^+$.

[00729] The following compounds were prepared analogous to the synthetic preparation in Example 95 (Compounds 417 and 418).

[00730] **Table 16.** Characterization data of compounds prepared analogously to compound 417/418.

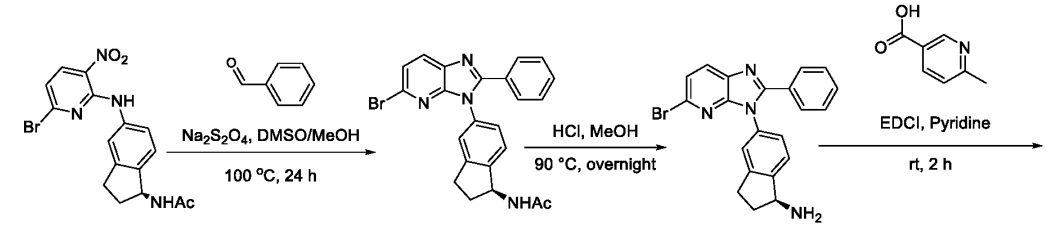
Cpd ID	Characterization Data
419	MS (ESI) calcd. for $C_{32}H_{28}N_{10}O$, 568.24 m/z, found, 569.40 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm); 9.00 - 9.09 (m, 1H), 8.91 - 8.97 (m, 1H), 8.44 - 8.58 (m, 2H), 8.02 - 8.10 (m, 1H), 7.88 - 7.93 (m, 1H), 7.80 - 7.82 (m, 1H), 7.69 - 7.76 (m, 1H), 7.47 - 7.52 (m, 1H), 7.40 - 7.46 (m, 1H), 7.32 - 7.39 (m, 1H), 6.81 - 6.92 (m, 1H), 5.56 - 5.68 (m, 1H), 3.03 - 3.15 (m, 1H), 2.88 - 3.02 (m, 1H), 2.67 (s, 3H), 2.58 - 2.63 (m, 1H), 2.02 - 2.18 (m, 2H), 1.00 - 1.10 (m, 2H), 0.86 - 0.95 (m, 2H). ^{19}FNMR (376 MHz, DMSO-d_6) δ (ppm); -73.98. (TFA salt)
420	MS (ESI) calcd. for $C_{32}H_{28}N_{10}O$, 568.24 m/z, found, 569.40 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ (ppm); 8.94 - 9.01 (m, 1H), 8.48 - 8.56 (m, 1H), 8.37 - 8.47 (m, 1H), 8.03 - 8.10 (m, 1H), 7.99 - 8.02 (m, 1H), 7.83 - 7.92 (m, 2H), 7.62 - 7.71 (m, 1H), 7.50 - 7.54 (m, 1H), 7.38 - 7.46 (m, 1H), 7.24 - 7.34 (m, 1H), 6.81 - 6.90 (m, 1H), 5.52 - 5.65 (m, 1H), 2.98 - 3.10 (m, 1H), 2.86 - 2.98 (m, 1H), 2.70 - 2.81 (m, 1H), 2.65 (s, 3H), 2.58 - 2.63 (m, 1H), 2.02 - 2.18 (m, 1H), 0.98 - 1.10 (m, 4H). ^{19}FNMR (376 MHz, DMSO-d_6) δ (ppm); -73.95. (TFA salt)
430	MS (ESI) calcd. for $C_{30}H_{24}F_2N_{10}O$, 578.21 m/z, found, 579.35 $[M+H]^+$.^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.21 - 9.34 (m, 1H), 8.83 - 8.99 (m, 1H), 8.39 - 8.52 (m, 1H), 8.11 - 8.21 (m, 1H), 7.99 - 8.09 (m, 1H), 7.85 - 7.96 (m, 1H), 7.37 - 7.49 (m, 3H), 7.33 - 7.36 (m, 1H), 7.02 - 7.32 (m, 2H), 6.47 - 6.59 (m, 1H), 5.54 - 5.68 (m, 1H), 3.01 - 3.11 (m, 1H), 2.87 - 2.99 (m, 1H), 2.58 - 2.63 (m, 1H), 2.51 - 2.55 (m, 3H), 2.04 - 2.16 (m, 1H). ^{19}F NMR (376 MHz, DMSO-d_6) δ (ppm); -116.80.

[00731] **Example 96: (S)-N-(5-(5-(1-cyclopropyl-1H-pyrazol-3-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 431)**

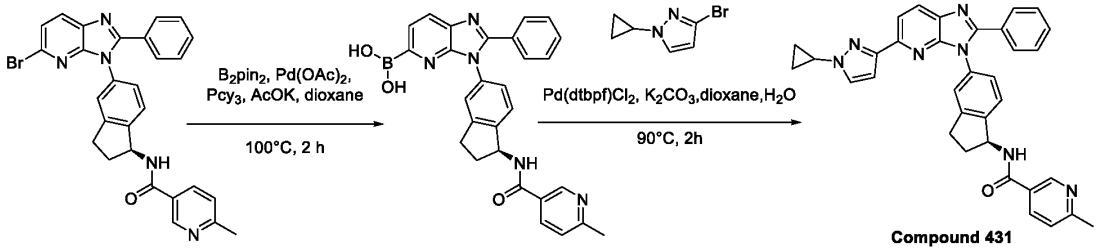


Compound 431

[00732] Synthetic Route:



Intermediate 245-5



Compound 431

[00733] Step 1: Synthesis of (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide

[00734] To a stirred solution of (S)-N-(5-((6-bromo-3-nitropyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)acetamide (Intermediate 245-5) (3 g, 7.668 mmol, 1 equiv) in DMSO (30 mL, 422.373 mmol, 55.08 equiv) and MeOH (5 mL, 123.494 mmol, 16.10 equiv) were added benzaldehyde (3.26 g, 30.672 mmol, 4 equiv) and $Na_2S_2O_4$ (3.34 g, 19.170 mmol, 2.5 equiv) and the resulting mixture was stirred for 24 h at 100°C. The mixture was allowed to cool to room temperature. The mixture was concentrated. To this mixture, sodium bicarbonate (150 mL) solution was added. After separation of phases, the aqueous phase was extracted with ethyl acetate (200 mL x 2). The combined organic layers were washed with brine (2 x 200 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with petroleum ether / ethyl acetate (1:1) to afford (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (1.4 g, 33.45% yield) as yellow solid.: MS (ESI) calcd. for $C_{23}H_{19}BrN_4O$, 446.07m/z, found 447.00 $[M+H]^+$.

[00735] Step 2: Synthesis of (S)-5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-amine

[00736] A solution of (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)acetamide (10 g, 22.355 mmol, 1 equiv) in HCl (70 mL) and MeOH (70 mL) was stirred at 100°C overnight. The mixture was allowed to cool to room temperature. The resulting mixture was concentrated under reduced pressure. The mixture was basified to pH 8~9 with $NaHCO_3/H_2O$. The precipitated solids were collected by filtration and washed with H_2O (500 mL x 3) to afford (S)-5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-amine (7.5 g, 74.50% yield) as a red solid. The crude product was used in the next step directly without further purification.: MS (ESI) calcd. for $C_{21}H_{17}BrN_4$, 404.06 m/z, found, 405.10 $[M+H]^+$.

[00737] Step 3: Synthesis of (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide

[00738] A solution of (S)-5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-amine (3 g, 7.402 mmol, 1 equiv), 6-methylpyridine-3-carboxylic acid (1.22 g, 8.882 mmol, 1.2 equiv) and EDCI (2.13 g, 11.103 mmol, 1.5 equiv) in Pyridine (30 mL) was stirred at room temperature for 1h. The reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (2.5 g, 59.25% yield) as a yellow solid.: MS (ESI) calcd. for $C_{28}H_{22}BrN_5O$, 523.10 m/z, found, 524.10 $[M+H]^+$.

[00739] Step 4: Synthesis of (S)-(3-(1-(6-methylnicotinamido)-2,3-dihydro-1H-inden-5-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-5-yl)boronic acid

[00740] To a solution of (S)-N-(5-(5-bromo-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (1.4 g, 2.670 mmol, 1 equiv) in dioxane (15 mL) were added 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (1.36 g, 5.340 mmol, 2 equiv), $Pd(OAc)_2$ (0.12 g, 0.534 mmol, 0.2 equiv) and PCy_3 (0.15 g, 0.534 mmol, 0.2 equiv). The resulting mixture was maintained under nitrogen and stirred at 100°C for 2 h. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-(3-(1-(6-

methylnicotinamido)-2,3-dihydro-1H-inden-5-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-5-yl)boronic acid (760 mg, 54.11% yield) as a yellow solid.: MS (ESI) calcd. for $C_{28}H_{24}BN_5O_3$, 489.19 m/z, found, 490.25 $[M+H]^+$.

[00741] Step 5: Synthesis of (S)-N-(5-(5-(1-cyclopropyl-1H-pyrazol-3-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 431)

[00742] To a solution of (S)-(3-(1-(6-methylnicotinamido)-2,3-dihydro-1H-inden-5-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-5-yl)boronic acid (200 mg, 0.409 mmol, 1 equiv) in dioxane (4 mL) was added 3-bromo-1-cyclopropylpyrazole (114.67 mg, 0.613 mmol, 1.5 equiv), $Pd(dtbpf)Cl_2$ (53.28 mg, 0.082 mmol, 0.2 equiv) and K_2CO_3 (169.46 mg, 1.227 mmol, 3 equiv). The resulting mixture was maintained under nitrogen and stirred at 90°C for 2 h. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(5-(1-cyclopropyl-1H-pyrazol-3-yl)-2-phenyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 431) (58.6 mg, 25.81% yield) as a yellow solid.: MS (ESI) calcd. for $C_{34}H_{29}N_7O$, 551.24 m/z, found, 552.35 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.80 - 9.13 (m, 1H), 8.05 - 8.31 (m, 2H), 7.88 - 8.02 (m, 1H), 7.70 - 7.85 (m, 1H), 7.52 - 7.65 (m, 2H), 7.31 - 7.51 (m, 6H), 7.12 - 7.30 (m, 1H), 6.50 - 6.63 (m, 1H), 5.53 - 5.82 (m, 1H), 3.72 - 3.92 (m, 1H), 2.80 - 3.20 (m, 2H), 2.53 - 2.60 (m, 4H), 1.96 - 2.23 (m, 1H), 0.81 - 1.28 (m, 4H).

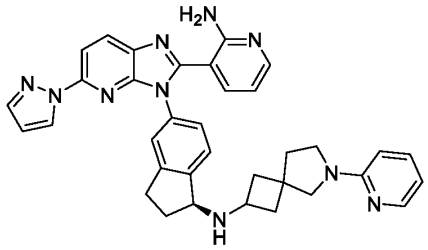
The following compounds were prepared analogous to the synthetic preparation in Example 96 (Compound 431).

Table 17. Characterization data of compounds prepared analogously to compound 431.

Cpd ID	Characterization Data
432	.: MS (ESI) calcd. for $C_{34}H_{27}F_2N_7O$, 587.22 m/z, found 588.40 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 9.15 (s, 1H), 8.40 - 8.50 (m, 1H), 8.15 - 8.25 (m, 1H), 7.90 - 8.00 (m, 1H), 7.82 - 7.90 (m, 1H), 7.75 - 7.82 (m, 1H), 7.55 - 7.70 (m, 2H), 7.35 - 7.50 (m, 5H), 7.20 - 7.30 (m, 1H), 6.85 - 7.20 (m, 1H), 6.63 (s, 1H), 5.60 - 5.70 (m, 1H), 3.70 - 3.80 (m, 1H), 2.85 - 3.15 (m, 2H), 2.55 - 2.65 (m, 1H), 2.00 - 2.20 (m, 1H), 0.95 - 1.15 (m, 4H). ^{19}F NMR (376 MHz, DMSO-d_6) δ -116.05.
555	Observed mass (ESI): 644.35 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.20 - 8.24 (m, 1H), 7.97 - 8.02 (m, 2H), 7.85 - 7.87 (m, 1H), 7.45 - 7.53 (m, 1H), 7.29 - 7.34 (m, 1H), 7.19 - 7.28 (m, 2H), 6.93 - 7.01 (m, 2H), 6.62 - 6.65 (m, 1H), 6.42 - 6.45 (m,1H), 4.45 - 4.52 (m,1H), 4.33 - 4.40 (m,1H), 4.25 - 4.29 (m, 2H), 3.95 - 4.04 (m, 2H), 3.43 - 3.52 (m, 2H), 3.17 - 3.37 (m, 1H), 2.89 - 3.01 (m, 2H), 2.72 - 2.89 (m, 2H), 2.35 - 2.65 (m, 2H), 1.71 - 2.08 (m, 8H), 1.13 - 1.37 (m, 2H), 0.63 - 0.75 (m, 4H).

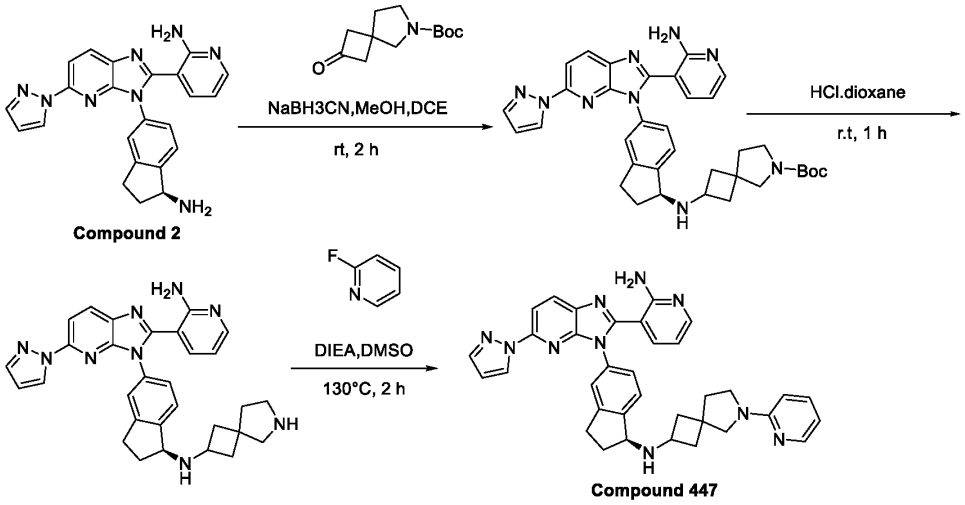
516	Observed mass (ESI): 592.2 [M+H]+. 1H NMR (400 MHz, DMSO+D2O)8.29 - 8.32 (m, 1H), 8.21 – 8.19 (m, 1H), 8.10 (m, 1H), 7.55 – 7.60 (m, 1H), 7.30 – 7.35 (s, 1H), 7.21 -7.26 (m, 2H), 6.51 (m, 1H), 4.62 (m, 1H), 4.25 – 4.31 (m, 2H), 3.14 (m, 2H), 2.94 – 3.09 (m, 1H), 2.81 – 2.90 (m, 1H), 2.65 – 2.71 (m, 4H), 2.44 – 2.49 (m, 1H), 1.92 – 2.15 (m, 4H), 1.23 – 1.45 (m, 2H), 0.75 – 0.80 (m, 4H).

[00743] Example 97: N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-(pyridin-2-yl)-6-azaspiro[3.4]octan-2-amine (Compound 447)



Compound 447

[00744] Synthetic Route:



[00745] Step 1: Synthesis of tert-butyl 2-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}-6-azaspiro[3.4]octane-6-carboxylate

[00746] A solution of (*S*)-3-(3-(1-amino-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (Compound 2) (300 mg, 0.761 mmol, 1 equiv) and tert-butyl 2-oxo-6-azaspiro[3.4]octane-6-carboxylate (171.35 mg, 0.761 mmol, 1 equiv) in DCE (3 mL) and MeOH (0.3 mL) was stirred for 1 h at 40 °C. Then, $NaBH_3CN$ (191.18 mg, 3.044 mmol, 4 equiv) was added to the reaction mixture. The obtained suspension was stirred at 40°C for 1 h. The mixture was purified by reverse-phase flash chromatography on C18 silica gel

using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl 2-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}-6-azaspiro[3.4]octane-6-carboxylate (200 mg, 42.57%) as a yellow solid.MS (ESI) calcd. for $C_{35}H_{39}N_9O_2$: 617.32 m/z, found, 616.30 $[M+H]^-$.

[00747] Step 2: Synthesis of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-azaspiro[3.4]octan-2-amine

[00748] A solution of tert-butyl 2-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}-6-azaspiro[3.4]octane-6-carboxylate (200 mg, 0.324 mmol, 1 equiv) in HCl (5 mL, 4 M in 1,4-dioxane) was stirred at room temperature for 1 h. The solvent was removed by distillation under vacuum to afford N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-azaspiro[3.4]octan-2-amine (100 mg, crude) as a yellow solid.: MS (ESI) calcd. for $C_{30}H_{31}N_9$: 517.27 m/z, found, 518.35 $[M+H]^+$.

[00749] Step 3: Synthesis of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-(pyridin-2-yl)-6-azaspiro[3.4]octan-2-amine (Compound 447)

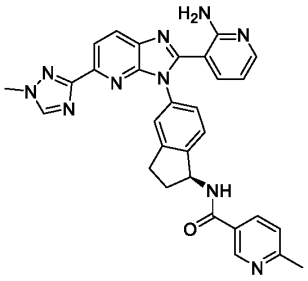
[00750] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-azaspiro[3.4]octan-2-amine (90 mg, 0.174 mmol, 1 equiv) in DMSO (5 mL) was added DIEA(112.36 mg, 0.870 mmol, 5 equiv) and 2-fluoropyridine (18.57 mg, 0.191 mmol, 1.1 equiv). The resulting mixture was stirred at 130°C for 2 h. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) .The material was further purified by Prep-HPLC on a XSelect CSH OBD Column using a gradient of acetonitrile in water (+ 0.05% TFA) to afford N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-(pyridin-2-yl)-6-azaspiro[3.4]octan-2-amine (Compound 447) (16.7 mg, 15.84%) as a light yellow solid.: MS (ESI) calcd. for $C_{35}H_{34}N_{10}$: 594.30 m/z, found, 595.20 $[M+H]^+$. ^{1}H-NMR (400 MHz, DMSO) δ (ppm); 8.40 - 8.48 (m, 1H), 8.30 - 8.39 (m, 1H), 7.91 - 8.10 (m, 4H), 7.80 - 7.85 (m, 1H), 7.65 - 7.78 (m, 2H), 7.55 - 7.61 (m, 1H), 7.40 - 7.45 (m, 1H), 6.98 - 7.10 (m, 1H), 6.88 - 6.95 (m, 1H), 6.65 - 6.75 (m, 1H), 6.52 - 6.60 (m, 1H), 4.75 - 4.85 (m, 1H), 3.90 - 4.10 (m, 2H), 3.48 - 3.60 (m, 3H), 3.11 - 3.25 (m, 1H), 2.90 - 3.05 (m, 1H), 2.55 - 2.70 (m, 1H), 2.26 - 2.43 (m, 4H), 2.15 - 2.25 (m, 2H), 2.05 - 2.14 (m, 1H).

[00751] The following compounds were prepared analogous to the synthetic preparation in Example 97 (Compound 447).

[00752] **Table 18.** Characterization data of compounds prepared analogously to compound 447.

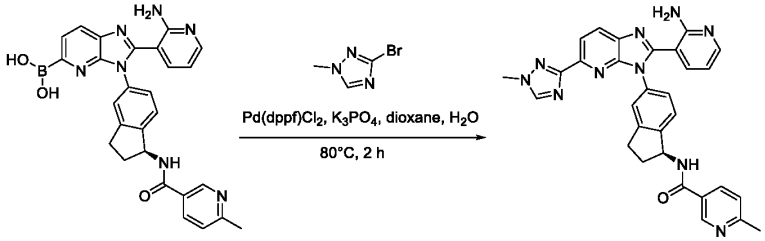
Cpd ID	Characterization Data
448	MS (ESI) calcd. for $C_{34}H_{32}N_{10}$: 580.28m/z, found, 581.40 $[M+H]^+$. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm); 8.32 - 8.39 (m, 2H), 8.00 - 8.02 (m, 1H), 7.92 - 7.99 (m, 2H), 7.79 - 7.81 (m, 1H), 7.44 - 7.51 (m, 2H), 7.30 - 7.33 (m, 1H), 7.19 - 7.28 (m, 2H), 6.97 - 7.01 (m, 2H), 6.58 - 6.62 (m, 1H), 6.53 - 6.55 (m, 1H), 6.37 - 6.41 (m, 1H), 6.31 - 6.36 (m, 1H), 4.12 - 4.19 (m, 1H), 3.88 - 3.96 (m, 1H), 3.79 - 3.87 (m, 1H), 3.20 - 3.21 (m, 1H), 2.88 - 2.95 (m, 1H), 2.70 - 2.81 (m, 1H), 2.29 - 2.34 (m, 4H), 1.91 - 1.99 (m, 2H), 1.71 - 1.82 (m, 1H).
449	MS (ESI) calcd. for $C_{36}H_{36}N_{10}$,608.31 m/z, found 609.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.28 - 8.47 (m, 2H), 8.07 - 8.18 (m, 1H), 7.91 - 8.07 (m, 2H),7.70 - 7.87(m, 1H), 7.38 - 7.63 (m, 2H),7.12 - 7.38 (m, 3H), 6.71 - 6.88 (m, 1H),6.56 - 6.71 (m, 1H), 6.49 - 6.54 (m, 1H),6.32 - 6.48 (m, 1H), 4.16 - 4.23 (m, 1H), 3.31 - 3.54 (m, 5H), 2.92 - 3.08 (m, 1H),2.71 - 2.84 (m, 1H),2.26 - 2.42 (m, 1H), 2.09 - 2.21 (m, 1H),1.98 - 2.11 (m, 1H), 1.76 - 1.92 (m, 1H), 1.41 - 1.68 (m, 6H).
450	MS (ESI) calcd. for $C_{36}H_{36}N_{10}$: 608.31 m/z, found, 609.45 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO-d_6) δ (ppm); 8.31 - 8.46 (m, 2H), 7.92 - 8.23 (m, 3H), 7.77 - 7.82 (m, 1H), 7.44 - 7.56 (m, 2H), 7.37 - 7.39 (m, 1H), 7.22 - 7.29 (m, 2H), 6.52 - 6.61 (m, 2H), 6.31 - 6.45 (m, 2H), 4.51 - 4.55 (m, 1H), 3.61 - 3.72 (m, 3H), 2.95 - 3.05 (m, 1H), 2.75 - 2.83 (m, 2H), 2.39 - 2.48 (m, 1H), 1.72 - 2.01 (m, 5H), 1.43 - 1.58 (m, 3H), 1.22 - 1.33 (m, 2H).
465	MS (ESI) calcd. for $C_{35}H_{34}N_{10}$: 594.30 m/z, found, 595.20 $[M+H]^+$. ^1H-NMR (400 MHz, DMSO) δ (ppm); 8.45 - 8.55 (m, 2H), 8.35 - 8.41 (m, 1H), 8.23 - 8.30 (m, 1H), 8.01 - 8.15 (m, 2H), 7.80 - 7.90 (m, 2H), 7.70 - 7.79 (m, 1H), 7.55 - 7.65 (m, 2H), 7.32 - 7.40 (m, 1H), 7.20 - 7.30 (m, 1H), 7.11 - 7.19 (m, 1H), 6.55 - 6.62 (m, 1H), 4.62 - 4.72 (m, 1H), 3.75 - 4.05 (m, 1H), 3.05 - 3.25 (m, 3H), 2.79 - 2.92 (m, 1H), 2.62 - 2.78 (m, 2H), 2.32 - 2.50 (m, 2H), 2.09 - 2.20 (m, 1H), 2.00 - 2.08 (m, 2H), 1.85 - 1.99 (m, 3H).
467	MS (ESI) calcd. for $C_{36}H_{36}N_{10}$,608.31 m/z, found 609.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ (ppm); 8.24 - 8.56 (m, 2H), 7.88 - 8.16 (m, 4H), 7.79 - 7.88 (m, 1H), 7.62 - 7.79 (m, 2H), 7.49 - 7.62 (m, 1H), 7.29 - 7.49 (m, 2H), 6.82 - 7.05 (m, 1H), 6.55 - 6.82 (m, 1H), 6.48 - 6.55 (m, 1H), 4.68 - 4.91 (m, 1H), 4.08 - 4.15 (m, 1H), 3.57 - 3.81 (m, 2H), 3.38 - 3.57 (m, 2H),3.09 - 3.33 (m, 1H), 2.85 - 3.09 (m, 1H), 2.48 - 2.56 (m, 1H), 2.15 - 2.38 (m, 2H), 2.06 - 2.15 (m, 1H), 1.85 - 2.06 (m, 2H), 1.71 - 1.85 (m, 2H), 1.46 - 1.71 (m, 2H).
468	MS (ESI) calcd. for $C_{36}H_{36}N_{10}$,608.31 m/z, found 609.25 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ (ppm); 8.41- 8.58 (m, 1H), 8.25 - 8.41 (m, 1H), 7.98 - 8.16 (m, 2H), 7.89 - 7.98 (m, 2H), 7.77 - 7.89 (m, 1H), 7.66 - 7.77 (m, 2H), 7.48 - 7.66 (m, 1H), 7.38 - 7.48 (m, 1H), 7.20 - 7.38 (m, 1H), 6.83 - 7.05 (m, 1H), 6.65 - 6.83 (m, 1H), 6.48 - 6.65 (m, 1H), 4.62 - 4.92 (m, 1H), 3.86 - 4.02 (m, 1H), 3.55 - 3.75 (m, 2H),3.35 - 3.75 (m, 2H), 3.09 - 3.32 (m, 1H), 2.85 - 3.09 (m, 1H), 2.49 - 2.53 (m, 1H), 2.09 - 2.36 (m, 3H), 1.91 - 2.09 (m, 2H), 1.75 - 1.91 (m, 2H), 1.51 - 1.75 (m, 2H).

[00753] **Example 98: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1-methyl-1H-1,2,4-triazol-3-yl)-3H-imidazo[4,5-b] pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 455)**



Compound 455

[00754] Synthetic Route:

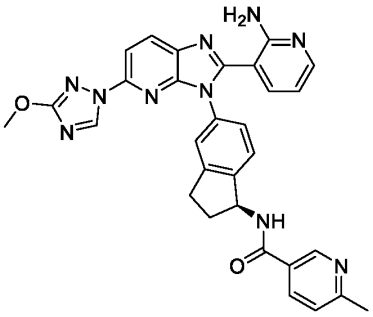


Intermediate 267-1 Compound 455

[00755] Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(1-methyl-1H-1,2,4-triazol-3-yl)-3H-imidazo[4,5-b] pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 455)

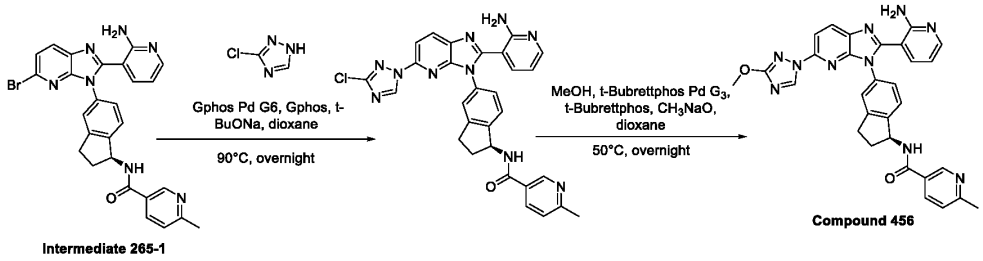
[00756] A mixture of 2-(2-aminopyridin-3-yl)-3-[(1S)-1-(6-methylpyridine-3-amido)-2,3-dihydro-1H-inden-5-yl] imidazo[4,5-b] pyridin-5-ylboronic acid (**Intermediate 267-1**) (100 mg, 0.198 mmol, 1 equiv), 3-bromo-1-methyl-1,2,4-triazole (32.06 mg, 0.198 mmol, 1 equiv), K_3PO_4 (126.01 mg, 0.594 mmol, 3 equiv) and $Pd(dppf)Cl_2$ (14.48 mg, 0.020 mmol, 0.1 equiv) in water (0.5 mL) and dioxane (2 mL) was stirred overnight at 80°C under N_2 atmosphere. The reaction was quenched with H_2O (10 mL). The resulting mixture was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with NaCl/H_2O (3x20 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with MeOH/DCM (0-10%) to afford crude product. The crude product was purified by Prep-HPLC on a XBridge Prep Shield RP OBD C18 Column using gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(1-methyl-1,2,4-triazol-3-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-methylpyridine-3-carboxamide (**Compound 455**) (16.5 mg, 15.29%) as a white solid.MS (ESI) calcd. for $C_{30}H_{26}N_{10}O$, 542.23 m/z, found 543.20 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm); 8.97 (s, 1H), 8.53 (s, 1H), 8.08 - 8.29 (m, 3H), 8.00 - 8.06 (m, 1H), 7.15 - 7.55 (m, 5H), 6.34 - 6.67 (m, 1H), 5.57 - 5.82 (m, 1H), 3.91 (s, 3H), 3.01 - 3.15 (m, 1H), 2.83 - 2.98 (m, 1H), 2.55 - 2.63 (m, 1H), 2.53 (s, 3H), 2.02 - 2.17 (m, 1H).

[00757] Example 99: (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methoxy-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 456)



Compound 456

[00758] Synthetic Route:



[00759] **Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-chloro-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide**

[00760] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-bromoimidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-methylpyridine-3-carboxamide (**Intermediate 265-1**) (200 mg, 0.370 mmol, 1 equiv) in dioxane (5 mL) was added 3-chloro-1H-1,2,4-triazole (76.61 mg, 0.740 mmol, 2 equiv), GPhos (19.86 mg, 0.037 mmol, 0.1 equiv), GPhos Pd G6 TES (34.99 mg, 0.037 mmol, 0.1 equiv) and t-BuONa (88.91 mg, 0.925 mmol, 2.5 equiv). The resulting mixture was maintained under nitrogen and stirred at 90°C overnight. After cooling to room temperature, the reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-chloro-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (100 mg, 43.19% yield) as a yellow solid.: MS (ESI) calcd. for $C_{29}H_{23}ClN_{10}O$, 562.17 m/z, found, 563.25 $[M+H]^+$.

[00761] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methoxy-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Compound 456)

[00762] To a solution of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-chloro-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (60 mg, 0.107 mmol, 1 equiv) in dioxane (2 mL) was added MeOH (17.07 mg, 0.535 mmol, 5 equiv), tBuBrettPhos (5.17 mg, 0.011 mmol, 0.1 equiv), tBuBrettPhos Pd G3 (9.25 mg, 0.011 mmol, 0.1 equiv) and t-BuONa (14.34 mg, 0.150 mmol, 1.4 equiv). The resulting mixture was maintained under nitrogen and stirred at 50°C overnight. After cooling to room temperature, the reaction was quenched with water (10 mL). The resulting mixture was extracted with ethyl acetate (3 x 10 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-(3-methoxy-1H-1,2,4-triazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (**Compound 456**) (10.7 mg, 17.97% yield) as an off-white solid.: MS (ESI) calcd. for $C_{30}H_{26}N_{10}O_2$, 558.22 m/z, found, 559.35 $[M+H]^+$. ^{1}H-NMR (300 MHz, DMSO-d_6) δ (ppm); 9.94 - 9.95 (m, 1H), 8.83 - 8.85 (m, 1H), 8.39 - 8.41 (m, 1H), 8.18 - 8.21 (m, 1H), 8.00 - 8.05 (m, 1H), 7.75 - 7.78 (m, 1H), 7.36 - 7.40 (m, 3H), 7.30 - 7.33 (m, 2H), 6.45 - 6.49 (m, 1H), 5.60 - 5.65 (m, 1H), 3.99 (s, 3H), 3.02 - 3.04 (m, 1H), 2.91 - 2.97 (m, 1H), 2.55 - 2.62 (m, 4H), 2.03 - 2.20 (m, 1H).

[00763] The following compounds were prepared analogous to the synthetic preparation in Example 99 (Compound 456).

[00764] **Table 19A.** Characterization data of compounds prepared analogously to compound 456.

Cpd ID	Characterization Data
346	MS (ESI) calcd. for $C_{29}H_{24}N_{10}O$: 528.21 m/z, found: 529.15 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6+D_2O) δ (ppm): 9.13 (s, 1H), 8.92 - 8.98 (m, 1H), 8.42 - 8.49 (m, 1H), 8.29 - 8.32 (m, 1H), 8.15 - 8.19 (m, 1H), 8.03 - 8.07 (m, 1H), 7.88 - 7.91 (m, 1H), 7.36 - 7.45 (m, 3H), 7.26 - 7.31 (m, 2H), 6.46 - 6.71 (m, 1H), 5.61 - 5.69 (m, 1H), 3.01 - 3.13 (m, 1H), 2.85 - 2.97 (m, 1H), 2.58 - 2.61 (m, 1H), 2.55 (s, 3H), 2.02 - 2.19 (m, 1H)
483	MS (ESI) calcd. for $C_{33}H_{33}F_2N_9O_2$: 625.27 m/z, found, 626.20 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-*d6*) δ(ppm): 8.37 (d, J = 8.8 Hz, 1H), 8.30 (s, 1H), 8.00 - 8.01 (m, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.33 - 7.65 (m, 3H), 7.21 - 7.30 (m, 2H), 6.93 (s, 2H), 6.41 - 6.44 (m, 1H), 6.34 - 6.35 (m, 1H), 4.35 - 4.37 (m, 1H), 4.19 - 4.21 (m, 2H), 3.22 - 3.23 (m, 1H), 2.92 - 2.94 (m, 2H), 2.76 - 2.82 (m, 2H), 2.42 - 2.47 (m, 1H), 1.77 - 2.02 (m, 5H), 1.18 - 1.30 (m, 2H), 0.68 - 0.72 (m, 4H).
485	MS (ESI) calcd. for $C_{33}H_{35}N_9O_2$: 589.29 m/z, found, 590.25 $[M+H]^+$. ^{1}H NMR (300 MHz, DMSO-*d6*) δ(ppm): 8.30 (d, J = 8.4 Hz, 1H), 8.17 - 8.18 (m, 1H), 7.98 - 8.00 (m, 1H), 7.77 (d, J = 8.7 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.25 (m, 2H), 6.94 (s, 2H), 6.39 - 6.44 (m, 1H), 6.04 - 6.05 (m, 1H), 4.33 - 4.35 (m, 1H), 4.19 - 4.22 (m, 2H), 3.92 (s, 3H), 3.15

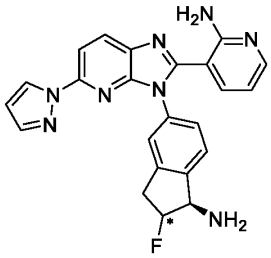
Cpd ID	Characterization Data
	- 3.23 (m, 1H), 2.75 - 2.93 (m, 4H), 2.43 - 2.46 (m, 1H), 1.77 - 2.07 (m, 5H), 1.23 - 1.28 (m, 2H), 0.67 - 0.72 (m, 4H).
486	MS (ESI) calcd. for $C_{34}H_{37}N_9O_2$: 603.31 m/z, found, 604.25[M+H]+. ^{1}H NMR (300 MHz, DMSO-*d6*) δ(ppm): 8.30 (d, *J* = 8.7 Hz, 1H), 8.15 (s, 1H), 7.98 - 8.00 (m, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.24 (m, 2H), 6.94 (s, 2H), 6.39 - 6.43 (m, 1H), 6.03 - 6.04 (m, 1H), 4.20 - 4.35 (m, 5H), 3.15 - 3.23 (m, 1H), 2.80 - 2.93 (m, 2H), 2.75 - 2.77 (m, 2H), 2.42 - 2.46 (m, 1H), 1.78 - 2.06 (m, 5H), 1.23 - 1.38 (m, 5H), 0.67 - 0.72 (m, 4H).
487	MS (ESI) calcd. for $C_{37}H_{41}N_9O_2$, 643.34 m/z, found 644.45 $[M+H]^+$.^{1}H NMR (300 MHz, DMSO-*d6*) δ ppm: 8.32 (d, *J* = 8.7 Hz, 1H), 8.24 (d, *J* = 2.7 Hz, 1H), 8.00 (d, *J* = 1.5 Hz, 1H), 7.87 - 7.99 (m, 1H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.33 (s, 1H), 7.20 - 7.25 (m, 2H), 6.93 (s, 2H), 6.39 - 6.44 (m, 2H), 4.36 (s, 1H), 4.20 (s, 2H), 3.92 (d, *J* = 9.9 Hz, 2H), 3.42 - 3.49 (m, 2H), 3.22 - 3.32 (m, 2H), 2.92 - 2.98 (m, 3H), 2.80 - 2.90 (m, 2H), 2.35 - 2.45 (m, 1H), 1.98 - 2.00 (m, 2H), 1.84 - 1.89 (m, 3H), 1.60 - 1.75 (m, 3H), 1.10 - 1.41 (m, 2H), 0.63 - 0.71 (m, 4H).
488	MS (ESI) calcd. for $C_{36}H_{40}N_{10}O_2$, 644.33 m/z, found 645.20 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-*d6*) δ (ppm); 8.27 (d, *J* = 8.6 Hz, 1H), 8.15 (d, *J* = 2.7 Hz, 1H), 7.99 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.77 (d, *J* = 8.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.31 (s, 1H), 7.16 - 7.25 (m, 2H), 6.96 (s, 2H), 6.41 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.16 (d, *J* = 2.7 Hz, 1H), 4.27 - 4.40 (m, 1H), 4.11 - 4.26 (m, 2H), 3.66 - 3.78 (m, 4H), 3.16 - 3.26 (m, 5H), 2.86 - 3.01 (m, 2H), 2.72 - 2.85 (m, 2H), 2.40 - 2.48 (m, 1H), 2.10 - 2.22 (m, 1H), 1.71 - 2.05 (m, 4H), 1.09 - 1.40 (m, 2H), 0.64 - 0.76 (m, 4H).
497	Observed mass (ESI): 616.25 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ ppm: 8.31 (d, J = 8.7 Hz, 1H), 8.18 (d, J = 2.7 Hz, 1H), 8.00 (d, J = 4.8 Hz, 1H), 7.76 (d, J = 8.7 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.25 (m, 2H), 6.94 (s, 2H), 6.41 (d, J = 7.5 Hz, 1H), 6.14 (s, 1H), 4.33 - 4.35 (m, 1H), 4.19 (s, 2H), 4.09 - 4.14 (m, 1H), 3.20 - 3.26 (m, 1H), 2.91 - 2.94 (m, 2H), 2.75 - 2.83 (m, 2H), 2.43 - 2.46 (m, 1H), 1.77 - 2.10 (m, 5H), 1.19 - 1.30 (m, 2H), 0.67 - 0.76 (m, 8H).
504	Observed mass (ESI): 634.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.31 (d, J = 8.6 Hz, 1H), 8.17 (d, J = 2.7 Hz, 1H), 8.00 (dd, J = 4.8, 1.9 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 1.9 Hz, 1H), 7.19 - 7.25 (m, 2H), 6.95 (s, 2H), 6.42 (dd, J = 7.7, 4.8 Hz, 1H), 6.06 (d, J = 2.7 Hz, 1H), 4.30 - 4.38 (m, 3H), 4.13 - 4.26 (m, 2H), 3.65 - 3.71 (m, 2H), 3.31 (s, 3H), 3.16 - 3.27 (m, 1H), 2.86 - 2.99 (m, 2H), 2.72 - 2.85 (m, 2H), 2.40 - 2.48 (m, 1H), 1.73 - 2.11 (m, 5H), 1.11 - 1.36 (m, 2H), 0.66 - 0.75 (m, 4H).
505	Observed mass (ESI): 689.3 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ(ppm): 8.29 - 8.32 (m, 1H), 8.16 - 8.17 (m, 1H), 7.99 - 8.01 (m, 1H), 7.76 (d, J = 8.7 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.24 (m, 2H), 6.95 (s, 2H), 6.39 - 6.43 (m, 1H), 6.06 - 6.07 (m, 1H), 4.31 - 4.34 (m, 3H), 4.19 - 4.25 (m, 2H), 3.56 - 3.59 (m, 4H), 3.21 - 3.23 (m, 1H), 2.91 - 2.93 (m, 2H), 2.71 - 2.80 (m, 4H), 2.46 - 2.47 (m, 5H), 1.78 - 2.06 (m, 5H), 1.20 - 1.30 (m, 2H), 0.67 - 0.72 (m, 4H).
517	Observed mass (ESI): 660.45 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ ppm: 8.30 (d, J = 8.4 Hz, 1H), 8.16 (s, 1H), 8.00 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.31 (s, 1H), 7.19 - 7.24 (m, 2H), 6.95 - 6.98 (m, 2H), 6.42 (d, J = 7.6 Hz, 1H), 6.08 (s, 1H), 4.77 - 4.81 (m, 1H), 4.32 - 4.36 (m, 1H), 4.13 - 4.24 (m, 2H), 3.86 - 3.89 (m, 2H), 3.47 - 3.53 (m, 2H), 3.18 - 3.23 (m, 1H), 2.92 - 2.98 (m, 2H), 2.78 - 2.82 (m, 2H), 2.47 - 2.48 (m, 1H), 1.99 - 2.09 (m, 4H), 1.88 - 1.93 (m, 1H), 1.75 - 1.85 (m, 2H), 1.64 - 1.68 (m, 2H), 1.15 - 1.35 (m, 2H), 0.68 - 0.72 (m, 4H).
518	Observed mass (ESI): 606.15 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ(ppm): 8.25 - 8.52 (m, 2H), 7.96 - 8.09 (m, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.32 (s, 1H),

Cpd ID	Characterization Data
	7.16 - 7.30 (m, 2H), 6.55 (d, J = 2.8 Hz, 1H), 6.38 - 6.50 (m, 1H), 4.33 (t, J = 7.2 Hz, 1H), 4.10 - 4.30 (m, 2H), 3.11 - 3.31 (m, 1H), 2.86 - 3.03 (m, 2H), 2.70 - 2.85 (m, 2H), 2.55 - 2.59 (m, 3H), 2.40 - 2.49 (m, 1H), 1.70 - 2.09 (m, 4H), 1.06 - 1.41 (m, 2H), 0.62 - 0.80 (m, 4H).
525	Observed mass (ESI): 644.25 [M+H]+. 1H-NMR (400 MHz, DMSO+D2O) δ (ppm): 8.33 - 8.45 (m, 1H), 8.25 - 8.32 (m, 1H), 7.97 - 8.10 (m, 1H), 7.72 - 7.88 (m, 1H), 7.20 - 7.70 (m, 5H), 6.40 - 6.50 (m, 1H), 6.30 - 6.39 (m, 1H), 5.40 - 5.70 (m, 1H), 4.15 - 4.65 (m, 3H), 3.00 - 3.35 (m, 4H), 2.72 - 2.90 (m, 1H), 1.80 - 2.20 (m, 3H), 1.15 - 1.55 (m, 2H), 0.60 - 0.85 (m, 4H).19F NMR (376 MHz, DMSO-d6) δ (ppm): -196.84, -84.19.

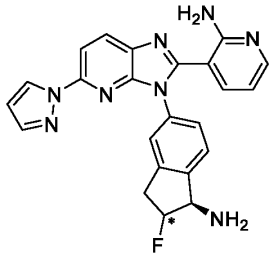
[00765] **Example 101: Synthetic Procedures for Intermediates**

[00766] **Intermediate 147-1: 3-(3-((1*R*,2*)-1-amino-2-fluoro-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine and**

[00767] **Intermediate 147-2: 3-(3-((1*R*,2*)-1-amino-2-fluoro-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine**

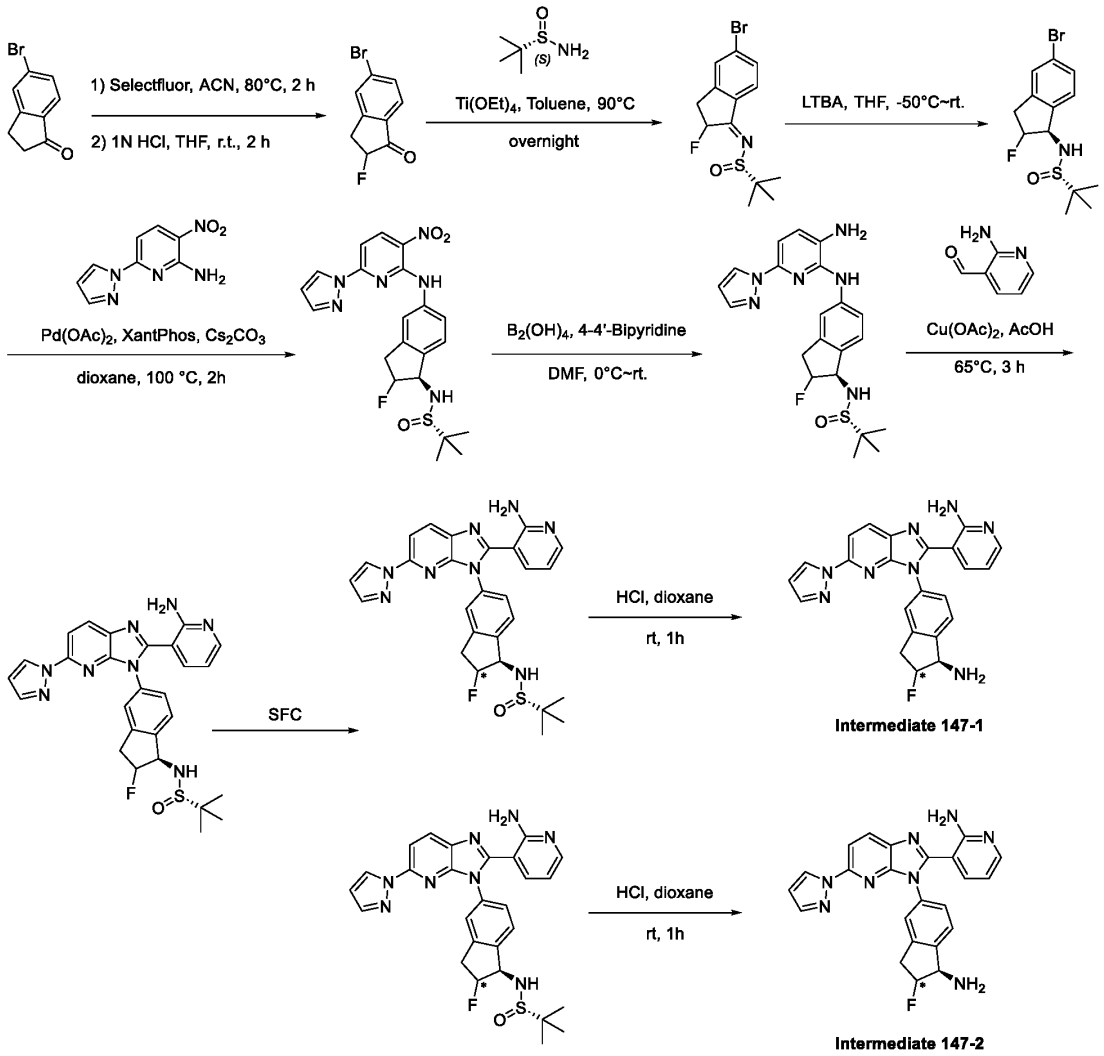


Intermediate 147-1



Intermediate 147-2

[00768] Synthetic Route:



[00769] **Step 1: Synthesis of 5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-one**

[00770] To a solution of 5-bromo-1-indanone (5.00 g, 23.8 mmol) in methanol (50 mL) was added SelectFluor (10.0 g, 28.2 mmol) and the resulting mixture was stirred under reflux for 2 hours. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was dissolved in tetrahydrofuran (50 mL) and 1 N hydrochloric acid (50 mL) was added followed by stirring at room temperature for 3 hours. To the reaction mixture, a 2 N aqueous sodium hydroxide solution (50 mL) was added, and the mixture was diluted with a saturated aqueous sodium bicarbonate solution. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure to afford 5-bromo-2-fluoro-2,3-dihydroinden-1-one (4.0 g, 74% yield) as a white solid. MS (ESI) calcd. for C_9H_6BrFO, 227.96 m/z, found: 229.00 $[M+H]^+$.

[00771] Step 2: Synthesis of (S)-N-((Z)-5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-ylidene)-2-methylpropane-2-sulfinamide

[00772] To a solution of 5-bromo-2-fluoro-2,3-dihydroinden-1-one (3.0 g, 13 mmol) in toluene (5 mL) was added (*S*)-2-methylpropane-2-sulfinamide (1.90 g, 15.7 mmol) and $Ti(OEt)_4$ (5.08 g, 22.2 mmol). The mixture was stirred at 90°C for 2 h. After cooling to room temperature, the reaction was quenched by the addition of 2M Rochelle's salt (30 mL). The resulting mixture was diluted with brine (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate in petroleum ether to afford (S)-N-(5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-ylidene)-2-methylpropane-2-sulfinamide (3.0 g, 69% yield) as a yellow solid. MS (ESI) calcd. for $C_{13}H_{15}BrFNOS$: 331.00 m/z, found: 332.10 $[M+H]^+$. *Note that the (S)- applies to the sulfur stereocenter and not the C-F bond for this and all instances vide infra.*

[00773] Step 3: Synthesis of (S)-N-((1R)-5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide

[00774] To a cooled (-50°C) solution of (S)-N-((Z)-5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-ylidene)-2-methylpropane-2-sulfinamide (3.0 g, 9.0 mmol) in THF was added LTBA (3.90 g, 15.4 mmol) and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched by the addition of 2M Rochelle's salt (30 mL). The mixture was diluted with brine (50 mL) and extracted with ethyl acetate (3×50 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate in petroleum ether to afford (S)-N-((1R)-5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide (2.0 g, 66% yield) as a yellow solid. MS (ESI) calcd. for $C_{13}H_{17}BrFNOS$: 333.02m/z, found: 334.10 $[M+H]^+$.

[00775] Step 4: Synthesis of (S)-N-((1R)-2-fluoro-5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide

[00776] A mixture of (S)-N-((1R)-5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide (2.0 g, 6.0 mmol), 3-nitro-6-(pyrazol-1-yl)pyridin-2-amine (1.35 g, 6.58 mmol), $Pd(OAc)_2$ (0.13 g, 0.60 mmol), Cs_2CO_3 (5.86g, 18.0 mmol) and XantPhos (0.35 g, 0.60 mmol) in dioxane (4.0 mL) was stirred at 100°C for 2 h under nitrogen atmosphere. The reaction was quenched with water (100 mL) and the mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were washed with brine (100 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using a gradient of methanol in

dichloromethane to afford (S)-N-((1R)-2-fluoro-5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide (2.5 g, 91% yield) as a yellow solid. MS (ESI) calcd. for $C_{21}H_{23}FN_6O_3S$, 458.15 m/z, found: 459.10 $[M+H]^+$.

[00777] Step 5: Synthesis of (S)-N-((1R)-5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide

[00778] To a solution of (S)-N-[(1R)-2-fluoro-5-{[3-nitro-6-(pyrazol-1-yl)pyridin-2-yl]amino}-2,3-dihydro-1H-inden-1-yl]-2-methylpropane-2-sulfinamide (2.5 g, 5.5 mmol) in DMF (30 mL) was added $B_2(OH)_4$ (1.47 g, 16.4 mmol) and 4-(pyridin-4-yl)pyridine (25.0 mg, 0.163 mmol). The resulting mixture was stirred at room temperature for 1 h. The reaction was quenched by the addition of water (200 mL) and then the mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were washed with brine (100 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure to afford (S)-N-((1R)-5-((3-amino-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide (2.0 g, 86% yield) as a yellow solid. MS (ESI) calcd. for $C_{21}H_{25}FN_6OS$: 428.17 m/z. found: 429.15 $[M+H]^+$.

[00779] Step 6: Synthesis of (S)-N-((1R)-5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide

[00780] To a solution of (S)-N-[(1R)-5-{[3-amino-6-(pyrazol-1-yl)pyridin-2-yl]amino}-2-fluoro-2,3-dihydro-1H-inden-1-yl]-2-methylpropane-2-sulfinamide (2.0 g, 4.7 mmol) and 2-aminopyridine-3-carbaldehyde (0.68 g, 5.6 mmol) in AcOH (60 mL) was added $Cu(OAc)_2$ (171 mg, 0.94 mmol). The mixture was stirred at 65°C for 1.0 h. After cooling to room temperature, the mixture was concentrated and the residue obtained was purified by reverse phase flash column chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05 mmol/L NH_4HCO_3) to afford (S)-N-((1R)-5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2-fluoro-2,3-dihydro-1H-inden-1-yl)-2-methylpropane-2-sulfinamide (1.47 g, 59% yield). MS (ESI) calcd. for $C_{27}H_{27}FN_8OS$, 530.20 m/z, found: 531.25 $[M+H]^+$. The two diastereomers were separated by chiral SFC on a (S,S)-Whelk-O 1 5µm Kromasil column using a 2:1 mix of CO_2 and [acetonitrile/methanol 4:1]. The first eluting peak was carried through step 7 below to afford Intermediate 147-1 and the second eluting peak was converted to Intermediate 147-2. *Denotes a stereocenter with undetermined absolute stereochemistry of a single diastereomer.

[00781] Step 7: Synthesis of 3-(3-((1*R*)-1-amino-2-fluoro-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (Intermediates 147-1 and 147-2)

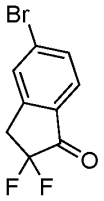
[00782] The two diastereomers of (*S*)-*N*-((1*R*)-5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2-fluoro-2,3-dihydro-1*H*-inden-1-yl)-2-methylpropane-2-sulfinamide (500 mg, 0.754 mmol) were dissolved separately in 4N HCl in dioxane (8mL) and the resulting mixtures were stirred at room temperature for 1h under nitrogen atmosphere. The solvent was removed under vacuum to afford 3-(3-((1*R*)-1-amino-2-fluoro-2,3-dihydro-1*H*-inden-5-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-2-yl)pyridin-2-amine (400 mg, crude) as a light yellow solid. MS (ESI) calcd. For $C_{23}H_{19}FN_8$: 426.17 m/z, found: 427.30 $[M+H]^+$.

[00783] The following compounds were prepared analogous to the synthetic preparation in Compound 147-1.

[00784] **Table 19B.** Characterization data of compounds prepared analogously to Compound 147-1.

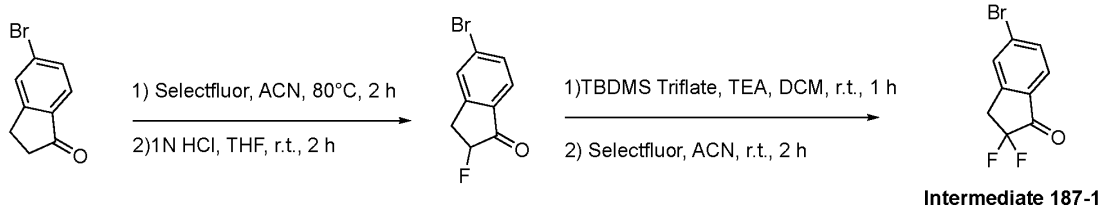
Cpd ID	Characterization Data
527	Observed mass (ESI): 411.25 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.25 - 8.46 (m, 2H), 7.91 - 8.04 (m, 1H), 7.76 - 7.89 (m, 1H), 7.62 - 7.75 (m, 1H), 7.52 - 7.62 (m, 1H), 7.18 - 7.48 (m, 5H), 6.44 - 6.63 (m, 1H), 4.18 - 4.32 (m, 1H), 2.82 - 2.93 (m, 1H), 2.69 - 2.81 (m, 1H), 2.33 - 2.42 (m, 1H), 1.58 - 1.73 (m, 1H).

[00785] **Intermediate 187-1: 5-bromo-2,2-difluoro-2,3-dihydro-1*H*-inden-1-one**



Intermediate 187-1

[00786] Synthetic Route:



Intermediate 187-1

[00787] **Step 1: Synthesis of 5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-one**

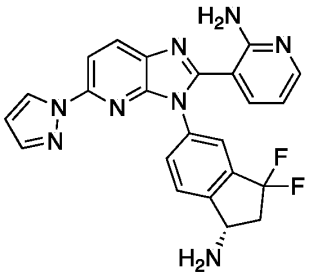
[00788] To a solution of 5-bromo-1-indanone (5.00 g, 23.8 mmol) in methanol (50 mL) was added SelectFluor (10.0 g, 28.2 mmol) and the resulting mixture was stirred under reflux for 2 hours. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The resulting residue was dissolved in tetrahydrofuran (50 mL), and 1 N

hydrochloric acid (50 mL) was added followed by stirring at room temperature for 3 hours. To the reaction mixture, a 2 N aqueous sodium hydroxide solution (50 mL) was added, and the mixture was diluted with a saturated aqueous sodium bicarbonate solution. The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure to afford 5-bromo-2-fluoro-2,3-dihydroinden-1-one (4.0 g, 74% yield) as a white solid. MS (ESI) calcd. for C_9H_6BrFO, 227.96 m/z, found: 229.00 $[M+H]^+$.

[00789] Step 2: 5-bromo-2,2-difluoro-2,3-dihydro-1H-inden-1-one (Intermediate 187-1)

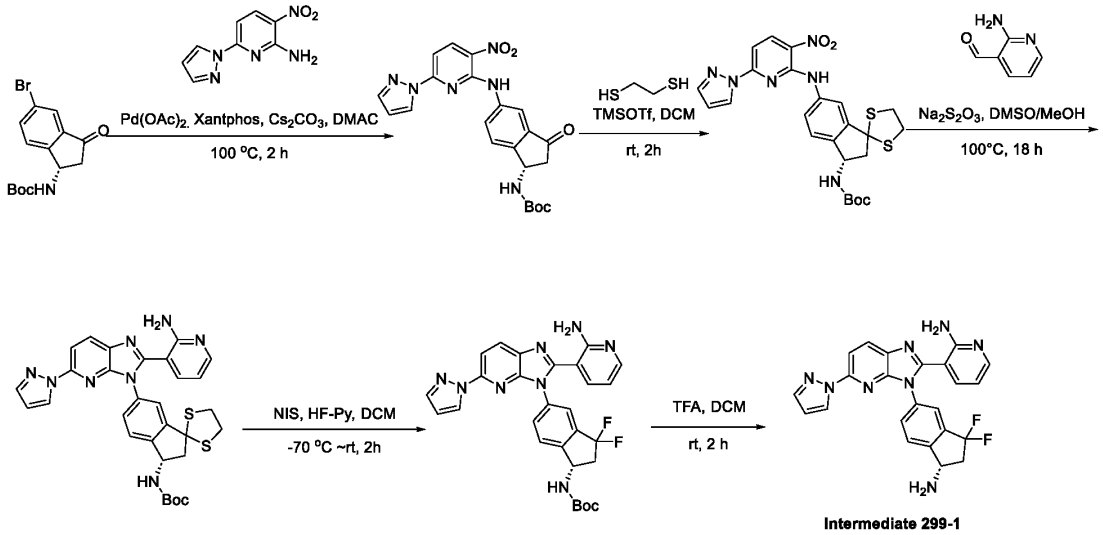
[00790] To a solution of 5-bromo-2-fluoro-2,3-dihydro-1H-inden-1-one (3.0 g, 13 mmol, 1 equiv) in DCM (30 mL) was added tert-butyldimethylsilyl trifluoromethanesulfonate (5.16 mL, 988 mmol, 70 equiv) and triethylamine (9.1 mL, 65.5 mmol, 5.0 equiv) and the resulting mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with saturated aqueous sodium bicarbonate and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The resulting residue was dissolved in acetonitrile (30 mL) and Selectfluor (5.57 g, 15.7 mmol, 1.2 equiv) was added. The resulting mixture was stirred at room temperature for 2 hours. The reaction mixture was diluted with saturated aqueous sodium bicarbonate and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. To the resulting residue, hexane was added, and the precipitate was collected by filtration to afford 5-bromo-2,2-difluoro-2,3-dihydro-1H-inden-1-one (Intermediate 187-1) (2.3 g, 71%). MS (ESI) calcd. for $C_9H_5BrF_2O$, 245.95 m/z, found: 247.00 $[M+H]^+$.

[00791] Intermediate 299-1: (S)-3-(3-(1-amino-3,3-difluoro-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine



Intermediate 299-1

[00792] Synthetic Route:



[00793] Step 1: Synthesis of tert-butyl (S)-(5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate

[00794] To a solution of tert-butyl (S)-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate (product of Step 4 of **Intermediate 312-2**) (1 g, 3.066 mmol, 1 equiv) and 3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-amine (0.69 g, 3.4 mmol, 1.1 equiv) in 1,4-dioxane (15 mL) were added Cs_2CO_3 (2.00 g, 6.13 mmol, 2 equiv), $Pd(OAc)_2$ (0.07 g, 0.3 mmol, 0.1 equiv) and XantPhos (0.35 g, 0.61 mmol, 0.2 equiv) at room temperature under N_2 atmosphere. After stirring for 2 h at 100°C under a nitrogen atmosphere, the mixture was allowed to cool to room temperature. The resulting mixture was filtered, the filter cake was washed with ethyl acetate (3 x 50 mL). The filtrate was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl (S)-(5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate (1 g, 72%) as a brown solid. MS (ESI) calcd. for $C_{22}H_{22}N_6O_5$, 450.17 m/z, found 451.15 $[M+H]^+$.

[00795] Step 2: Synthesis of tert-butyl (S)-(6-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate

[00796] To a stirred solution of tert-butyl (S)-(5-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate (1 g, 2.2 mmol, 1 equiv) and ethane-1,2-dithiol (0.42 g, 4.4 mmol, 2 equiv) in DCM (30 mL) was added TMSOTf (0.10 g, 0.44 mmol, 0.2 equiv) dropwise at 0°C. The resulting mixture was stirred for 2h at room temperature. The reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with ethyl acetate in

petroleum ether (0~50%) to afford tert-butyl (S)-(6-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate (900 mg, 77% yield) as a brown solid. MS (ESI) calcd. for $C_{24}H_{26}N_6O_4S_2$, 526.15 m/z, found 527.10 $[M+H]^+$.

[00797] Step 3: Synthesis of tert-butyl (S)-(6-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate

[00798] To a stirred solution of tert-butyl (S)-(6-((3-nitro-6-(1H-pyrazol-1-yl)pyridin-2-yl)amino)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate (900 mg, 1.709 mmol, 1 equiv) and 2-aminonicotinaldehyde (229.58 mg, 1.880 mmol, 1.1 equiv) in DMSO (24 mL) and MeOH (4 mL) was added $Na_2S_2O_4$ (654.57 mg, 3.760 mmol, 2.2 equiv) at room temperature. The resulting mixture was stirred for 18 h at 100°C. The mixture was allowed to cool to room temperature. The mixture was basified to pH 7 with sat. $NaHCO_3$. The resulting mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl (S)-(6-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate (500 mg, 48.86% yield) as a yellow solid. MS (ESI) calcd. for $C_{30}H_{30}N_8O_2S_2$, 598.19 m/z, found 599.20 $[M+H]^+$.

[00799] Step 4: Synthesis of tert-butyl (S)-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-3,3-difluoro-2,3-dihydro-1H-inden-1-yl)carbamate

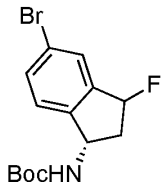
[00800] To a solution of NIS (338.19 mg, 1.503 mmol, 3 equiv) in DCM (5 mL) was added dropwise pyridine hydrofluoride (993.15 mg, 10.020 mmol, 20 equiv) (70% in Pyridine) at -78 °C under N_2 atmosphere. The reaction mixture was stirred at -78°C for 30 mins. Then a solution of tert-butyl (S)-(6-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydrospiro[indene-1,2'-[1,3]dithiolan]-3-yl)carbamate (300 mg, 0.501 mmol, 1 equiv) in 2 mL DCM was added dropwise and the mixture was stirred for another 10 mins at -78°C. The resulting mixture was stirred for 2 h at room temperature. The reaction was quenched with sat. $NaHCO_3$ (50 mL), and the mixture was extracted with ethyl acetate (2*50mL). The combined organic extracts were washed with brine (50mL), dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford tert-butyl (S)-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-3,3-difluoro-2,3-dihydro-1H-inden-1-

yl)carbamate (110 mg, 40.31% yield) as a yellow solid. MS (ESI) calcd. for $C_{28}H_{26}F_2N_8O_2$, 544.21 m/z, found 545.20 $[M+H]^+$.

[00801] Step 5: Synthesis of (S)-3-(3-(1-amino-3,3-difluoro-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (Intermediate 299-1)

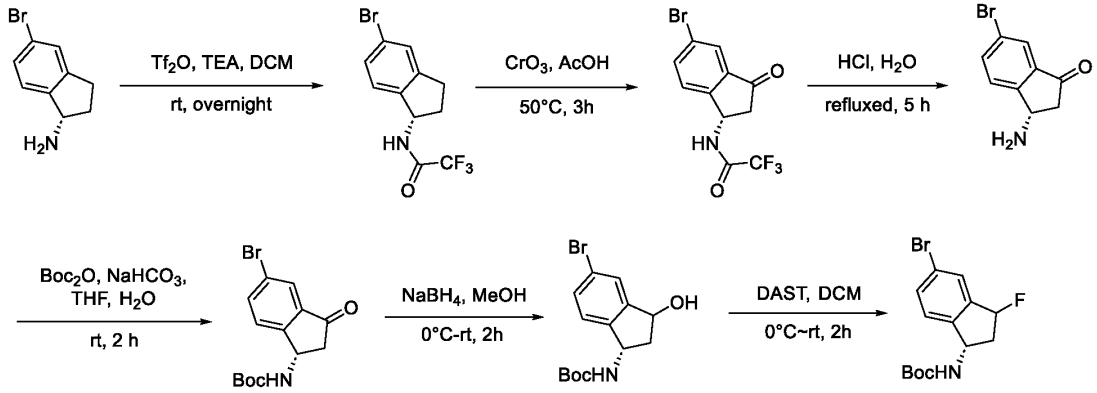
[00802] A solution of tert-butyl (S)-(5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-3,3-difluoro-2,3-dihydro-1H-inden-1-yl)carbamate (50 mg, 0.092 mmol, 1 equiv) in DCM (1.5 mL) was treated with TFA (0.5 mL) at room temperature. The resulting mixture was stirred for 2h at room temperature. The mixture was concentrated under vacuum and the residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-3-(3-(1-amino-3,3-difluoro-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Intermediate 299-1**) (9.5 mg, 22% yield) as a white solid. MS (ESI) calcd. for $C_{23}H_{18}F_2N_8$, 444.16 m/z, found 445.10 $[M+H]^+$.

[00803] Intermediate 312-2: *tert*-butyl ((1*S*)-5-bromo-3-fluoro-2,3-dihydro-1*H*-inden-1-yl)carbamate



Intermediate 312-2

[00804] Synthetic Route:



Intermediate 312-2

[00805] Step 1: Synthesis of (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide

[00806] A solution of (1S)-5-bromo-2,3-dihydro-1H-inden-1-amine (50 g, 236 mmol, 1 equiv) and TEA (55.7 g, 550 mmol, 2 equiv) in DCM (750 mL) was added TFAA (63.25 g, 301.1 mmol, 1.3 equiv) at 0°C. The resulting mixture was stirred overnight at room temperature. The reaction was quenched with H_2O (500 mL) at room temperature. The aqueous layer was extracted with DCM (2 x 500 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure to afford crude (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide (86 g) as a white solid. MS (ESI) calcd. for $C_{11}H_9BrF_3NO$, 306.98 m/z, found: 306.10 $[M-H]^-$.

[00807] **Step 2: Synthesis of (S)-N-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide**

[00808] A solution of (S)-N-(5-bromo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide (50 g, 162 mmol, 1.00 equiv) and CrO_3 (48.8 g, 488 mmol, 3.00 equiv) in AcOH (600 mL) was stirred for 2 h at 50°C under air atmosphere. The mixture was allowed to cool to room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with ethyl acetate in petroleum ether (0~20%) to afford (S)-N-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide (11.5 g, 22%) as a white solid. MS (ESI) calcd. for $C_{11}H_7BrF_3NO_2$, 320.96 m/z, found: 319.90 $[M-H]^-$.

[00809] **Step 3: Synthesis of (S)-3-amino-6-bromo-2,3-dihydro-1H-inden-1-one**

[00810] A solution of (S)-N-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoroacetamide (10 g, 31 mmol, 1 equiv) in 6M aqueous HCl (200 mL) was refluxed 5 h. The resulting mixture was concentrated under reduced pressure and the residue was triturated with Et_2O (200 mL). The residue was filtered and dried to afford (S)-3-amino-6-bromo-2,3-dihydro-1H-inden-1-one (7 g, crude quant.) as a white solid. MS (ESI) calcd. for C_9H_8BrNO, 224.98 m/z, found 224.05 $[M-H]^-$.

[00811] **Step 4: Synthesis of tert-butyl (S)-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate**

[00812] To a stirred solution of (S)-3-amino-6-bromo-2,3-dihydro-1H-inden-1-one (7 g, 31 mmol, 1 equiv) in THF (60 mL) and H_2O (15 mL) were added $NaHCO_3$ (5.20 g, 61.9 mmol, 2 equiv) and Boc_2O (8.11 g, 37.2mmol, 1.2 equiv) in portions at 0°C. The resulting mixture was stirred for 2h at room temperature. The reaction was quenched with water (100 mL). The resulting mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with ethyl acetate in petroleum ether (0~50%) to afford tert-butyl (S)-

(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate (7 g, 69% yield) as an off-white solid. MS (ESI) calcd. for $C_{14}H_{16}BrNO_3$, 325.03 m/z, found 324.10 $[M-H]^-$.

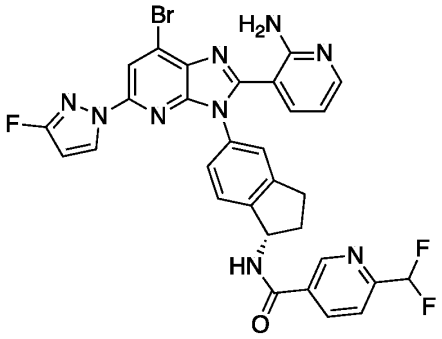
[00813] Step 5: Synthesis of tert-butyl ((1S)-5-bromo-3-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamate

[00814] To a stirred solution of tert-butyl (S)-(5-bromo-3-oxo-2,3-dihydro-1H-inden-1-yl)carbamate (7 g, 21mmol, 1 equiv) in MeOH (100 mL) was added $NaBH_4$ (1.62 g, 42.9 mmol, 2 equiv) in portions at 0°C. The resulting mixture was stirred for 2h at room temperature. The reaction was quenched by the addition of water (200 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 300 mL). The combined organic layers were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluting with ethyl acetate in petroleum ether (0~50%) to afford tert-butyl ((1S)-5-bromo-3-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamate (5 g, 71%) as a white solid. MS (ESI) calcd. for $C_{14}H_{18}BrNO_3$, 327.05 m/z, found 326.10 $[M-H]^-$.

[00815] Step 6: Synthesis of tert-butyl ((1S)-5-bromo-3-fluoro-2,3-dihydro-1H-inden-1-yl)carbamate (Intermediate 312-2)

[00816] To a stirred solution of tert-butyl ((1S)-5-bromo-3-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamate (5 g, 15 mmol, 1 equiv) in DCM (100 mL) was added DAST (4.91 g, 30.5 mmol, 2 equiv) in portions at 0°C. The resulting mixture was stirred for 2h at room temperature. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (200 mL) at room temperature. The resulting mixture was extracted with ethyl acetate (3 x 300 mL). The combined organic layers were washed with brine (300 mL) and dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with ethyl acetate in petroleum ether (0~30%) to afford tert-butyl ((1S)-5-bromo-3-fluoro-2,3-dihydro-1H-inden-1-yl)carbamate (**Intermediate 312-2**) (4 g, 80% yield) as a white solid. MS (ESI) calcd. for $C_{14}H_{17}BrFNO_2$, 329.04 m/z, found 310.15 $[M-F]^+$.

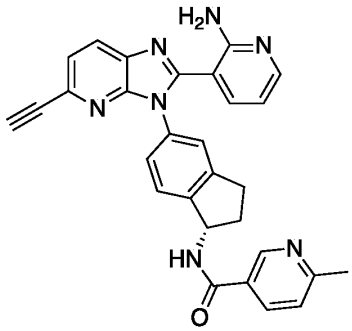
[00817] Intermediate 329-1: (S)-N-(5-(2-(2-aminopyridin-3-yl)-7-bromo-5-(3-fluoro-1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-(difluoromethyl)nicotinamide



Intermediate 329-1

[00818] **Intermediate 329-1** was prepared in a manner analogous to **Intermediate 122-2** (via **Intermediate 122-1**) using 3-fluoropyrazole in place of pyrazole. MS (ESI) calcd. for $C_{30}H_{21}BrF_3N_9O$, 659.10 m/z, found 660.08 $[M+H]^+$.

[00819] **Intermediate 341-1: (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-ethynyl-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-methylnicotinamide**



Intermediate 341-1

[00820] Synthetic Route:

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[00821] **Step 1: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-((trimethylsilyl)ethynyl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide**

[00822] To a stirred solution of (*S*)-*N*-(5-(2-(2-aminopyridin-3-yl)-5-bromo-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6-methylnicotinamide (**Intermediate 265-1**) (300 mg, 0.431 mmol, 1 equiv), CuI (16.41 mg, 0.086 mmol, 0.2 equiv), $Pd(PPh_3)_4$ (99.57 mg, 0.086 mmol, 0.2 equiv) and DIEA (167.04 mg, 1.293 mmol, 3 equiv) in DMF (2 mL) was added trimethylsilylacetylene (211.58 mg, 2.155 mmol, 5 equiv) under N_2 atmosphere. The reaction mixture was stirred at 90°C for 2 h. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-((trimethylsilyl)ethynyl)-

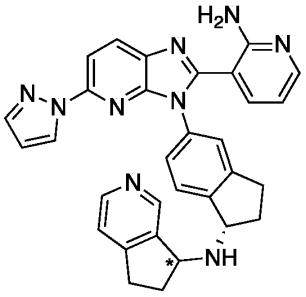
3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (147 mg, 11.37% yield) as an off-white solid. MS (ESI) calcd. for $C_{32}H_{31}N_7OSi$: 557.20 m/z, found: 558.30 $[M+H]^+$.

[00823] Step 2: Synthesis of (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-ethynyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (Intermediate 341-1)

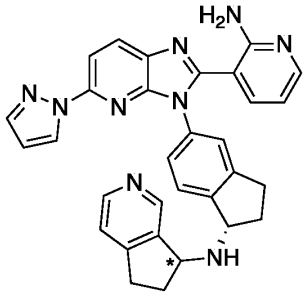
[00824] To a solution of N-[(1S)-5-[2-(2-aminopyridin-3-yl)-5-[2-(trimethylsilyl)ethynyl]imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]-6-methylpyridine-3-carboxamide (200 mg, 0.359 mmol, 1 equiv) in DMF (2 mL) was added triethylamine trihydrofluoride (173.43 mg, 1.077 mmol, 3 equiv) at rt. The resulting mixture was stirred for 2 h at rt. The crude product was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford (S)-N-(5-(2-(2-aminopyridin-3-yl)-5-ethynyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6-methylnicotinamide (**Intermediate 341-1**) (135 mg, 77.52% yield) as yellow oil. MS (ESI) calcd. for $C_{29}H_{23}N_7O$: 485.20 m/z, found: 486.30 $[M+H]^+$.

[00825] Example 495: (*S)-*N*-((*S*)-5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6,7-dihydro-5*H*-cyclopenta[*c*]pyridin-7-amine and**

[00826] Example 496: (*R)-*N*-((*S*)-5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)-6,7-dihydro-5*H*-cyclopenta[*c*]pyridin-7-amine**

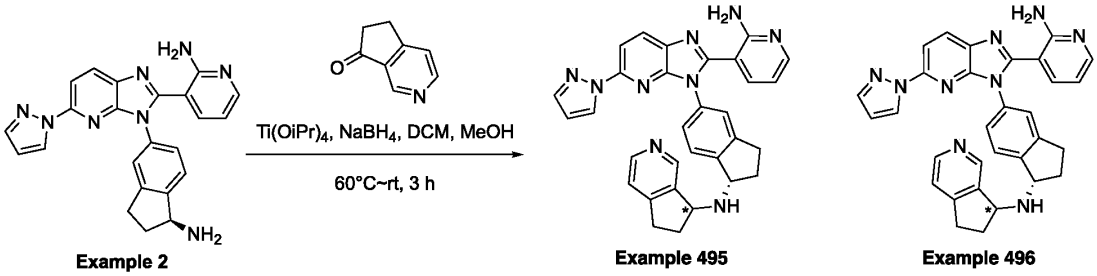


Example 495



Example 496

Synthetic Route:



Example 2 Example 495 Example 496

[00827] Step 1: Synthesis of N-((S)-5-(2-(2-aminopyridin-3-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-3-yl)-2,3-dihydro-1H-inden-1-yl)-6,7-dihydro-5H-cyclopenta[c]pyridin-7-amine

[00828] A solution of (S)-3-(3-(1-amino-2,3-dihydro-1H-inden-5-yl)-5-(1H-pyrazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine (**Example 2**) (500 mg, 1.224 mmol, 1 equiv), 5H,6H-cyclopenta[c]pyridin-7-one (325.9 mg, 2.448 mmol, 2 equiv) and tetrakis(propan-2-yloxy)titanium (1739.5 mg, 6.120 mmol, 5 equiv) in DCM (10 mL) and MeOH (2 mL) was stirred at 60°C for 1 h. Then to the mixture was added $NaBH_4$ (92.6 mg, 2.448 mmol, 2 equiv) at 0°C. The resulting mixture was stirred at room temperature for 2 h. The reaction was quenched with water (20 ml) at 0°C. The resulting mixture was extracted with DCM (3 x 50 ml). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by reverse-phase flash chromatography on C18 silica gel using a gradient of acetonitrile in water (+ 0.05% ammonium bicarbonate) to afford crude product. The diastereomers were separated by Chiral-HPLC on a CHIRALPAK IA column using a mixture of [Hex/DCM (3:1) (+ 0.5% 2M NH3-MeOH)] and IPA to afford **Example 496** (39.0 mg, 6.06% yield) as an off-white solid and

[00829] **Example 495** (59.7 mg, 9.28% yield) as an off-white solid. * Note that the stereochemistry of the newly formed stereocenter was assumed.

[00830] **Example 495**: MS (ESI) calcd. for $C_{31}H_{27}N_9$, 525.24 m/z, found 526.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.55 - 8.68 (m, 1H), 8.30 - 8.40 (m, 3H), 7.90 - 8.10 (m, 2H), 7.80 - 7.90 (m, 1H), 7.50 - 7.60 (m, 1H), 7.30 - 7.40 (m, 1H), 7.26 - 7.30 (m, 1H), 7.20 - 7.26 (m, 2H), 6.50 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 4.41 - 4.50 (m, 1H), 4.30 - 4.41 (m, 1H), 2.90 - 3.10 (m, 2H), 2.72 - 2.90 (m, 2H), 2.40 - 2.52 (m, 2H), 1.80 - 2.00 (m, 2H).

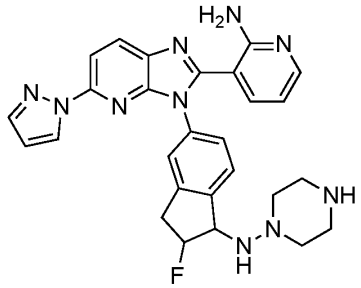
[00831] **Example 496**: MS (ESI) calcd. for $C_{31}H_{27}N_9$, 525.24 m/z, found 526.30 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.50 - 8.68 (m, 1H), 8.30 - 8.40 (m, 3H), 8.00 - 8.10 (m, 1H), 7.90 - 8.00 (m, 1H), 7.80 - 7.90 (m, 1H), 7.50 - 7.60 (m, 1H), 7.30 - 7.40 (m, 2H), 7.20 - 7.28 (m, 2H), 6.50 - 6.60 (m, 1H), 6.40 - 6.50 (m, 1H), 4.30 - 4.50 (m, 2H), 2.90 - 3.10 (m, 2H), 2.72 - 2.90 (m, 2H), 2.45 - 2.50 (m, 1H), 2.30 - 2.45 (m, 1H), 1.75 - 1.95 (m, 2H).

[00832] The following compounds were prepared analogous to the synthetic preparation in Example Compounds 495 and 496.

[00833] Table 19C. Characterization data of compounds prepared analogously to Compound 495 and Compound 496.

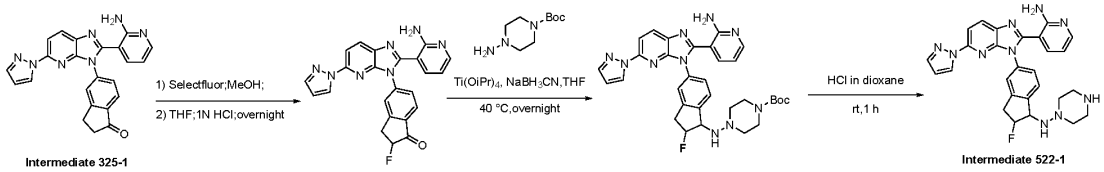
Cpd ID	Characterization Data
498	Observed mass (ESI): 541.15 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.31 - 8.38 (m, 2H), 8.16 - 8.20 (m, 1H), 7.99 - 8.02 (m, 1H), 7.95 - 7.98 (m, 1H), 7.78 - 7.82 (m, 1H), 7.57 - 7.62 (m, 1H), 7.38 - 7.40 (m, 1H), 7.19 - 7.30 (m, 3H), 6.84 - 6.96 (m, 2H), 6.64 - 6.68 (m, 1H), 6.54 - 6.62 (m, 1H), 6.50 - 6.53 (m, 1H), 6.38 - 6.46 (m, 1H), 4.50 - 4.61 (m, 1H), 4.35 - 4.47 (m, 1H), 2.96 - 3.06 (m, 1H), 2.79 - 2.92 (m, 2H), 2.65 - 2.76 (m, 1H), 2.48 - 2.53 (m, 1H), 2.38 - 2.46 (m, 1H), 1.91 - 2.05 (m, 2H).
499	Observed mass (ESI): 541.2 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.31 - 8.39 (m, 2H), 8.17 - 8.22 (m, 1H), 7.91 - 8.03 (m, 2H), 7.78 - 7.82 (m, 1H), 7.53 - 7.59 (m, 1H), 7.34 - 7.39 (m, 1H), 7.17 - 7.30 (m, 3H), 6.91 - 7.01 (m, 2H), 6.65 - 6.68 (m, 1H), 6.55 - 6.62 (m, 1H), 6.50 - 6.53 (m, 1H), 6.39 - 6.46 (m, 1H), 4.42 - 4.50 (m, 1H), 4.30 - 4.40 (m, 1H), 2.92 - 3.02 (m, 1H), 2.73 - 2.91 (m, 2H), 2.61 - 2.71 (m, 1H), 2.50 - 2.53 (m, 1H), 2.30 - 2.41 (m, 1H), 1.82 - 1.99 (m, 2H).

[00834] Intermediate 522-1: *N*-(5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2-fluoro-2,3-dihydro-1*H*-inden-1-yl)piperazin-1-amine



Intermediate 522-1

[00835] Synthetic Route:



[00836] Step 1: Synthesis of 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydroinden-1-one

[00837] A mixture of 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydroinden-1-one (**Intermediate 325-1**) (500 mg, 1.227 mmol, 1 equiv) and

SelectFluor (1 g, 2.823 mmol, 2.30 equiv) in MeOH was stirred for 2 hours under reflux. The reaction mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. The resulting residue was dissolved in tetrahydrofuran (30 mL), and 1 N hydrochloric acid (30 mL) was added. The mixture was stirred at room temperature for 3 hours. To the reaction mixture, a 2 N aqueous sodium hydroxide solution (20 mL) was added, and the mixture was diluted with saturated aqueous sodium bicarbonate then extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to afford 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydroinden-1-one as a white solid. MS (ESI) calcd. for $C_{23}H_{16}FN_7O$, 425.14 m/z, found: 426.10 $[M+H]^+$.

[00838] Step 2: Synthesis of tert-butyl 4-({5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydro-1H-inden-1-yl}amino)piperazine-1-carboxylate

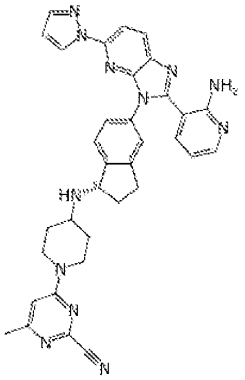
[00839] To a solution of 5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydroinden-1-one (450 mg, 1.058 mmol, 1 equiv) in THF (20 mL) was added tetrakis(propan-2-yloxy)titanium (600 mg, 2.111 mmol, 2.00 equiv) and tert-butyl 4-aminopiperazine-1-carboxylate (320 mg, 1.590 mmol, 1.50 equiv). The resulting mixture was stirred at 40°C for 4 h then cooled to 0°C. $NaBH_3CN$ (300 mg, 4.774 mmol, 4.51 equiv) was added and the resulting mixture was stirred at 40°C overnight. The reaction was quenched with H_2O (2 mL). The resulting mixture was concentrated under reduced pressure. The residue was purified by reverse phase column chromatography on C18 silica gel (0 – 41 % ACN/0.05 % TFA in water) to afford tert-butyl 4-({5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydro-1H-inden-1-yl}amino)piperazine-1-carboxylate (70 mg, 87% purity) as a yellow solid. MS (ESI) calcd. for $C_{32}H_{35}FN_{10}O_2$: 610.29 m/z, found: 611.30 $[M+H]^+$.

[00840] Step 3: Synthesis of N-{5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydro-1H-inden-1-yl}piperazin-1-amine (Intermediate 522-1)

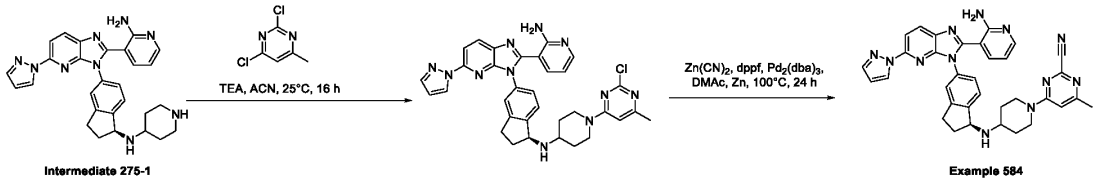
[00841] A solution of tert-butyl 4-({5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydro-1H-inden-1-yl}amino)piperazine-1-carboxylate (70 mg, 0.115 mmol, 1 equiv) in 4N HCl in 1,4-dioxane (3 mL) was stirred at r.t for 1h. The residue was adjusted to pH 8 with saturated $NaHCO_3$ and extracted with MeOH:DCM (1:10). The combined organic layers were washed with water and brine then dried over Na_2SO_4. After filtration, the filtrate was concentrated to afford N-{5-[2-(2-aminopyridin-3-yl)-5-

(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2-fluoro-2,3-dihydro-1H-inden-1-yl}piperazin-1-amine (**Intermediate 522-1**) (50 mg, 90%purity) as a yellow solid. MS (ESI) calcd. for $C_{27}H_{27}FN_{10}$: 510.24 m/z, found: 511.30 $[M+H]^+$.

[00842] Example 584: (*S*)-4-(4-((5-(2-(2-aminopyridin-3-yl)-5-(1*H*-pyrazol-1-yl)-3*H*-imidazo[4,5-*b*]pyridin-3-yl)-2,3-dihydro-1*H*-inden-1-yl)amino)piperidin-1-yl)-6-methylpyrimidine-2-carbonitrile



[00843] Synthetic Route:



[00844] Step 1: Synthesis of 3-{3-[(1S)-1-{[1-(2-chloro-6-methylpyrimidin-4-yl)piperidin-4-yl]amino}-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine

[00845] To a stirred solution of 3-{3-[(1S)-1-(piperidin-4-ylamino)-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (**Intermediate 275-1**) (510 mg, 1.037 mmol, 1 equiv) and 2,4-dichloro-6-methylpyrimidine (338.20 mg, 2.074 mmol, 2 equiv) in MeCN (30 mL) was added Et_3N (839.84 mg, 8.296 mmol, 8 equiv) at 25 °C. The resulting mixture was stirred at 25 °C for 16 h. The residue was purified by silica gel column chromatography, eluting with CH_2Cl_2 / MeOH (10:1) to afford 3-{3-[(1S)-1-{[1-(2-chloro-6-methylpyrimidin-4-yl)piperidin-4-yl]amino}-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (306 mg, 47.72%yield, 98%purity) as a yellow solid. Observed mass (ESI): 618.35 $[M+H]^+$.

[00846] Step 2: Synthesis of 4-(4-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}piperidin-1-yl)-6-

methylpyrimidine-2-carbonitrile (TER-6308)

[00847] To a stirred solution of 3-{3-[(1S)-1-{[1-(2-chloro-6-methylpyrimidin-4-yl)piperidin-4-yl]amino}-2,3-dihydro-1H-inden-5-yl]-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-2-yl}pyridin-2-amine (260 mg, 0.421 mmol, 1 equiv) and $Zn(CN)_2$ (74.08 mg, 0.631 mmol, 1.5 equiv) in N,N-dimethylacetamide (5 mL) were added Dppf (46.64 mg, 0.084 mmol, 0.2 equiv) and $Pd_2(dba)_3$ (77.03 mg, 0.084 mmol, 0.2 equiv) at 25 °C. To the above mixture was added Zn (13.75 mg, 0.210 mmol, 0.5 equiv) at 25 °C. The resulting mixture was stirred at 100 °C for 24 h under N_2 atmosphere. The residue was purified by Prep-TLC (CH_2Cl_2 / MeOH 10:1) to afford crude product. The crude product (200 mg) was purified by Prep-HPLC on a XBridge Prep OBD C18 Column using a gradient of acetonitrile in water (+ 10 mmol/L ammonium bicarbonate) to afford 4-(4-{[(1S)-5-[2-(2-aminopyridin-3-yl)-5-(pyrazol-1-yl)imidazo[4,5-b]pyridin-3-yl]-2,3-dihydro-1H-inden-1-yl]amino}piperidin-1-yl)-6-methylpyrimidine-2-carbonitrile (**Example 584**) (96.8 mg, 37.81%yield, 99.3%purity) as a white solid. Observed mass (ESI): 609.35 $[M+H]^+$. ^1H NMR (400 MHz, DMSO-d6) δ (ppm): 8.32 - 8.39 (m, 2H), 7.98 - 8.04 (m, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.81 (s, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.34 (s, 1H), 7.20 - 7.29 (m, 2H), 7.04 (s, 1H), 6.94 (s, 2H), 6.53 - 6.57 (m, 1H), 6.39 - 6.47 (m, 1H), 4.11 - 4.41 (m, 3H), 3.12 - 3.23 (m, 2H), 2.92 - 3.03 (m, 2H), 2.71 - 2.85 (m, 1H), 2.44 - 2.47 (m, 1H), 2.30 (s, 3H), 2.08 - 2.17 (m, 1H), 1.98 - 2.06 (m, 1H), 1.88 - 1.96 (m, 1H), 1.72 - 1.85 (m, 1H), 1.21 - 1.39 (m, 2H).

[00848] Table 19D. Characterization data of Compounds 594, 600, and 601.

Cpd ID	Characterization Data
594	Observed mass (ESI): 601.2 [M+H]+. 1H NMR (400 MHz, DMSO-d6) δ 9.41 (d, J = 8.3 Hz, 1H), 8.64 – 8.59 (m, 1H), 8.42 (d, J = 8.6 Hz, 1H), 8.04 (s, 1H), 7.96 – 7.91 (m, 1H), 7.81 (d, J = 0.9 Hz, 1H), 7.55 – 7.40 (m, 4H), 7.39 – 7.31 (m, 2H), 7.24 (s, 1H), 6.65 – 6.54 (m, 1H), 5.64 – 5.55 (m, 1H), 3.98 (s, 3H), 3.05 – 3.00 (m, 1H), 2.97 – 2.87 (m, 1H), 2.78 – 2.75 (m, 1H), 2.62 – 2.56 (m, 1H), 2.11 – 2.00 (m, 1H).
600	Observed mass (ESI): 582.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.33 - 8.41 (m, 2H), 8.02 - 8.06 (m, 1H), 7.98 - 8.01 (m, 1H), 7.82 - 7.85 (m, 1H), 7.51 - 7.59 (m, 1H), 7.39 - 7.42 (m, 1H), 7.32 - 7.37 (m, 1H), 7.20 - 7.29 (m, 2H), 6.55 - 6.59 (m, 1H), 6.51 - 6.57 (m, 1H), 4.59 - 4.65 (m, 1H), 4.30 - 4.41 (m, 1H), 2.97 - 3.07 (m, 2H), 2.74 - 2.90 (m, 3H), 2.48 - 2.51 (m, 1H), 2.30 - 2.38 (m, 1H), 1.89 - 1.99 (m, 1H).
601	Observed mass (ESI): 582.35 [M+H]+. 1H NMR (300 MHz, DMSO-d6) δ (ppm): 8.33 - 8.41 (m, 2H), 7.98 - 8.06 (m, 2H), 7.82 - 7.85 (m, 1H), 7.51 - 7.59 (m, 1H), 7.05 - 7.40 (m, 4H), 6.58 - 6.61 (m, 1H), 6.46 - 6.51 (m, 1H), 4.59 - 4.65 (m, 1H), 4.30 - 4.38 (m, 1H), 2.98 - 3.09 (m, 2H), 2.74 - 2.90 (m, 3H), 2.48 - 2.51 (m, 1H), 2.30 - 2.38 (m, 1H), 1.89 - 1.99 (m, 1H).

[00849] Example 102: AKT1 Inhibition Data

[00850] Antiproliferative effects in LAPC4 cells.

[00851] LAPC4 prostate cancer cells (Klein, K. A. et al. *Nat Med* 1997, 3, 402–408), which express the AKT1 E17K allele, were grown in IMDM media (Hyclone) supplemented with 12% FBS + 1% P/S. To assess compound effects on growth, 1,000 cells/well were seeded in 384 well assay plates, incubated with compound dilutions dissolved in DMSO. After 72 h, intracellular ATP content was assessed with CellTiter Glo reagent (Promega) according to the manufacturer's instructions. IC_{50} values were calculated by fitting luminescence values to a log(inhibitor) vs. response Hill equation.

[00852] **Determining live cell AKT1 E17K, AKT1 WT, and AKT2 target engagement by NanoBRET competitive probe displacement.** Live cell target engagement assays were performed as described (Vasta, J. D. et al. *Cell Chem Biol* 2018, 25(11), 206-214). Briefly, HEK293 cells were transfected with plasmids encoding kinase-NanoLuciferase fusion proteins overnight. Cells were then treated with serial dilutions of compound and an ~EC_{50} concentration of fluorescently-tagged ATP-competitive tracer (Promega). After incubation for 2 h at 37 °C, luciferase substrate and extracellular luciferase inhibitor were added to all wells, and luminescent intensity at 460 nm and 600 nm were measured on a multimode plate-reader. The ratio of E_{600}/E_{460} was calculated to give the tracer engagement signal (BRET). IC_{50} values were calculated by fitting BRET values to a log(inhibitor) vs. response Hill equation.

[00853] **Table 20** provides IC_{50} values for selected compounds of the present disclosure.

Cpd ID	AKT1 WT IC50 (nM)	AKT1 E17K IC50 (nM)	AKT2 IC50 (nM)	LAPC4 proliferation IC50 (nM)
1	> 737	> 1.00E+03	4310	
2	61.9	> 1.00E+03	858	8980
3	7.21	120	132	1710
4	19.7	172	295	1770
5	129	> 1.00E+03	1410	9300
6	10.8	179	307	1660
7	7.29	320	118	2600
8	2.97	10.8	55.8	523
9	> 1.00E+03	> 1.00E+03	8890	
10	390	> 1.00E+03	> 10.0E+03	> 10.0E+03
11	> 1.00E+03	> 1.00E+03	> 10.0E+03	
12	7.56	10.5	38.1	740
13	49.4	329	1270	3480
14	14.5	22.9	264	1290
15	215	> 1.00E+03	4030	> 10.0E+03
16	2.41	10.2	66.5	560
17	5.78	41.2	90.6	1020
18	10.5	44.4	55.5	733
19	43.5	167	2120	8030
20	126	137	713	8490
21	4.46	20.9	30.2	1050
22	11.2	31.9	67.6	1260

23	4.61	390	46.6	1200
24	55.1	232	846	6360
25	2.11	7.43	9.84	576
26	6.46	26.8	69.6	1060
27	> 1.00E+03		> 10.0E+03	
28	2.53	12.1	6.6	225
29	15.9	78.6	153	3650
30	10.6	51.1	127	721
31	33.9	366	470	7880
32	11	49	123	914
33	19.6	> 1.00E+03	321	3750
34	6.27	24.1	64	555
35	14.2	143	98.6	1750
36	58.6	164	1250	3460
37	175	> 1.00E+03	7720	> 10.0E+03
38	4.07	25.6	19	585
39	49.2	211	754	5190
40	9.21	36	179	1770
41	6.36	30.1	57.4	1170
42	2.84	14.4	40.7	631
43	14.1	44.2	139	1160
44	9.55	74.1	141	1400
45	17.4	170	139	1340
46	6.94	15	17	331
47	> 1.00E+03		> 10.0E+03	
48	155	> 1.00E+03	2850	> 10.0E+03
49	199	> 1.00E+03	2840	> 10.0E+03
50	279	> 1.00E+03	3740	> 10.0E+03
51	137	> 1.00E+03	4560	> 10.0E+03
52	11.6	357	128	915
53	18.1	142	118	1120
54	12	17.4	10.7	207
55	16.2	107	49.2	1510
56	12.2	143	43.3	1630
57	23.4	192	52.8	1320
58	30.7	157	2040	1900
59	48.8	261	3430	3620
60	2.5	62.1	31.5	741
61	4.75	72.6	49.7	921
62	4.97	64	59.5	692
63	2.57	73.9	12.6	970
64	4.63	159	183	2620
65	19.4	292	1070	925
66	8.95		15	
67	15	229	636	1140
68	5.29		15.2	
69	10.9		71.6	
70	49.4		576	
71	4.63		69.7	
72	7.95		28.1	

73	9.03		49.8	
74	4.94		34.8	
75	5.99		73.6	
76	6.86		39.4	
77	13.6		50.1	
78	106		1910	
79	19.5		540	
80	8.65		28.4	
81	121		2900	
82	65.8		2140	
83	139		867	
84	113		1960	
85	36.3		169	
86	46.8		427	
87	149		1900	
88	155		1810	
89	459		> 10.0E+03	
90	228		5850	
91	198		763	
92	42.8		1140	
93	38.8		1790	
94	7.33		18.8	
95	6.98		9.41	
96	18.6		94.7	
97	21.9		83.5	
98	13.2		52.6	
99	28.4		260	
100	17.2		24.9	
101	11.9		8.02	
102	31.5		836	
103	25.2		316	
104	317		> 10.0E+03	
105	11.2		109	
106	6.39		36	
107	118		> 10.0E+03	
108	18.8		223	
109	257		5830	
110	46.2		963	
111	178		4500	
112	9.53		52.7	
113	21		537	
114	9.15		102	
115	5.16		31.7	
116	10.2	157	303	5240
117	5.32		103	
118	66.2		3230	
119	90.8		3160	
120	5.61		103	
121	36.6		1590	
122	10.6		34.6	

123	9.84		114	
124	13.9		54.8	
125	13.3		201	
126	721		532	
127	12.6		126	
128	34.4		442	
129	111		> 10.0E+03	
130	46.4		2290	
131	42.5		785	
132	> 1.00E+03		2550	
133	76.2		1340	
134	> 1.00E+03		> 10.0E+03	
135	83.1		1110	
136	19.8		284	
137	21.5		174	
138	13.5		284	
139	89.6		5850	
140	31.5		576	
141	52.6		734	
142	43.8		886	
143	24.9		138	
144	43.6		520	
145	170		> 10.0E+03	
146	508		> 10.0E+03	
147	19.6		131	
148	16.7		107	
149	50.3		1580	
150	18.2		107	
151	22.8		366	
152	61.7		984	
153	120		2220	
154	508		3180	
155	16.5		197	
156	39.3		722	
157	40.5		521	
158	13.5		124	
159	4.65		22.1	
160	53.5		560	
161	94.6		1910	
162	9.12		37.8	
163	20.4		363	
164	15.3		180	
165	11.6		100	
166	29.9		687	
167	40.9		830	
168	41.1		1010	
169	12		228	
170	69.6		1380	
171	7.74		82.9	
172	203		2390	

173	30.2		226	
174	13.2	52	431	1440
175	13		79.7	
176	24.7		315	
177	10.6		47.2	
178	88.2		3520	
179	80		1270	
180	91.8		1150	
181	78.4		3680	
182	11.5		219	
183	330		> 10.0E+03	
184	114		4740	
185	65.3		1540	
186	76.3		3270	
187	6.73		21.3	
188	20		650	
189	554		2850	
190	25.5		122	
191	9.23		78.6	
192	9.54		86.4	
193	6.71		42.3	
194	9.37		39.5	
195	12.4		48.9	
196	9.31		72.4	
197	14.7		95.3	
198	9.5		113	
199	10.6		83.1	
200	14.7		212	
201	9.27		66.5	
202	5.59		29.4	
203	10.5		99.6	
204	9.42		53.1	
205	168		2340	
206	121		1780	
207	151		2520	
208	32.4		1030	
209	37.7		316	
210	95.8		596	
211	32.1		824	
212	57.8		158	
213	13.8		60.6	
214	56.9		2690	
215	21.5		381	
216	58.4		1390	
217	38.9		328	
218	643		4400	
219	119		6640	
220	68.2		6260	
221	10.9	5.8	449	1280
222	146		1400	

223	38.7		586	
224	32.1		342	
225	11.3	408	343	8430
226	45.5		2020	
227	> 1.00E+03		> 10.0E+03	
228	586		2030	
229	95.9		2850	
230	13.6		68.2	
231	504		3870	
232	13.5		46.6	
233	12.3		24.2	
234	168		4550	
235	22.8		111	
236	12.1		158	
237	7.29		28.1	
238	9.1		57.7	
239	117		1090	
240	5.82		59.3	
241	4.06		15.7	
242	70		3220	
243	75		8230	
244	221		> 10.0E+03	
245	41.8		1960	
246	65.5		2370	
247	60.4		1570	
248	20.2		107	
249	21.8		368	
250	> 1.00E+03		> 10.0E+03	
251	363		5810	
252	599		2610	
253	65.8		2120	
254	23.9		753	
255	3.42		30.4	
256	5.19		73.8	
257	8.26	16.5	273	1430
258	3.06		60.3	
259	204		1210	
260	7.55		164	
261	4.75		46.7	
262	8.14	68.1	211	2340
263	9.18		120	
264	9.54		163	
265	35.9		1870	
266	18.3		468	
267	14.6		286	
268	7.96		100	
269	3.21		9.39	
270	535		> 10.0E+03	
271	285		> 10.0E+03	
272	38.6		604	

273	11.6		165	
274	593	> 1.00E+03	5000	> 10.0E+03
275	51	570	1070	4380
276	47.4	> 1.00E+03	1200	> 10.0E+03
277	25.1	365	486	2440
278	93	> 1.00E+03	3290	> 10.0E+03
279	45.4	> 1.00E+03	2400	9360
280	2.75	33.7	7.09	516
281	3.63	75.5	18.3	950
282	5.86	84.2	68.9	1310
283	2.75	10.6	2.91	264
284	5.1	143	10.5	1070
285	23.7	39.5	608	2230
286	40.5	897	589	4810
287	16.9	259	636	3000
288	112	> 1.00E+03	> 10.0E+03	3680
289	69.9	283	2990	4780
290	3.83		18.9	
291	5.14		56.5	
292	12.9		73.2	
293	12.3		83.8	
294	5.27		29.1	
295	5.59		81.3	
296	56.2		660	
297	163		4220	
298	7.16		51.6	
299	> 1.00E+03		> 10.0E+03	
300	3.32		8.47	
301	189		2050	
302	20.9		456	
303	45.6		1720	
304	80.8		4750	
305	32.1		1160	
306	34.5		132	
307	10.8		123	
308	15.1		296	
309	10.8		8.38	
310	22.1		351	
311	19.1		191	
312	80.5		1870	
313	11.2		41.1	
314	10.5		70.4	
315	23.9		617	
316	16.9		201	
317	131		1730	
318	149	181	931	3600
319	7.5	22.1	28.5	571
320	83.7	472	2330	2250
321	6.84	127	207	628
322	63.5	274	1330	2550

323	45.6	112	594	713
324	23.1		502	
325	120		4290	
326	18.2		1320	
327	526		6850	
328	17.9		181	
329	14.7		143	
330	55.1		1190	
331	19.1		41.3	
332	7.58		60.2	
333	6.14		58.7	
334	8.16		21.4	
335	5.88		31.5	
336	17.7		305	
337	8.65		82.2	
338	5.01		13.2	
339	126		5170	
340	37.7		1010	
341	391		2850	
342	43.9		979	
343	16.6		240	
344	7.97		19.6	
345	51.6		752	
346	24.7		987	
347	23.7		824	
348	58.2		2600	
349	10.3	49.6	222	408
350	11.5	94.4	423	885
351	20.3	82.5	497	1140
352	141		4290	
353	25		1270	
354	39.8		900	
355	16.8	734	74.4	2770
356	52.3	> 1.00E+03	1070	> 10.0E+03
357	5.79	23.8	20	875
358	208	> 1.00E+03	4640	7530
359	231	> 1.00E+03	> 10.0E+03	> 10.0E+03
360	483	> 1.00E+03	8140	> 10.0E+03
361	24.7	486	411	4290
362	36.1	138	1270	6960
363	7.74	57.9	67.2	1420
364	20.7	260	1110	2320
365	8.58	26.5	24.9	444
366	70.9	818	4380	> 10.0E+03
367	74.4	735	2520	6330
368	36.8	406	768	6620
369	117	> 1.00E+03	5590	> 10.0E+03
370	58.4	810	1720	> 10.0E+03
371	15.4	47.8	1280	1050
372	> 1.00E+03		> 10.0E+03	

373	704		9910	
374	27.8		389	
375	7.52		68.9	
376	8.07		151	
377	2.9		22.2	
378	16.9		392	
379	12.6	248	1280	4240
380	13.9		312	
381	3.48	15.8	90.1	687
382	13.1	92.3	546	4150
383	12.8		214	
384	13.2	93.9	525	1260
385	34.3	> 856	1790	> 7.50E+03
386	17.6	> 487	1310	> 7.16E+03
387	9.48	376	351	4430
388	28.7	247	674	3140
389	7.01	55.9	63.3	1710
390	15.8	31.8	105	> 10.0E+03
391	19.7	257	103	2250
392	41.3	> 1.00E+03	5530	> 10.0E+03
393	125	> 1.00E+03	3850	> 10.0E+03
394	101	> 1.00E+03	1480	> 10.0E+03
395	7.78	120	137	1650
396	14.7		250	
397	16.5		1440	
398	17.8		1090	
399	15	177	656	2730
400	14.4		2100	
401	10.9	108	2730	4210
402	7.99	53.3	477	3000
403	6.13		20.1	
404	33.7		2820	
405	46.2		1580	
406	20.4		903	
407	421		3550	
408	91.1		2300	
409	36		1290	
410	7.43		57.6	
411	976		> 10.0E+03	
412	26.4		686	
413	21.7		1470	
414	26.1		562	
415	2.96		70	
416	1.43		34	
417	19.6		561	
418	76		2680	
419	35.9		540	
420	336		3100	
421	3.52		37.9	
422	67.9		2080	

423	188		2620	
424	122		5380	
425	109		3090	
426	3.17	59	360	1510
427	9.56	101	1080	1710
428	58.9		1730	
429	5.64		57	
430	83.5		2490	
431	16.7		900	
432	14.6	145	1450	3500
433	190		3530	
434	57.7		1300	
435	19.6		1390	
436	40		4660	
437	80.7		1570	
438	25.3		795	
439	15	655	794	3820
440	24.3	> 1.00E+03	1750	5270
441	21.7	> 1.00E+03	1340	3710
442	72.6		1600	
443	23.2		940	
444	23.5		499	
445	20.2		980	
446	31.9		1330	
447	78.5		1490	
448	47.8		1760	
449	79.7		1200	
450	198		4470	
451	8.14		198	
452	6.63		131	
453	28		3770	
454	37.5		> 10.0E+03	
455	195		3020	
456	52.3		715	
457	235		6740	
458	93.4		2800	
459	26.6		782	
460	33.6		6180	
461	109		3030	
462	225		2370	
463	27		1080	
464	19.2		167	
465	> 1.00E+03		> 10.0E+03	
466	25.9		1570	
467	358		3560	
468	74.7		1960	
469	93.4		1130	
470	68.2		777	
471	39		1040	
472	18		404	

473	19		281	
474	14.9	196	423	2730
475	130		2780	
476	209		> 10.0E+03	
477	170		4360	
478	126		3170	
479	89.3		> 10.0E+03	
480	38.9		3140	
481	13.9		278	
482	5.39	140	194	827
483	30.9		7440	
484	28.4		3850	
485	50.9		997	
486	25.1		1070	
487	42.8		> 10.0E+03	
488	7.99	30.6	98	624
489	92.6		5410	
490	74.3		3200	
491	5.37	23.6	351	285
492	24.1		2120	
493	57.6		973	
494	199		6860	
495	9.4		197	
496	28.2		1070	
497	18.9		1280	
498	43		620	
499	45.6		897	
500	81.5		> 10.0E+03	
501	20.5		695	
502	134		2090	
503	74.1		2930	
504	14.3	> 1.00E+03	665	4410
505	17.6	485	547	4360
506	96.9		8940	
507	125		3760	
508	75.9		627	
509	28.7		928	
510	14.6		262	
511	10.4		196	
512	19.7		409	
513	13.9		240	
514	26.4		1130	
515	12.1		452	
516	102		6240	
517	31.6		973	
518	32		1290	
519	39.2		1220	
520	9.92		198	
521	105		> 10.0E+03	
522	524		> 10.0E+03	

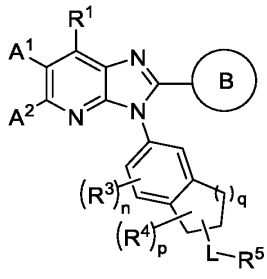
523	48.4		1740	
524	48.4		1740	
525	33.5		1330	
526	20.2		1260	
527	19.5		1150	
528	17.2		320	
529	8.2		621	
530	21.2		422	
531	50.6		1280	
532	177		> 10.0E+03	
533	> 1.00E+03		7230	
534	38.9		507	
535	6.42		42.1	
536	26.2		1570	
537	2.77		15.3	
538	25.1		2910	
539	5.11		430	
540	107		3180	
541	5.46		556	
542	117		2330	
543	81	526	1210	
544	6.24		130	
545	20.8		730	
546	9.86		221	
547	28.3		1740	
548	27.4		4080	
549	27.6		723	
550	7.1		75.7	
551	13.1		296	
552	9.18		166	
553	7.04		344	
554	339		9260	
555	64.4		1570	
556	124		1330	
557	15.9		1760	
558	71.5		7510	
559	5.67		268	
560	249		2520	
561	93.3		3090	
562	9.77		430	
563	1.83		37.8	
564	2.28		84.4	
565	9.86		274	
566	10.5		246	
567	11.3		455	
568	8.72		458	
569	77.4		808	
570	47.5		679	
571	2.22		176	
572	16.1		945	

573	318		5640	
574	52.4		2420	
575	221		3300	
576	133		4300	
577	87.9		904	
578	74.9		1690	
579	5.42	9.88	26.6	
580	11.2	11.4	24.4	
581	6.51	20.8	38.4	
582	> 1.00E+03		> 10.0E+03	
583	805		3780	
584	6.1	11.8	62.5	
585	4.77	8.23	10.7	
586	6.98	17.3	43	
587	116		1010	
588	27		764	
589	16.8		650	
590	45.2		1540	
591	25.2		962	
592	4.32	5.5	11	
593	4.56	22	23.7	
594	27.6		2690	
595	15		520	
596	12.9		689	
597	66.1		3780	
598	3.8		40.5	
599	25.4		1280	
600	418		7070	
601	102		2500	
602	34	61.4	351	
603	7.65	16.5	76.8	

CLAIMS

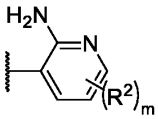
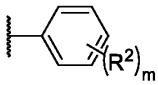
WHAT IS CLAIMED IS:

1. A compound represented by the structure of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

Ring B is selected from:  and ;

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, -CN, optionally substituted C_{3-8} carbocycle, optionally substituted 4- to 8-membered heterocycle, and optionally substituted C_{1-6} alkyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-SR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-C(O)OR^{11A}$, $-OC(O)R^{11A}$, $-NO_2$, =O, =S, $=N(R^{11A})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NS(O)_2N(R^{11})_2$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-6} alkynyl, C_{3-8} carbocycle, or 4- to 8-membered heterocycle, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected

from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN;

L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

wherein L^1, L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN;

R^{10}, R^{11}, R^{11A}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl,C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, -CN, and C_{3-8} carbocycle or 4- to 8-membered heterocycle, either of which is optionally further substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

2. The compound or salt of claim 1, wherein A^2 is selected from C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, =O, and $-NO_2$, -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-NO_2$, =O, and -CN.

3. The compound or salt of claim 1 or claim 2, wherein A^2 is selected from C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-N(R^{11A})S(O)_2R^{11A}$, $-NO_2$, =O, and -CN.

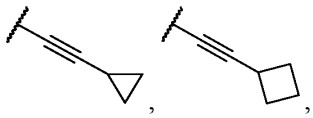
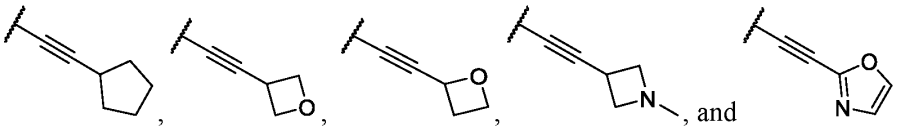
4. The compound or salt of any one of claims 1-3, wherein A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$,-CN; C_{3-10} carbocycle and 4- to 10-membered heterocycle, the C_{3-10} carbocycle and 3- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-NO_2$, =O, and -CN.

5. The compound or salt of claim 4, wherein A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from C_{3-6} carbocycle and 4- to 6-membered

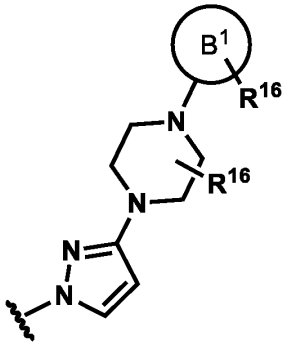
heterocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$,=O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$,=O, and -CN.

6. The compound or salt of claim 4, wherein A^2 is C_{2-6} alkynyl optionally substituted with one or more substituents independently selected from: C_{3-6} carbocycle and 4- to 6-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

7. The compound or salt of claim 6, wherein A^2 is C_{2-6} alkynyl optionally substituted with cyclopropyl, cyclopentyl, oxetanyl, azetidinyl, and oxazolyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, $-N(R^{11A})_2$, $-C(O)R^{11A}$, $-C(O)N(R^{11A})_2$, $-N(R^{11A})C(O)R^{11A}$, $-NO_2$, =O, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11A}$, and $-N(R^{11A})_2$.

8. The compound or salt of claim 7, wherein A^2 is selected from , , and .

9. The compound or salt of any one of claims 1-8, wherein L^1, L^2, L^3, and L^4 are all absent.

10. The compound or salt of any one of claims 1-9, wherein A^2 is , wherein ring B^1 is C_{3-8} carbocycle or 4- to 8-membered heterocycle, either of which is

optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN.

11. The compound or salt of any one of claims 1-10, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

12. The compound or salt of claim 11, wherein R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

13. The compound or salt of claim 12, wherein R^5 is 4- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, -

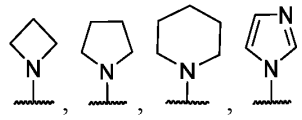
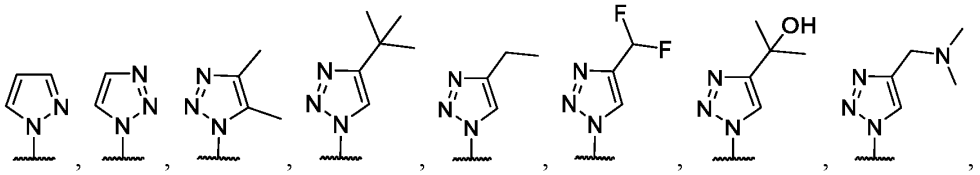
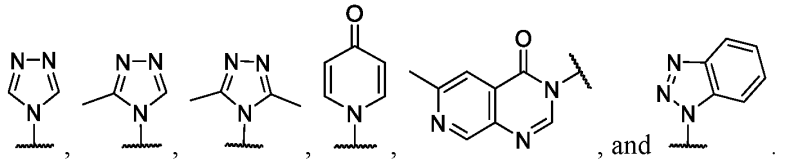
$N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

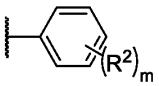
C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

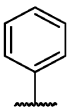
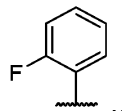
14. The compound or salt of claim 13, wherein R^5 is selected from azetidinyl, cyclopentyl, cyclohexyl, imidazolyl, pyrazolyl, 1H-1,2,3-triazolyl, 4H-1,2,4-triazolyl, 1,4-dihydropyridinyl, 3,4-dihydropyrido[3,4-d]pyrimidinyl, 1H-benzo[d][1,2,3]triazolyl, each of which is optionally substituted with one or more substituents independently selected from:

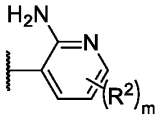
halogen, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

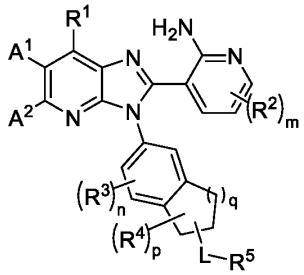
15. The compound or salt of claim 14, wherein R^5 is selected from , , , and .

16. The compound or salt of any one of claims 1-15, wherein Ring B is .

17. The compound or salt of claim 16, wherein Ring B is selected from  and ,.

18. The compound or salt any one of claims 1-15, wherein Ring B is .

19. The compound or salt of claim 1, wherein the structure of Formula (I) is represented by the structure of Formula (II):



(II),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})_2$, $-NO_2$, and -CN;

A^1 and A^2 are each independently selected from (i), (ii), and (iii):

(i) hydrogen, halogen, C_{1-4} haloalkyl, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, and -CN;

(ii) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$,$-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

(iii) 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, -

$N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-N(R^{11})C(O)OR^{11}$, $-OC(O)N(R^{11})_2$, $-N(R^{11})C(O)N(R^{11})_2$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, -CN; and

C_{1-6} alkyl C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-SR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-C(O)OR^{11}$, $-OC(O)R^{11}$, $-NO_2$, =O, =S, $=N(R^{11})$, and -CN;

q is selected from 1, 2, and 3;

m and n are each independently selected from 0, 1, 2, and 3;

R^2 is independently selected at each instance from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{12}$, $-SR^{12}$, $-N(R^{12})_2$, $-NO_2$, and -CN;

R^3 is independently selected at each instance from:

halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{13}$, $-SR^{13}$, $-N(R^{13})_2$, $-C(O)R^{13}$, $-C(O)N(R^{13})_2$, $-N(R^{13})C(O)R^{13}$, $-C(O)OR^{13}$, $-OC(O)R^{13}$, $-NO_2$, =O, =S, $=N(R^{13})$, and -CN;

p is selected from 0, 1, 2, 3, 4, and 5;

R^4 is independently selected at each instance from:

halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, =O, =S, $=N(R^{14})$, and -CN; or

two R^4 attached to the same atom are taken together to form a group selected from: =O, =S, and $=N(R^{14})$; or

two R^4 attached to the same atom or to adjacent atoms are taken together with the carbons to which they are attached to form a group selected from 4- to 8-membered heterocycle and C_{3-8} carbocycle, any of which is optionally substituted

with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-NO_2$, and -CN;

L is represented by $-L^1-L^2-L^3-L^4-$, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, $-N(R^{15})-$, -S-, -S(O)-, $-S(O)_2-$, $-S(O)(NR^{15})-$, $-N(R^{15})C(O)-$, $-N(R^{15})C(O)O-$, $-N(R^{15})S(O)_2-$, $-N(R^{15})S(O)_2N(R^{15})-$, $-S(O)(NR^{15})N(R^{15})-$, $-N(R^{15})N(R^{15})-$, $-(R^{15})NC(O)N(R^{15})-$, and $-(R^{15})NC(O)N(R^{15})N(R^{15})-$; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-8} carbocyclene, and 4- to 8-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{15}$, $-SR^{15}$, =O, =S, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent;

R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-N(R^{16})C(O)N(R^{16})_2$, $-N(R^{16})C(O)OR^{16}$, $-OC(O)N(R^{16})_2$, $-S(O)R^{16}$, $-S(O)_2R^{16}$, $-NO_2$, =O, =S, $=N(R^{16})$, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN;

R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, and R^{15} are each independently selected at each occurrence from: hydrogen, C_{1-4} alkyl, C_{3-8} carbocycle, 4- to 8-membered heterocycle, and C_{1-4} haloalkyl;

R^{16} is independently selected at each occurrence from (iv), (v), and (vi):

(iv) hydrogen;

(v) C_{1-4} alkyl, wherein the C_{1-4} alkyl is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, -

$N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

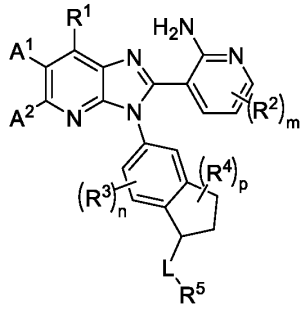
C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-C(O)N(R^{20})_2$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-S(O)_2N(R^{20})_2$, $-NO_2$, and -CN; and

(vi) C_{3-8} carbocycle and 4- to 8-membered heterocycle, either of which is optionally substituted with one or more substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{20}$, $-SR^{20}$, $-N(R^{20})_2$, $-C(O)R^{20}$, $-C(O)N(R^{20})_2$, $-C(O)OR^{20}$, $-OC(O)R^{20}$, $-N(R^{20})C(O)R^{20}$, $-N(R^{20})S(O)_2R^{20}$, $-N(R^{20})C(O)N(R^{20})_2$, $-N(R^{20})C(O)OR^{20}$, $-OC(O)N(R^{20})_2$, $-S(O)R^{20}$, $-S(O)_2R^{20}$, $-NO_2$, and -CN; and

R^{20} is independently selected at each occurrence from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{3-8} carbocycle, and 4- to 8-membered heterocycle.

20. The compound or salt of claim 19, wherein q is 1.

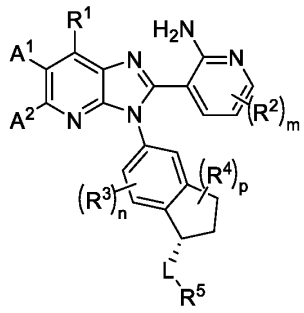
21. The compound or salt of claim 19 or claim 20 represented by the structure of Formula (III):



(III);

or a pharmaceutically acceptable salt thereof.

22. The compound or salt of any one of claims 19-21, represented by the structure of Formula (III-A):



(III-A);

or a pharmaceutically acceptable salt thereof.

23. The compound or salt of any one of claims 19-22, wherein m is 0.

24. The compound or salt of any one of claims 19-23, wherein n is 0.

25. The compound or salt of any one of claims 19-24, wherein p is selected from 0, 1, and 2.

26. The compound or salt of any one of claims 19-25, wherein R^4 is independently selected at each instance from: halogen, $-OR^{14}$, $-SR^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)R^{14}$, $-C(O)OR^{14}$, $-OC(O)R^{14}$, $-NO_2$, and -CN.

27. The compound or salt of claim 26, wherein R^4 is independently selected at each instance fluoro, chloro, and bromo.

28. The compound or salt of claim 25, wherein p is 0.

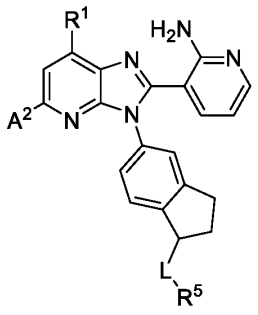
29. The compound or salt of any one of claims 19-28, wherein A^1 is selected from hydrogen, halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{11}$, $-N(R^{11})_2$, and -CN.

30. The compound or salt of claim 29, wherein A^1 is selected from hydrogen, halogen, C_{1-4} alkyl, and C_{1-4} haloalkyl.

31. The compound or salt of claim 29 or claim 30, wherein A^1 is selected from hydrogen, fluoro, and methyl.

32. The compound or salt of any one of claims 29-31, wherein A^1 is hydrogen.

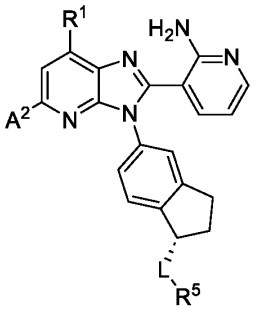
33. The compound or salt according to any one of claims 19-32 represented by the structure of Formula (IV):



(IV);

or a pharmaceutically acceptable salt thereof.

34. The compound or salt according to any one of claims 19-33 represented by the structure of Formula (IV-A):



(IV-A);

or a pharmaceutically acceptable salt thereof.

35. The compound or salt of any one of claims 19-34, wherein R^1 is selected from hydrogen, halogen, $-OR^{10}$, $-N(R^{10})_2$, $-NO_2$, -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{10}$, and $-N(R^{10})_2$.

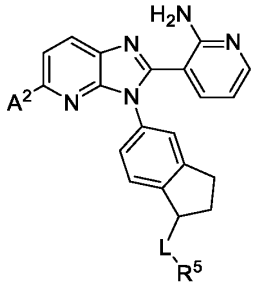
36. The compound or salt of claim 35, wherein R^1 is selected from hydrogen, $-OR^{10}$, and -CN; and C_{1-6} alkyl optionally substituted with one or more $-OR^{10}$.

37. The compound or salt of claim 35 or claim 36, wherein R^1 is selected from hydrogen, methoxy, -CN, methyl, ethyl, and (methoxy)methyl.

38. The compound or salt of claim 35 or claim 36, wherein R^1 is selected from hydrogen, fluoro, methoxy, -CN, methyl, ethyl, (methoxy)methyl, and .

39. The compound or salt of any one of claims 35-38, wherein R^1 is hydrogen.

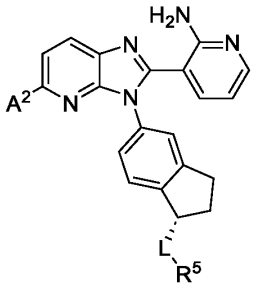
40. The compound or salt according to any one of claims 19-39 represented by the structure of Formula (V):



(V);

or a pharmaceutically acceptable salt thereof.

41. The compound or salt according to any one of claims 19-40 represented by the structure of Formula (V-A):



(V-A);

or a pharmaceutically acceptable salt thereof.

42. The compound or salt of any one of claims 19-41, wherein A^2 is selected from:

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN; and

5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each

optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

43. The compound or salt of claim 42, wherein A^2 is selected from:

C_{1-6} alkyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-S(O)_2N(R^{11})_2$, $-NO_2$, =O, and -CN; and

5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

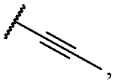
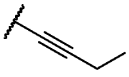
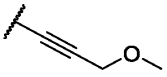
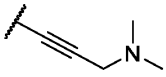
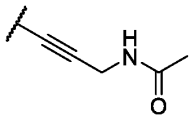
C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

C_{3-8} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O, -CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

44. The compound or salt of claim 42 or claim 43, wherein A^2 is selected from C_{1-6} alkyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN.

45. The compound or salt of claim 44, wherein A^2 is selected from methyl, ethyl, propyl, isopropyl, ethylnyl, propylnyl, and isopropylnyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-NO_2$, =O, and -CN.

46. The compound or salt of claim 45, wherein A^2 is selected from:

-CH_3, , , , , , and .

47. The compound or salt of claim 42 or claim 43, wherein A^2 is selected from 5- to 10-membered heteroaryl, 5- to 10-membered heterocycloalkyl, C_{4-8} aryl, and C_{3-10} cycloalkyl, each of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

48. The compound or salt of claim 47, wherein A^2 is selected from pyrazolyl, triazolyl, oxazolyl, thiazolyl, morpholinyl, phenyl, and cyclopropyl, each of which is optionally substituted with one or more substituents independently selected from:

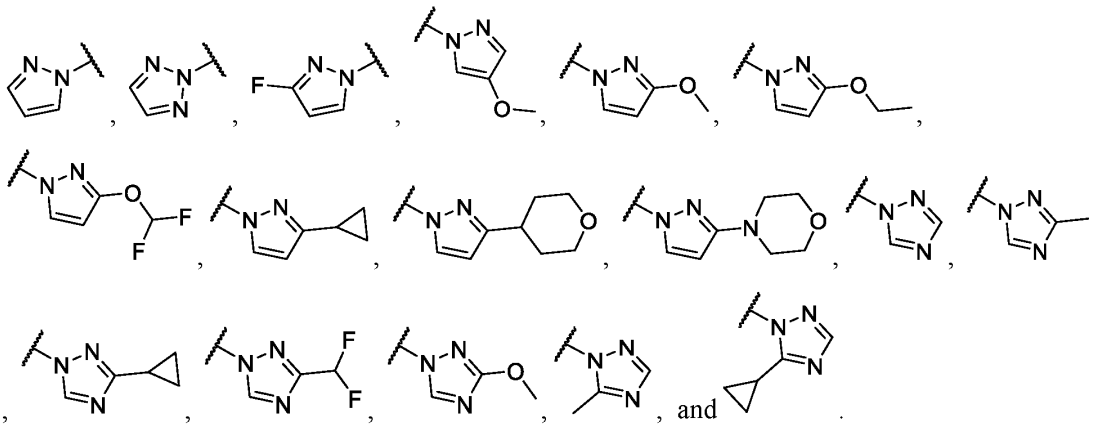
halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, $-NO_2$, =O, and -CN; and

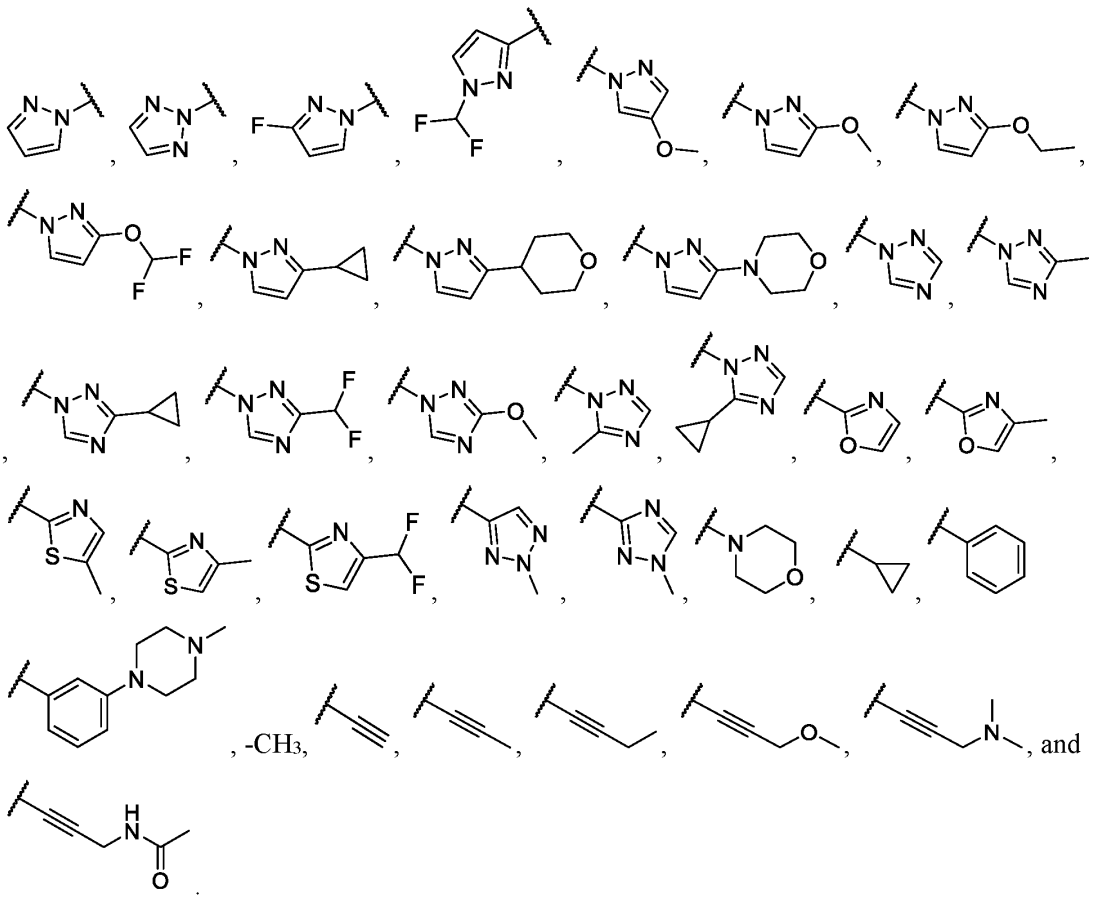
C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-NO_2$, =O,-CN; C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, are each optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, -

$N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN.

49. The compound or salt of claim 42, wherein A^2 is selected from:



50. The compound or salt of claim 42, wherein A^2 is selected from:



51. The compound or salt of any one of claims 19-41, wherein A^2 is selected from 5- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN.

52. The compound or salt of claim 51, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, $-NO_2$, =O, and -CN; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle, any of which is each optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{3-6} alkynyl, any one of which is optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, $-N(R^{11})S(O)_2R^{11}$, =O, and -CN.

53. The compound or salt of claim 51 or claim 52, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from:

halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, and =O; and

C_{3-10} carbocycle and 4- to 10-membered heterocycle; wherein the C_{3-10} carbocycle and 4- to 10-membered heterocycle are each optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, and =O.

54. The compound or salt of any one of claims 51-53, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, and =O.

55. The compound or salt of any one of claims 51-54, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from halogen, $-OR^{11}$, $-N(R^{11})_2$, $-C(O)R^{11}$, $-C(O)N(R^{11})_2$, $-N(R^{11})C(O)R^{11}$, =O, and -CN; and C_{1-6} alkyl optionally substituted with one or more substituents independently selected from: halogen, $-OR^{11}$, and $-N(R^{11})_2$.

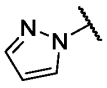
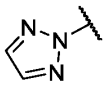
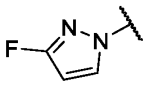
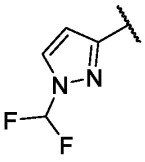
56. The compound or salt of any one of claims 51-55, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from halogen.

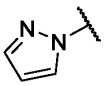
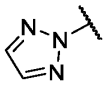
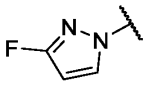
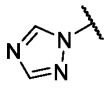
57. The compound or salt of any one of claims 51-56, wherein A^2 is 5- to 10-membered heterocycle optionally substituted with one or more substituents independently selected from fluoro.

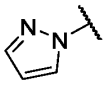
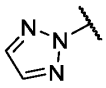
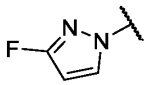
58. The compound or salt of any one of claims 51-57, wherein the optionally substituted 5- to 10-membered heterocycle is optionally substituted 5- to 10-membered heteroaryl.

59. The compound or salt of any one of claims 51-58, wherein the optionally substituted 5- to 10-membered heterocycle is optionally substituted 5-membered heteroaryl.

60. The compound or salt of any one of claims 51-59, wherein the optionally substituted 5-membered heteroaryl is selected from optionally substituted pyrazolyl and optionally substituted triazolyl.

61. The compound or salt of any one of claims 51-58, wherein A^2 is selected from , , , and .

62. The compound or salt of any one of claims 51-58, wherein A^2 is selected from , , , and .

63. The compound or salt of any one of claims 51-62, wherein A^2 is selected from , , and .

64. The compound or salt of any one of claims 19-63, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -N(R^{15})-, -S-, -N(R^{15})C(O)-, -N(R^{15})C(O)O-, -N(R^{15})S(O)$_2$, -N(R^{15})N(R^{15})-, and -(R^{15})NC(O)N(R^{15})-; and

(b) C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-6} carbocyclene, and 4- to 6-membered heterocyclene, any of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{15}, =O, and -CN;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent.

R^{15} is selected from hydrogen and C_{1-4} alkyl.

65. The compound or salt of claim 64, wherein L^1, L^2, L^3, and L^4 are each independently selected from (a) and (b):

(a) -O-, -N(R^{15})-, and -N(R^{15})C(O)-; and

(b) C_{1-6} alkylene;

wherein L^2, L^3, and L^4 are each optionally absent;

wherein no more than two of L^1, L^2, L^3, and L^4 are selected from (a) and the two selected are not adjacent; and

R^{15} is selected from hydrogen and C_{1-4} alkyl.

66. The compound or salt of claim 64 or claim 65, wherein L^4 is absent.

67. The compound or salt of any one of claims 64-66, wherein L^3 is absent or -O-.

68. The compound or salt of any one of claims 64-66, wherein L^3 is absent, -O-, ethynyl, or methylene substituted with =O.

69. The compound or salt of any one of claims 64-68, wherein L^2 is absent or methylene.

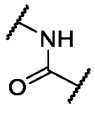
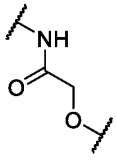
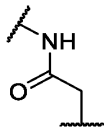
70. The compound or salt of any one of claims 64-68, wherein L^2 is absent, methylene, (methyl)methylene, ethylene, or -O-.

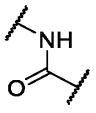
71. The compound or salt of any one of claims 64-70, wherein L^1 is $-N(R^{15})C(O)-$.

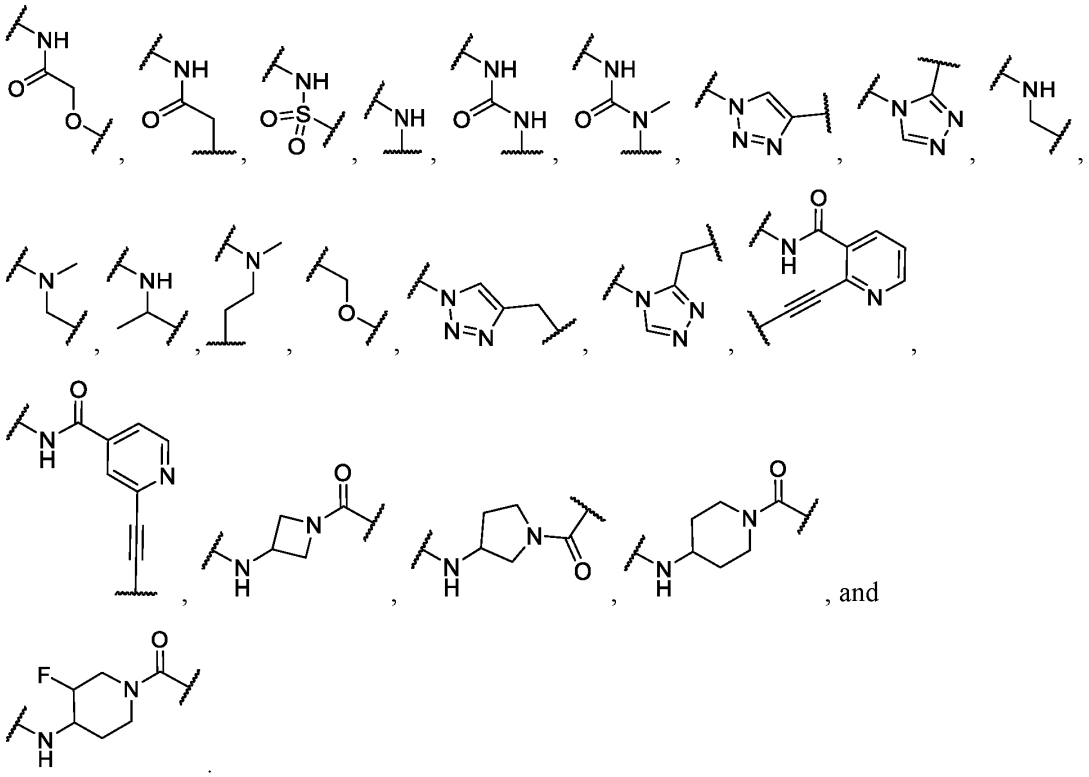
72. The compound or salt of any one of claims 64-70, wherein L^1 is selected from $-N(R^{15})C(O)-$, $-N(R^{15})-$, $-N(R^{15})S(O)-$, $-(R^{15})NC(O)N(R^{15})-$, and 4- to 6-membered heterocyclene optionally substituted with one or more halogen atoms.

73. The compound or salt of any one of claims 64-72, wherein R^{15} is hydrogen.

74. The compound or salt of any one of claims 64-72, wherein R^{15} is selected from hydrogen and $-CH_3$.

75. The compound or salt of claim 64 or claim 65, wherein L is selected from , , and .

76. The compound or salt of claim 64 or claim 65, wherein L is selected from ,



, and

.

77. The compound or salt of any one of claims 19-76, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

78. The compound or salt of any one of claims 19-76, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, -

$N(R^{16})C(O)R^{16}$, $-N(R^{16})S(O)_2R^{16}$, $-S(O)_2R^{16}$, $-S(O)_2N(R^{16})_2$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

4- to 6-membered heterocycle and C_{3-8} carbocycle, each of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

79. The compound or salt of claim 77, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

halogen, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-C(O)N(R^{16})_2$, $-C(O)OR^{16}$, $-OC(O)R^{16}$, $-N(R^{16})C(O)R^{16}$, $-NO_2$, =O, and -CN;

C_{1-4} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, any of which is optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-SR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN; and

C_{3-8} carbocycle optionally substituted with one or more substituents independently selected from: halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, $-NO_2$, and -CN.

80. The compound or salt of claim 77 or claim78, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from:

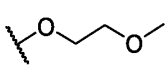
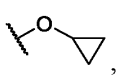
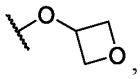
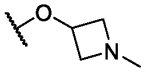
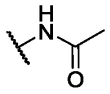
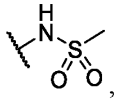
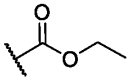
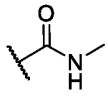
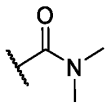
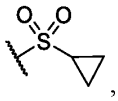
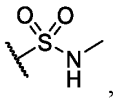
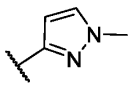
halogen, C_{2-6} alkynyl, C_{1-4} haloalkyl, $-OR^{16}$, $-N(R^{16})_2$, =O, and -CN;

C_{1-4} alkyl optionally substituted with one or more substituents independently selected from: $-N(R^{16})_2$; and

C_{3-8} carbocycle optionally substituted with one or more substituents independently selected from: halogen.

81. The compound or salt of any one of claims 77-80, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: fluoro, chloro, methyl, ethyl, ethynyl, difluoromethyl, hydroxy, methoxy, trifluoromethoxy, dimethylamino, =O, -CN, cyclopropyl, and pyrazolyl.

82. The compound or salt of any one of claims 77-80, wherein R^5 is selected from 4- to 10-membered heterocycle and C_{3-10} carbocycle, any of which is optionally substituted with one or more substituents independently selected from: fluoro, chloro, methyl, ethyl, ethynyl, propynyl,

fluoromethyl, difluoromethyl, trifluoromethyl, hydroxy, -CH_2OH, methoxy, -CH_2OCH_3, , , , , difluoromethoxy, trifluoromethoxy, -NH_2, dimethylamino, -$CH_2N(CH_3)_2$, , , , , , , , =O, -CN, cyclopropyl, phenyl, morpholinyl, pyrazolyl, , and pyridinyl.

83. The compound or salt of any one of claims 77-82, wherein R^5 is optionally substituted 4- to 10-membered heterocycle.

84. The compound or salt of any one of claims 77-83, wherein R^5 is optionally substituted 4- to 10-membered heteroaryl.

85. The compound or salt of claim 84, wherein R^5 is selected from: optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl.

86. The compound or salt of claim 84, wherein R^5 is selected from: optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted oxazolyl, optionally substituted pyridyl, optionally substituted pyrimidyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, optionally substituted benzo[d]isoxazolyl, optionally substituted imidazo[1,2-a]pyridinyl, optionally substituted 1H-benzo[d]imidazolyl, optionally substituted 1H-pyrazolo[3,4-b]pyridinyl, optionally substituted 2H-pyrrolo[3,4-c]pyridinyl, and optionally substituted isoquinolinyl, optionally substituted isoxazolyl, optionally substituted isothiazole, optionally substituted 1,2,3-thiadiazolyl, optionally substituted 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazolyl, optionally substituted 2,3-dihydropyrazolo[5,1-b]oxazolyl, optionally substituted 5,6-dihydro-3H-furo[2,3-d]imidazolyl, optionally substituted indolizinyl, optionally substituted pyrazolo[1,5-a]pyridinyl, optionally substituted pyrrolo[1,2-a]pyrimidinyl, optionally substituted pyrazolo[1,5-a]pyrimidinyl, optionally substituted imidazo[1,2-a]pyrimidinyl, optionally substituted imidazo[1,2-b]pyridazinyl, optionally substituted [1,2,4]triazolo[1,5-a]pyridinyl, optionally substituted 6,7-dihydro-5H-cyclopenta[b]pyridinyl, optionally substituted 6,7-

dihydro-5H-cyclopenta[c]pyridinyl, optionally substituted 5,6,7,8-tetrahydroisoquinolinyl, optionally substituted 3,4-dihydro-2H-pyrano[2,3-b]pyridinyl, optionally substituted 2,3-dihydro-[1,4]dioxino[2,3-b]pyridinyl, optionally substituted 5,7-dihydrofuro[3,4-b]pyridinyl, optionally substituted 2,3-dihydrofuro[2,3-c]pyridinyl, optionally substituted 2,3-dihydrofuro[2,3-b]pyridinyl, optionally substituted [1,3]dioxolo[4,5-b]pyridinyl, optionally substituted furo[2,3-b]pyridinyl, optionally substituted thieno[2,3-b]pyridinyl, optionally substituted 1,2-dihydro-3H-indazol-3-onyl, optionally substituted 1H-benzo[d][1,2,3]triazolyl, optionally substituted 1,3-dihydro-2H-benzo[d]imidazol-2-onyl, optionally substituted benzo[d]oxazol-2(3H)-onyl, optionally substituted benzo[d]thiazol-2(3H)-onyl, optionally substituted 1H-indazolyl, optionally substituted indolin-2-onyl, and optionally substituted 1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-onyl.

87. The compound or salt of claims 77-83, wherein R^5 is an optionally substituted 6- to 10-membered bicyclic heterocycle selected from optionally substituted 6- to 10-membered fused heterocycle, optionally substituted 6- to 10-membered bridged heterocycle, and optionally substituted 6- to 10-membered spirocyclic heterocycle.

88. The compound or salt of claim 87, wherein R^5 is optionally substituted 6- to 10-membered spirocyclic heterocycle selected from optionally substituted 2-azaspiro[3.3]heptanyl, optionally substituted 6-azaspiro[3.4]octanyl, optionally substituted 5-azaspiro[3.4]octanyl, optionally substituted 2-azaspiro[3.5]nonanyl, optionally substituted 7-azaspiro[3.5]nonanyl, and optionally substituted 6-azaspiro[3.5]nonanyl.

89. The compound or salt of any one of claims 77-83, wherein R^5 is optionally substituted 3- to 8-membered heterocycloalkyl.

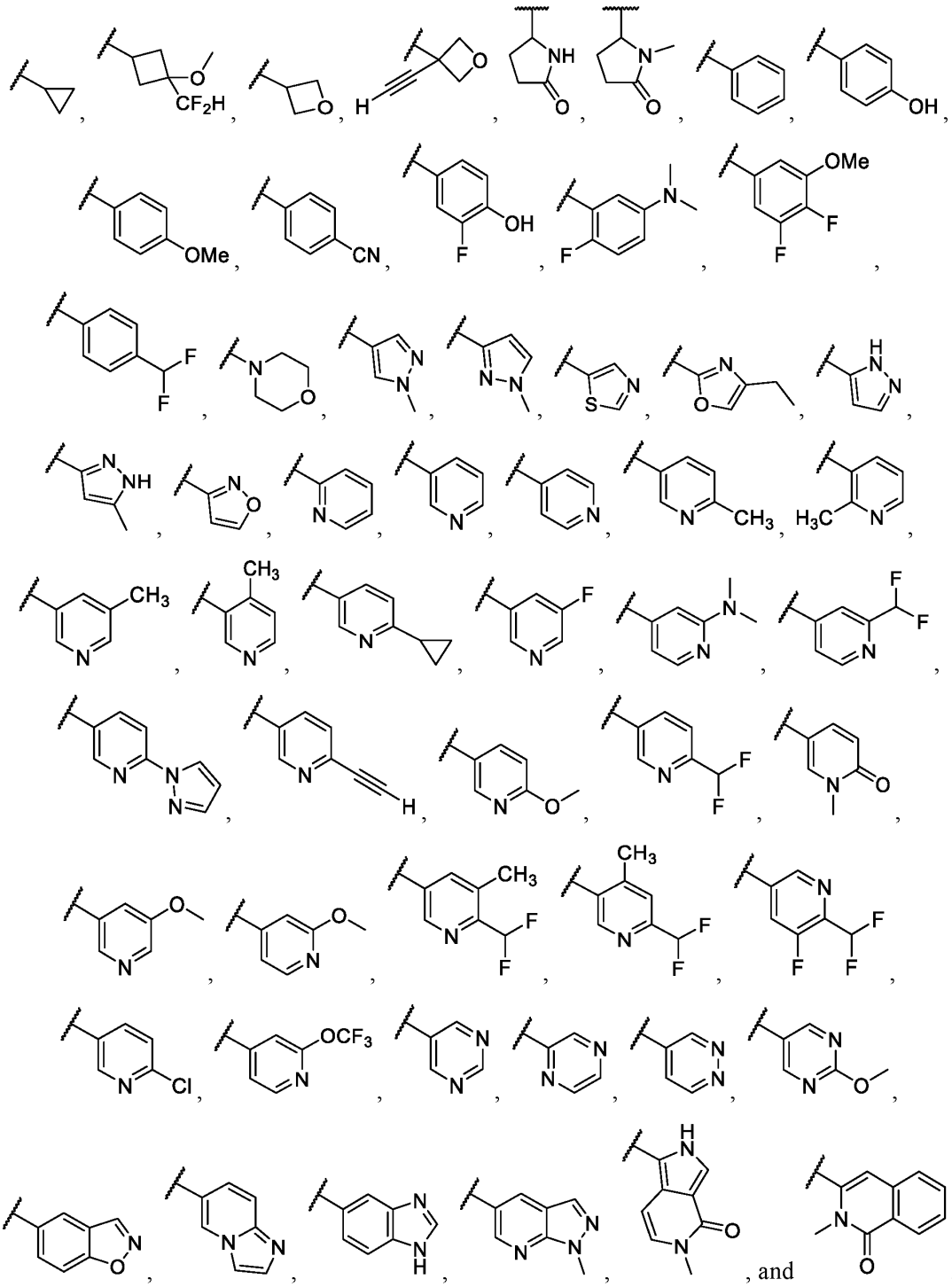
90. The compound or salt of claim 89, wherein R^5 is selected from optionally substituted oxetanyl, optionally substituted pyrrolyl, and optionally substituted morpholinyl.

91. The compound or salt of claim 89, wherein R^5 is selected from optionally substituted oxetanyl, optionally substituted pyrrolyl, optionally substituted morpholinyl, optionally substituted azetidinyl, optionally substituted pyrrolidinyl, optionally substituted tetrahydro-2H-thiopyranyl, and optionally substituted piperidinyl.

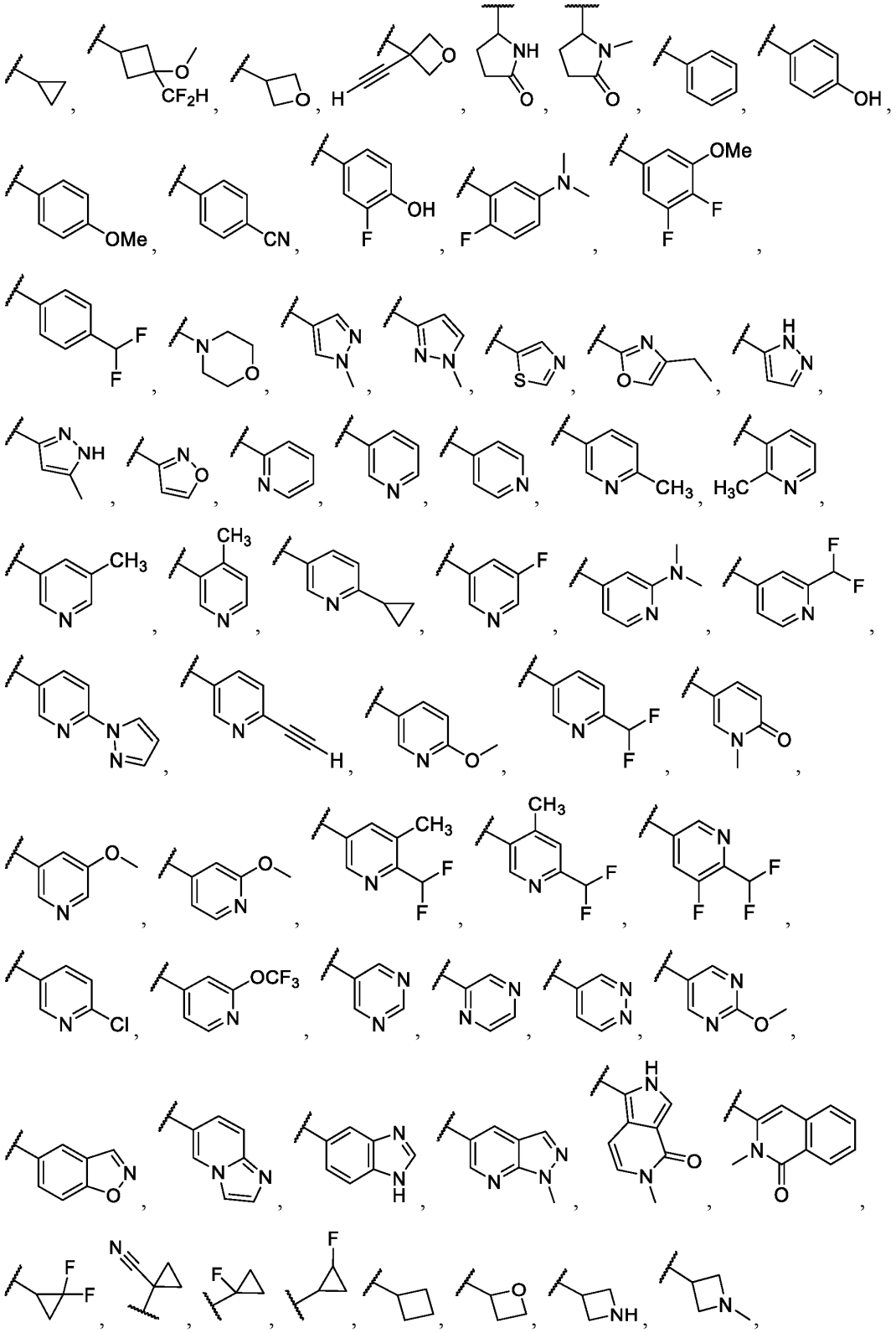
92. The compound or salt of any one of claims 77-81, wherein R^5 is selected from optionally substituted C_{3-6} cycloalkyl and optionally substituted phenyl.

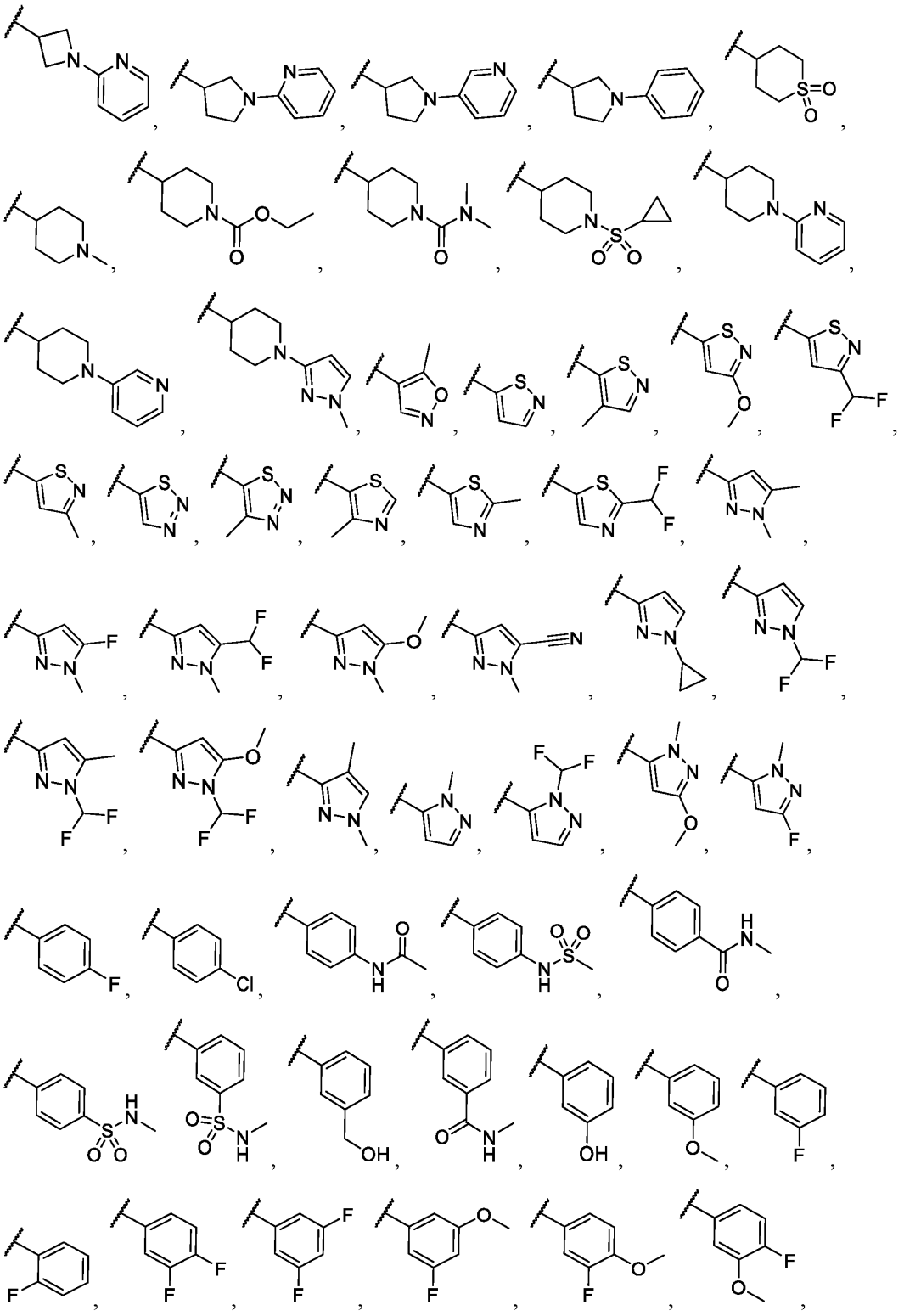
93. The compound or salt of claim 92, wherein R^5 is selected from optionally substituted cyclopropyl, optionally substituted cyclobutyl, and optionally substituted phenyl.

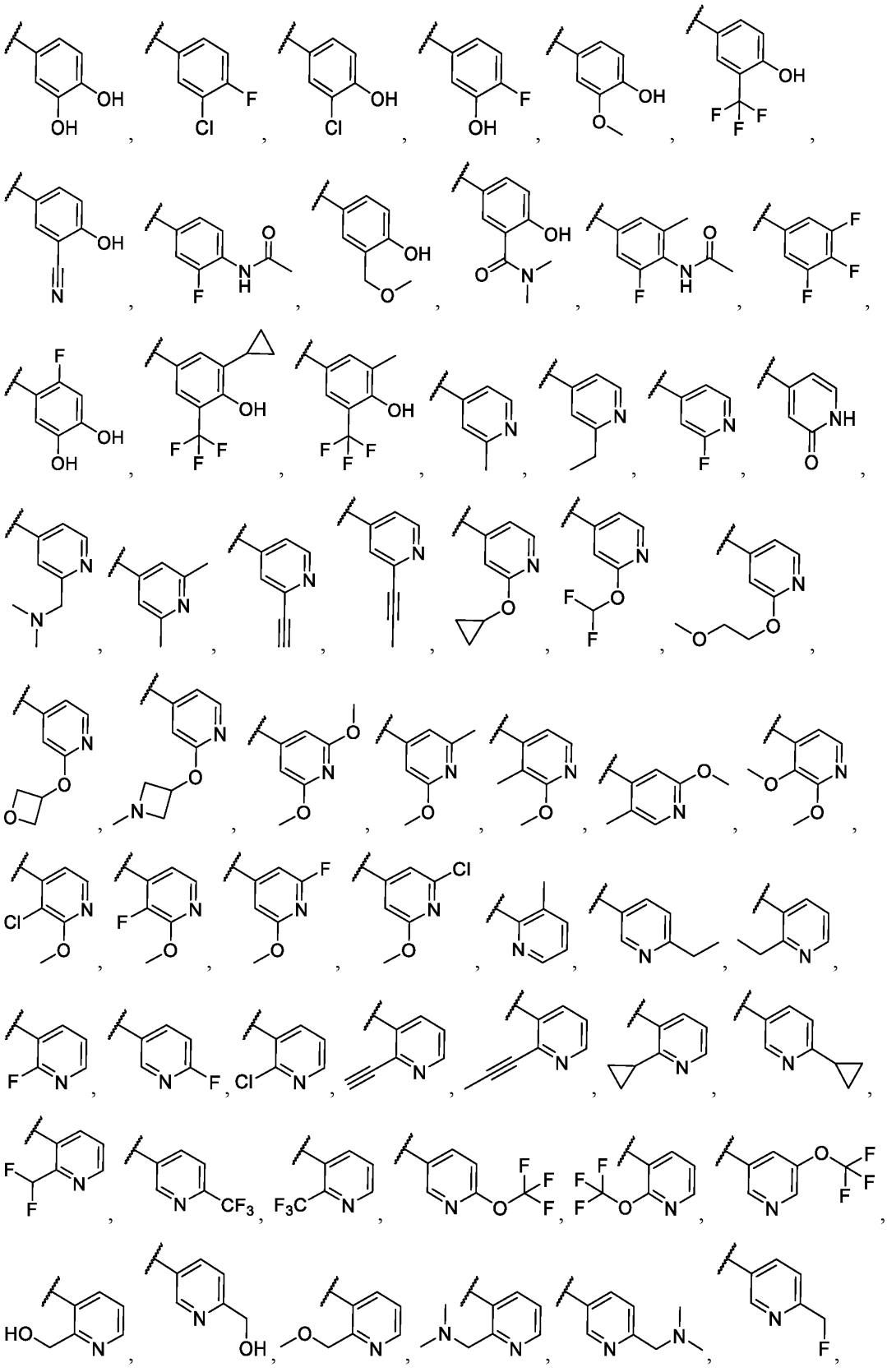
94. The compound or salt of claim 77 or claim 78, wherein R^5 is selected from:

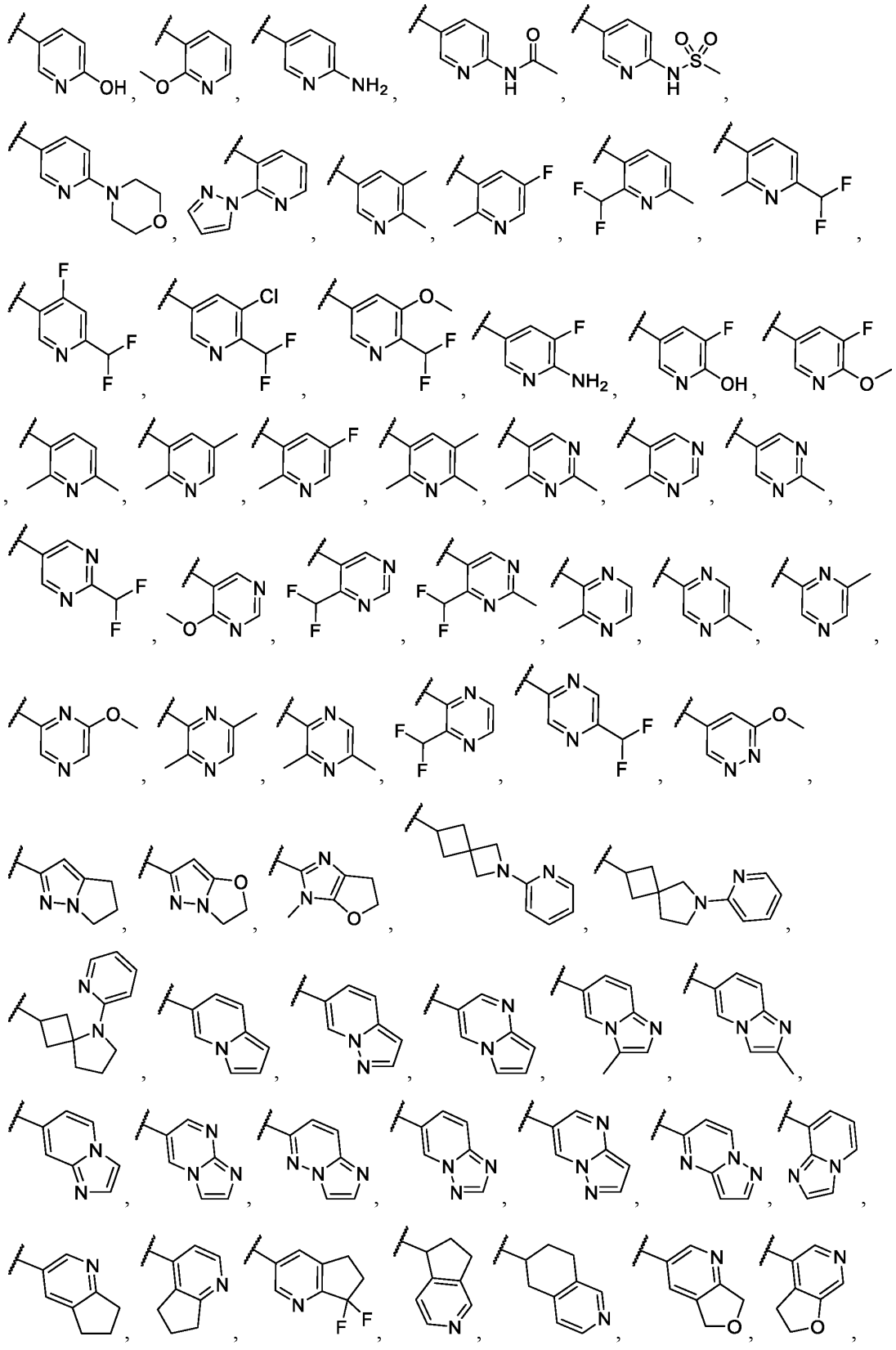


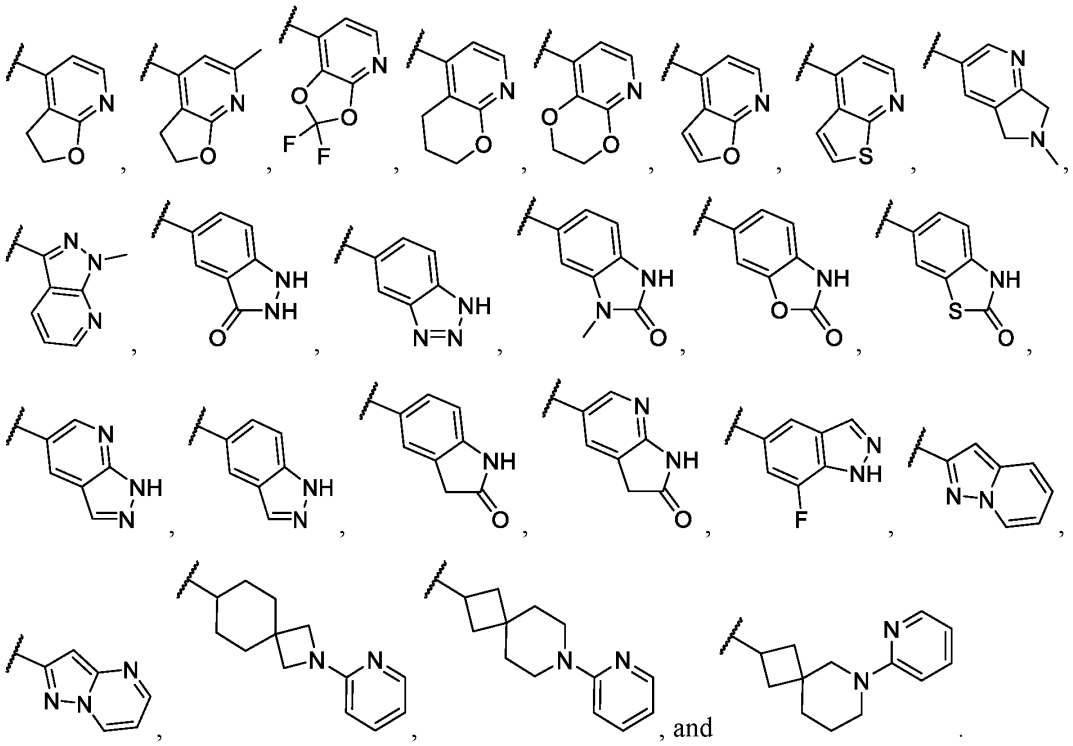
95. The compound or salt of claim 77 or claim 78, wherein R^5 is selected from:











96. The compound or salt of any one of claims 1 to 95, wherein the compound is selected from a compound of Table 1, or a pharmaceutically acceptable salt thereof.

97. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound or salt of any one of claims 1-96.

98. A method of modulating activity of wild-type AKT1 comprising, administering to a subject in need thereof a compound or salt of any of claims 1-96, or a pharmaceutical composition of claim 97.

99. A method of modulating activity of mutant AKT1 comprising, administering to a subject in need thereof a compound or salt of any of claims 1-96, or a pharmaceutical composition of claim 97.

100. A method of selectively modulating activity of wild-type AKT1 over wild-type AKT2 comprising administering to a subject in need thereof a compound or salt of any of claims 1-96, or a pharmaceutical composition of claim 97.

101. A method of selectively modulating activity of a mutant AKT1 over wild-type AKT2 comprising administering to a subject in need thereof a compound or salt of any of claims 1-96, or a pharmaceutical composition of claim 97.

102. A method of treating cancer in a subject in need thereof, the method comprising administering to the subject a compound or salt of any of claims 1-96, or a pharmaceutical composition of claim 97.

103. The method of claim 102, wherein the cancer is selected from breast cancer, colorectal cancer, and meningioma.

104. The method of claim 103, wherein the administration modulates activity of a mutant AKT1.

105. The method of claim 98, 101, or 104, wherein the mutant AKT1 is AKT1 E17K.