

5-OXO-4,5-DIHYDROIMIDAZO[1,5-A]QUINAZOLINE COMPOUNDS AS PI3K[ALPHA] INHIBITORS

TECHNICAL FIELD

The present disclosure provides tricyclic compounds as well as their pharmaceutical compositions that modulate the activity of PI3K α and are useful in the treatment of various diseases related to PI3K α , including cancer.

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BACKGROUND

In the past few decades, signal transduction events have been studied to demonstrate critical roles in regulating almost all aspects of biological responses. Aberrant activation of the signaling pathways regulating cell survival and proliferation is commonly observed in many human cancers. The phosphoinositide 3-kinases (PI3Ks) signaling pathway is documented to be one of the highly mutated pathways in human cancers (Vogelstein et al., *Science*, 2013, 339(6127), 1546-1558). The PI3K signaling pathway regulates cell survival and proliferation. Increased activity of this pathway is associated with tumor progression and resistance to cancer therapies (Fusco et al., *Front Oncol.*, 2021, 11, 644737).

PI3Ks belong to a lipid kinase family which catalyzes the phosphorylation of lipids contained in or associated with cell membranes. The PI3K family has fifteen kinases with distinct substrates, expression pattern, and modes of regulation. The class-I PI3Ks (p110 α , p110 β , p110 δ , and p110 γ) are typically activated by tyrosine receptor kinases or G-protein coupled receptors to generate PIP3, which activates downstream effectors of Akt, mTOR, or Rho GTPases (Fruman et al., *Nat. Rev. Drug Discov.*, **2014**, 13(2), 140-156)

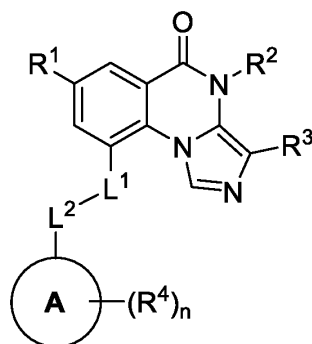
Genetic mutations in the gene coding for PI3K α are hotspot point mutations within helical and kinase domains, such as E542K, E545K, and H1047R. These mutations have been observed to occur in many cancer types such as lung, stomach, endometrial, ovarian, bladder, breast, colon, brain, prostate, and skin cancers. Because these gain-of-function mutations in PI3K α are associated with tumor progression, targeting this pathway may provide valuable therapeutic opportunities (Courtney et al., *J. Clin. Oncol.*, **2010**, 28 (6), 1075-1083). While multiple inhibitors of PI3Ks have been developed (for example, taselisib, alpelisib, buparlisib and others), these molecules inhibit multiple PI3K isoforms. These “pan-PI3K” inhibitors have

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encountered major hurdle in the clinical development due to inability to achieve the required level of target inhibition in tumors while avoiding toxicity in cancer patients (Fruman et al., *Nat. Rev. Drug Discov.*, **2014**, 13(2), 140-156). The toxicity of PI3K inhibitors is dependent on their isoform selectivity profile. Inhibition of PI3K α is associated with hyperglycemia and rash, while inhibition of PI3K δ or PI3K γ is associated with diarrhea, myelosuppression, and transaminitis (Hanker et al., *Cancer Discov.*, **2019**, 9(4), 482-491). Therefore, selective inhibitors of PI3K α may increase the therapeutic window, enabling sufficient target inhibition in the tumor while avoiding dose-limiting toxicity in cancer patients. However, given the central role of PI3K α in regulating glucose homeostasis and other critical physiological process, current PI3K α selective inhibitors, which are equally potent to wild-type and mutant PI3K α , often cause hyperglycemia and/or hyperinsulinemia (Busaidy et al., *J. Clin. Oncol.*, **2012**, 30, 2919-2928). In summary, developing inhibitors with enhanced selectivity for mutant PI3K α against wild-type PI3K α would be able to overcome the problem of compensatory insulin production and hyperglycemia.

SUMMARY

The present disclosure provides, *inter alia*, compounds of Formula I:



I

or pharmaceutically acceptable salts thereof, wherein constituent members are defined herein.

The present disclosure further provides a pharmaceutical composition comprising a compound of the disclosure, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

The present disclosure further provides methods of inhibiting PI3K α activity, comprising contacting the PI3K α with a compound described herein, or a pharmaceutically acceptable salt thereof.

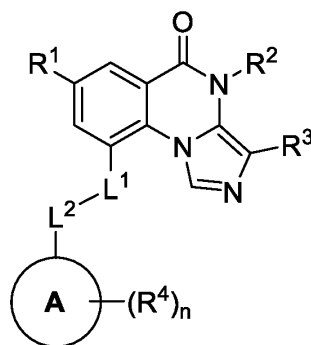
The present disclosure further provides methods of treating a disease or a disorder associated with PI3K α in a patient by administering to the patient a therapeutically effective amount of a compound of the disclosure, or a pharmaceutically acceptable salt thereof.

The present disclosure further provides a compound described herein, or a pharmaceutically acceptable salt thereof, for use in any of the methods described herein.

The present disclosure further provides use of a compound described herein, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for use in any of the methods described herein.

DETAILED DESCRIPTION

The present disclosure provides a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

n is 0, 1, 2, 3, 4, 5, or 6;

Ring A is C₃₋₁₄ cycloalkyl, C₆₋₁₀ aryl, 4-14 membered heterocycloalkyl, or 5-10 membered heteroaryl;

L¹ is C₁₋₄ alkylene, wherein the C₁₋₄ alkylene is optionally substituted with 1, 2, 3, or 4 independently selected R^G substituents;

L² is selected from bond, -O-, and -N(R^L)-;

R^L is selected from H, C₁₋₆ alkyl, and C₁₋₆ haloalkyl;

R¹ is selected from H, halo, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, and -CN;

R² is selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₇ cycloalkyl, and C₃₋₇ cycloalkyl-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₇ cycloalkyl, and C₃₋₇ cycloalkyl-C₁₋₄ alkyl of R² are each optionally substituted with 1, 2, 3, or 4

independently selected R^G substituents;

R³ is selected from H, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a3}, -SR^{a3}, -NR^{c3}R^{d3}, -NO₂, -C(O)R^{a3}, -C(O)OR^{a3}, -C(O)NR^{c3}R^{d3}, -C(O)NR^{c3}(OR^{a3}), -OC(O)R^{a3}, -OC(O)NR^{c3}R^{d3}, -OC(O)OR^{a3}, -OS(O)₂R^{b3}, -OS(O)₂NR^{c3}R^{d3}, -NR^{c3}C(O)R^{a3}, -NR^{c3}C(O)OR^{a3}, -NR^{c3}C(O)NR^{c3}R^{d3}, -NR^{c3}S(O)₂R^{b3}, -NR^{c3}S(O)₂NR^{c3}R^{d3}, -NR^{c3}OR^{a3}, -NR^{c3}S(O)R^{b3}, -NR^{c3}S(O)NR^{c3}R^{d3}, -S(O)R^{b3}, -S(O)₂R^{b3}, -S(O)NR^{c3}R^{d3}, -S(O)₂NR^{c3}R^{d3}, -C(=NR^{e3})R^{a3}, -C(=NR^{e3})NR^{c3}R^{d3}, -NR^{c3}C(=NR^{e3})R^{a3}, -NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}, -NR^{c3}S(O)(=NR^{e3})R^{b3}, -NR^{c3}S(O)(=NR^{e3})NR^{c3}R^{d3}, -OS(O)(=NR^{e3})R^{b3}, -S(O)(=NR^{e3})R^{b3}, -S(O)(=NR^{e3})NR^{c3}R^{d3}, -C(O)NR^{c3}S(O)₂R^{b3}, -C(O)NR^{c3}S(O)₂NR^{c3}R^{d3}, -S(O)₂NR^{c3}C(O)R^{b3}, -NR^{c3}S(O)NR^{c3}C(O)R^{b3}, and -P(O)R^{f3}R^{g3}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R³ are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{a3}, R^{c3}, and R^{d3} is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{a3}, R^{c3},

and R^{d3} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

or, any R^{e3} and R^{d3} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{b3} is independently selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{b3} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{e3} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^{f3} and R^{g3} are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^{3A} is independently selected from oxo, H, halo, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, (5-10 membered heteroaryl)- C_{1-4} alkyl, -CN, -OR^{a3A}, -SR^{a3A}, -NR^{c3A}R^{d3A}, -NO₂, -C(O)R^{a3A}, -C(O)OR^{a3A}, -C(O)NR^{c3A}R^{d3A}, -C(O)NR^{c3A}(OR^{a3A}), -OC(O)R^{a3A}, -OC(O)NR^{c3A}R^{d3A}, -OC(O)OR^{a3A}, -OS(O)₂R^{b3A}, -OS(O)₂NR^{c3A}R^{d3A}, -NR^{c3A}C(O)R^{a3A}, -NR^{c3A}C(O)OR^{a3A}, -

$\text{NR}^{\text{c3A}}\text{C}(\text{O})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{NR}^{\text{c3A}}\text{S}(\text{O})_2\text{R}^{\text{b3A}}$, $-\text{NR}^{\text{c3A}}\text{S}(\text{O})_2\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{NR}^{\text{c3A}}\text{OR}^{\text{a3A}}$, -
 $\text{NR}^{\text{c3A}}\text{S}(\text{O})\text{R}^{\text{b3A}}$, $-\text{NR}^{\text{c3A}}\text{S}(\text{O})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{S}(\text{O})\text{R}^{\text{b3A}}$, $-\text{S}(\text{O})_2\text{R}^{\text{b3A}}$, $-\text{S}(\text{O})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, -
 $\text{S}(\text{O})_2\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{C}(=\text{NR}^{\text{c3A}})\text{R}^{\text{a3A}}$, $-\text{C}(=\text{NR}^{\text{c3A}})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{NR}^{\text{c3A}}\text{C}(=\text{NR}^{\text{c3A}})\text{R}^{\text{a3A}}$, -
 $\text{NR}^{\text{c3A}}\text{C}(=\text{NR}^{\text{c3A}})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{NR}^{\text{c3A}}\text{S}(\text{O})(=\text{NR}^{\text{c3A}})\text{R}^{\text{b3A}}$, -
5 $\text{NR}^{\text{c3A}}\text{S}(\text{O})(=\text{NR}^{\text{c3A}})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{OS}(\text{O})(=\text{NR}^{\text{c3A}})\text{R}^{\text{b3A}}$, $-\text{S}(\text{O})(=\text{NR}^{\text{c3A}})\text{R}^{\text{b3A}}$, -
 $\text{S}(\text{O})(=\text{NR}^{\text{c3A}})\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, $-\text{C}(\text{O})\text{NR}^{\text{c3A}}\text{S}(\text{O})_2\text{R}^{\text{b3A}}$, $-\text{C}(\text{O})\text{NR}^{\text{c3A}}\text{S}(\text{O})_2\text{NR}^{\text{c3A}}\text{R}^{\text{d3A}}$, -
 $\text{S}(\text{O})_2\text{NR}^{\text{c3A}}\text{C}(\text{O})\text{R}^{\text{b3A}}$, $-\text{NR}^{\text{c3A}}\text{S}(\text{O})\text{NR}^{\text{c3A}}\text{C}(\text{O})\text{R}^{\text{b3A}}$, and $-\text{P}(\text{O})\text{R}^{\text{f3A}}\text{R}^{\text{g3A}}$, wherein the
 C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10
membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl,
10 C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10
membered heteroaryl)- C_{1-4} alkyl of R^{a3A} are each optionally substituted with 1, 2, 3, 4,
5, or 6 independently selected R^{G} substituents;
each R^{a3A} , R^{c3A} , and R^{d3A} is independently selected from H, C_{1-6} alkyl, C_{1-6}
haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered
15 heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4}
 C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered
heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl,
 C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered
heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered
20 heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{a3A} , R^{c3A} ,
and R^{d3A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected
 R^{G} substituents;
or, any R^{c3A} and R^{d3A} attached to the same N atom, together with the N atom
to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein
25 the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5,
or 6 independently selected R^{G} substituents;
each R^{b3A} is independently selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6}
alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-
10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10
membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl,
wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10}
aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl-

C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{b3A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{e3A} is independently selected from H, OH, CN, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{f3A} and R^{g3A} are independently selected from H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

R⁴ is selected from oxo, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a4}, -SR^{a4}, -NR^{c4}R^{d4}, -NO₂, -C(O)R^{a4}, -C(O)OR^{a4}, -C(O)NR^{c4}R^{d4}, -C(O)NR^{c4}(OR^{a4}), -OC(O)R^{a4}, -OC(O)NR^{c4}R^{d4}, -OC(O)OR^{a4}, -OS(O)₂R^{b4}, -OS(O)₂NR^{c4}R^{d4}, -NR^{c4}C(O)R^{a4}, -NR^{c4}C(O)OR^{a4}, -NR^{c4}C(O)NR^{c4}R^{d4}, -NR^{c4}S(O)₂R^{b4}, -NR^{c4}S(O)₂NR^{c4}R^{d4}, -NR^{c4}OR^{a4}, -NR^{c4}S(O)R^{b4}, -NR^{c4}S(O)NR^{c4}R^{d4}, -S(O)R^{b4}, -S(O)₂R^{b4}, -S(O)NR^{c4}R^{d4}, -S(O)₂NR^{c4}R^{d4}, -C(=NR^{e4})R^{a4}, -C(=NR^{e4})NR^{c4}R^{d4}, -NR^{c4}C(=NR^{e4})R^{a4}, -NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}, -NR^{c4}S(O)(=NR^{e4})R^{b4}, -NR^{c4}S(O)(=NR^{e4})NR^{c4}R^{d4}, -OS(O)(=NR^{e4})R^{b4}, -S(O)(=NR^{e4})R^{b4}, -S(O)(=NR^{e4})NR^{c4}R^{d4}, -C(O)NR^{c4}S(O)₂R^{b4}, -C(O)NR^{c4}S(O)₂NR^{c4}R^{d4}, -S(O)₂NR^{c4}C(O)R^{a4}, -NR^{c4}S(O)NR^{c4}C(O)R^{a4}, and -P(O)R^{f4}R^{g4}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R⁴ are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{a4} , R^{c4} , and R^{d4} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{a4} , R^{c4} , and R^{d4} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

or, any R^{c4} and R^{d4} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{b4} is independently selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{b4} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{e4} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^{f4} and R^{g4} are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4}

alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{4A} is independently selected from oxo, H, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a4A}, -SR^{a4A}, -NR^{c4A}R^{d4A}, -NO₂, -C(O)R^{a4A}, -C(O)OR^{a4A}, -C(O)NR^{c4A}R^{d4A}, -C(O)NR^{c4A}(OR^{a4A}), -OC(O)R^{a4A}, -OC(O)NR^{c4A}R^{d4A}, -OC(O)OR^{a4A}, -OS(O)₂R^{b4A}, -OS(O)₂NR^{c4A}R^{d4A}, -NR^{c4A}C(O)R^{a4A}, -NR^{c4A}C(O)OR^{a4A}, -NR^{c4A}C(O)NR^{c4A}R^{d4A}, -NR^{c4A}S(O)₂R^{b4A}, -NR^{c4A}S(O)₂NR^{c4A}R^{d4A}, -NR^{c4A}OR^{a4A}, -NR^{c4A}S(O)R^{b4A}, -NR^{c4A}S(O)NR^{c4A}R^{d4A}, -S(O)R^{b4A}, -S(O)₂R^{b4A}, -S(O)NR^{c4A}R^{d4A}, -S(O)₂NR^{c4A}R^{d4A}, -C(=NR^{e4A})R^{a4A}, -C(=NR^{e4A})NR^{c4A}R^{d4A}, -NR^{c4A}C(=NR^{e4A})R^{a4A}, -NR^{c4A}C(=NR^{e4A})NR^{c4A}R^{d4A}, -NR^{c4A}S(O)(=NR^{e4A})R^{b4A}, -NR^{c4A}S(O)(=NR^{e4A})NR^{c4A}R^{d4A}, -OS(O)(=NR^{e4A})R^{b4A}, -S(O)(=NR^{e4A})R^{b4A}, -S(O)(=NR^{e4A})NR^{c4A}R^{d4A}, -C(O)NR^{c4A}S(O)₂R^{b4A}, -C(O)NR^{c4A}S(O)₂NR^{c4A}R^{d4A}, -S(O)₂NR^{c4A}C(O)R^{b4A}, -NR^{c4A}S(O)NR^{c4A}C(O)R^{b4A}, and -P(O)R^{f4A}R^{g4A}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{a4A}, R^{c4A}, and R^{d4A} is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{a4A}, R^{c4A}, and R^{d4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

or, any R^{c4A} and R^{d4A} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

5 each R^{b4A} is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{b4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{e4A} is independently selected from H, OH, CN, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{f4A} and R^{g4A} are independently selected from H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^G is independently selected from H, D, OH, CN, halo, oxo, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ haloalkyl, cyano-C₁₋₄ alkyl, HO-C₁₋₄ alkyl, C₁₋₄ alkoxy-C₁₋₄ alkyl, C₃₋₇ cycloalkyl, 4-7 membered heterocycloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, amino, C₁₋₃ alkylamino, di(C₁₋₃ alkyl)amino, thio, C₁₋₃ alkylthio, C₁₋₃ alkylsulfinyl, C₁₋₃ alkylsulfonyl, carbamyl, C₁₋₃ alkylcarbamyl, di(C₁₋₃ alkyl)carbamyl, carboxy, C₁₋₃ alkylcarbonyl, C₁₋₃ alkoxycarbonyl, C₁₋₃ alkylcarbonyloxy, C₁₋₃ alkylcarbonylamino, C₁₋₃ alkoxycarbonylamino, aminocarbonyloxy, C₁₋₃ alkylaminocarbonyloxy, di(C₁₋₃ alkyl)aminocarbonyloxy, C₁₋₃ alkylsulfonylamino, aminosulfonyl, C₁₋₃ alkylaminosulfonyl, di(C₁₋₃ alkyl)aminosulfonyl,

aminosulfonylamino, C₁₋₃ alkylaminosulfonylamino, di(C₁₋₃ alkyl)aminosulfonylamino, aminocarbonylamino, C₁₋₃ alkylaminocarbonylamino, and di(C₁₋₃ alkyl)aminocarbonylamino.

In some embodiments, L¹ is ethylene, wherein the ethylene is optionally substituted with one R^G substituent.

In some embodiments, L¹ is ethylene, wherein the ethylene is optionally substituted with deuterium.

In some embodiments, L² is -N(R^L)-.

In some embodiments, L² is -NH-.

In some embodiments, R¹ is selected from halo, C₁₋₃ alkyl, and C₁₋₃ haloalkyl.

In some embodiments, R¹ is selected from chloro, methyl, and trifluoromethyl.

In some embodiments, R¹ is halo or C₁₋₃ alkyl.

In some embodiments, R¹ is chloro or methyl.

In some embodiments, R¹ is chloro.

In some embodiments, R¹ is methyl.

In some embodiments, R¹ is trifluoromethyl.

In some embodiments, R² is C₁₋₃ alkyl.

In some embodiments, R² is selected from methyl and trideuteromethyl.

In some embodiments, R² is methyl.

In some embodiments, R² is trideuteromethyl.

In some embodiments, R³ is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and C(O)NR^{c3}R^{d3}, wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl of R³ are each optionally substituted with 1, 2, 3, or 4 independently selected R^{3A} substituents.

In some embodiments, R³ is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl,

thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and C(O)NR^{c3}R^{d3}, wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl
 5 of R³ are each optionally substituted with 1 or 2 independently selected R^{3A} substituents.

In some embodiments, R³ is selected from pyrazolyl, pyrimidinyl, piperidinyl, azetidylmethyl, pyridinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, and C(O)NR^{c3}R^{d3}, wherein the
 10 pyrazolyl, pyrimidinyl, piperidinyl, azetidylmethyl, pyridinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl of R³ are each optionally substituted with 1, 2, 3, or 4 independently selected R^{3A} substituents.

In some embodiments, R³ is selected from pyrazolyl, pyrimidinyl, piperidinyl, and C(O)NR^{c3}R^{d3}, wherein the pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl of
 15 R³ are each optionally substituted with one R^{3A} substituent.

In some embodiments, each R^{3A} is independently selected from halo, C₁₋₃ alkyl, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxy, oxetanyl, amino, C₁₋₃ alkylamino, di(C₁₋₃ alkyl)amino, -C(O)C₁₋₃ alkyl, -C(O)C₁₋₃ hydroxyalkyl, -C(O)C₃₋₆ cycloalkyl, and -
 20 S(O)₂C₁₋₃ alkyl;

In some embodiments, R³ is selected from pyrazolyl, pyrimidinyl, piperidinyl, and C(O)NR^{c3}R^{d3}, wherein the pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl of
 R³ are each optionally substituted with one R^{3A} substituent selected from C₁₋₃ alkyl, amino, and -C(O)C₁₋₃ alkyl.

In some embodiments, R³ is selected from pyrazolyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R³ are each
 25 optionally substituted with one R^{3A} substituent selected from C₁₋₃ alkyl, amino, and -C(O)C₁₋₃ alkyl.

In some embodiments, R³ is selected from pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R³ are each
 30 optionally substituted with one R^{3A} substituent selected from methyl, amino, and methylcarbonyl.

In some embodiments, R^3 is selected from methylpyrazolyl, aminopyrimidinyl, and (methylcarbonyl)piperidinyl.

In some embodiments, R^3 is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, and $C(O)NR^{c3}R^{d3}$,
 5 wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents.

10 In some embodiments, R^3 is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl, wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents.
 15

In some embodiments, each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl.

20 In some embodiments, R^3 is selected from (difluoroazetidyl)methyl, oxetanylpiperidinyl, (methylcarbonyl)piperidinyl, (isopropylcarbonyl)piperidinyl, (hydroxymethylcarbonyl)piperidinyl, (cyclopropylcarbonyl)piperidinyl, (methylsulfonyl)piperidinyl, (isopropylsulfonyl)piperidinyl, (cyclopropylsulfonyl)piperidinyl, pyrazolyl, methylpyrazolyl, (hydroxyethyl)pyrazolyl, pyridinyl, (hydroxymethyl)pyridinyl, aminopyridinyl, (amino)(chloro)pyridinyl, (methylamino)pyridinyl, (dimethylamino)pyridinyl, aminopyrimidinyl, (hydroxymethyl)pyrimidinyl, (amino)(fluoro)pyrimidinyl, (amino)(methyl)pyrimidinyl, (amino)(methoxy)pyrimidinyl, methyl-2H-pyrazolo[3,4-b]pyridine, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, (amino)(fluoro)pyridinyl, methylimidazolyl, aminothiazolyl,
 25 (amino)(methyl)thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl.
 30

In some embodiments, R^3 is selected from (difluoroazetidiny)methyl, oxetanylpiperidinyl, (methylcarbonyl)piperidinyl, (isopropylcarbonyl)piperidinyl, (hydroxymethylcarbonyl)piperidinyl, (cyclopropylcarbonyl)piperidinyl, (methylsulfonyl)piperidinyl, (isopropylsulfonyl)piperidinyl, (cyclopropylsulfonyl)piperidinyl, pyrazolyl, methylpyrazolyl, (hydroxyethyl)pyrazolyl, pyridinyl, (hydroxymethyl)pyridinyl, aminopyridinyl, (methylamino)pyridinyl, (dimethylamino)pyridinyl, (amino)(chloro)pyridinyl, aminopyrimidinyl, (hydroxymethyl)pyrimidinyl, (amino)(fluoro)pyrimidinyl, (amino)(methyl)pyrimidinyl, (amino)(methoxy)pyrimidinyl, methyl-2H-pyrazolo[3,4-b]pyridine, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl.

In some embodiments, R^3 is $C(O)NR^{c3}R^{d3}$.

In some embodiments, R^{c3} and R^{d3} are each independently selected from C_{1-3} alkyl.

In some embodiments, R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl.

In some embodiments, R^{c3} and R^{d3} are each methyl.

In some embodiments, R^{c3} and R^{d3} are each trideuteromethyl.

In some embodiments, Ring A is selected from phenyl and pyridinyl.

In some embodiments, Ring A is phenyl.

In some embodiments, Ring A is pyridinyl.

In some embodiments, n is 1, 2, or 3.

In some embodiments, n is 1 or 2.

In some embodiments, n is 2.

In some embodiments, each R^4 is independently selected from H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, $C(O)NR^{c4}R^{d4}$, and tetrazolyl, wherein the tetrazolyl of R^4 is optionally substituted with one R^{4A} substituent.

In some embodiments, each R^{c4} and R^{d4} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl.

In some embodiments, each R^{c4} and R^{d4} is H.

In some embodiments, each R^4 is independently selected from H, halo, C_{1-3} alkyl, C_{1-3} alkoxy, $C(O)NH_2$, and tetrazolyl, wherein the tetrazolyl of R^4 is optionally substituted with one R^{4A} substituent.

In some embodiments, at least one R^4 is $C(O)NH_2$.

5 In some embodiments, at least one R^4 is tetrazolyl, wherein the tetrazolyl of R^4 is optionally substituted with one R^{4A} substituent.

In some embodiments, at least one R^4 is $C(O)NH_2$; and each additional R^4 is independently selected from H, halo, C_{1-3} alkyl, and C_{1-3} alkoxy.

10 In some embodiments, at least one R^4 is tetrazolyl, wherein the tetrazolyl of R^4 is optionally substituted with one R^{4A} substituent; and each additional R^4 is independently selected from H, halo, C_{1-3} alkyl, and C_{1-3} alkoxy.

In some embodiments, each R^4 is independently selected from H, halo, C_{1-3} alkyl, and C_{1-3} alkoxy.

15 In some embodiments, each R^4 is independently is selected from H, fluoro, chloro, methyl, and methoxy.

In some embodiments, R^4 is halo.

In some embodiments, R^4 is fluoro or chloro.

In some embodiments, R^4 is fluoro.

In some embodiments, R^4 is chloro.

20 In some embodiments, R^4 is H.

In some embodiments, R^4 is methyl.

In some embodiments, R^4 is methoxy.

25 In some embodiments, each R^{4A} is independently selected from C_{1-3} alkyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^4 are each optionally substituted with C_{1-3} alkyl.

In some embodiments, each R^{4A} is selected from C_{1-3} alkyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^4 are each optionally substituted with C_{1-3} alkyl.

30 In some embodiments, R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl.

In some embodiments, R^{4A} is selected from methyl, trideuteromethyl, ethyl, methylazetidiny, and methylpiperidiny.

In some embodiments, R^{4A} is methyl.

In some embodiments, R^{4A} is ethyl.

5 In some embodiments, R^{4A} is trideuteromethyl.

In some embodiments, R^{4A} is selected methylazetidiny.

In some embodiments, R^{4A} is methylpiperidiny.

In some embodiments, R^G is H or D.

In some embodiments, R^G is H.

10 In some embodiments, R^G is D.

In some embodiments:

R^1 is selected from chloro, methyl, and trifluoromethyl;

R^2 is selected from methyl and trideuteromethyl;

15 R^3 is selected from pyrazolyl, pyridinyl, pyrimidinyl, piperidinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from methyl, amino, and methylcarbonyl;

R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

20 R^4 is fluoro or chloro; and

R^G is H or D.

In some embodiments:

R^1 is chloro or methyl;

R^2 is methyl or trideuteromethyl;

25 R^3 is selected from pyrimidinyl, azetidinylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidinyl, azetidinylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl of R^3 are each optionally substituted with 1 or 2 independently selected R^{3A} substituents;

30

each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl;

5 R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

R^4 is selected from H, fluoro, chloro, methyl, and methoxy;

R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl; and

10

R^G is H or D.

In some embodiments:

R^1 is chloro or methyl;

R^2 is methyl or trideuteromethyl;

15 R^3 is selected from pyrimidiny, azetidiny, methyl, pyrazoly, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, imidazo[1,5-a]pyridiny, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidiny, azetidiny, methyl, pyrazoly, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny of

20 R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl;

25 R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

R^4 is selected from H, fluoro, chloro, methyl, and methoxy;

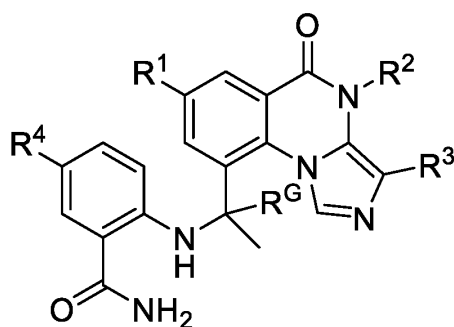
R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl; and

30

R^G is H or D.

In some embodiments, the compound of Formula I is a compound of Formula

II:

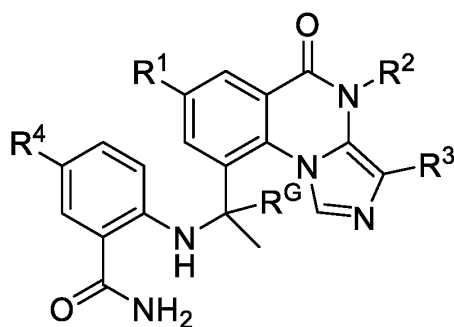


II

5 or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula I is a compound of Formula

II:



II

10 or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from halo, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^2 is C_{1-3} alkyl;

R^3 is selected from pyrazolyl, pyrimidinyl, piperidinyl, and $C(O)NR^{c3}R^{d3}$,

wherein the pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl of R^3 are each

15 optionally substituted with one R^{3A} substituent selected from C_{1-3} alkyl, amino, and -
 $C(O)C_{1-3}$ alkyl;

each R^{c3} and R^{d3} is independently selected from C_{1-3} alkyl and C_{1-3} haloalkyl;

R^4 is halo; and

R^G is H or D.

In some embodiments of Formula II, R^1 is selected from chloro, methyl, and trifluoromethyl.

In some embodiments of Formula II, R^1 is chloro.

In some embodiments of Formula II, R^1 is methyl.

5 In some embodiments of Formula II, R^1 is trifluoromethyl.

In some embodiments of Formula II, R^2 is selected from methyl and trideuteromethyl.

In some embodiments of Formula II, R^2 is methyl.

In some embodiments of Formula II, R^2 is trideuteromethyl.

10 In some embodiments of Formula II, R^3 is $C(O)NR^{c3}R^{d3}$.

In some embodiments of Formula II, R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl.

In some embodiments of Formula II, R^{c3} and R^{d3} are each methyl.

In some embodiments of Formula II, R^{c3} and R^{d3} are each trideuteromethyl.

15 In some embodiments of Formula II, R^3 is selected from pyrazolyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from C_{1-3} alkyl, amino, and $-C(O)C_{1-3}$ alkyl.

20 In some embodiments of Formula II, R^3 is selected from pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from methyl, amino, and methylcarbonyl.

In some embodiments of Formula II, R^3 is selected from methylpyrazolyl, aminopyrimidinyl, and (methylcarbonyl)piperidinyl.

25 In some embodiments of Formula II, R^3 is methylpyrazolyl.

In some embodiments of Formula II, R^3 is aminopyrimidinyl.

In some embodiments of Formula II, R^3 is (methylcarbonyl)piperidinyl.

In some embodiments of Formula II, R^4 is fluoro or chloro.

In some embodiments of Formula II, R^4 is fluoro.

30 In some embodiments of Formula II, R^4 is chloro.

In some embodiments of Formula II, R^G is H.

In some embodiments of Formula II, R^G is D.

In some embodiments of Formula II:

R^1 is selected from chloro, methyl, and trifluoromethyl;

R^2 is selected from methyl and trideuteromethyl;

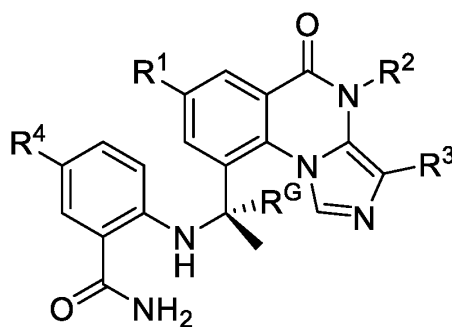
R^3 is selected from pyrazolyl, pyridinyl, pyrimidinyl, piperidinyl, and
 5 $C(O)NR^{c3}R^{d3}$, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each
 optionally substituted with one R^{3A} substituent selected from methyl, amino, and
 methylcarbonyl;

R^{c3} and R^{d3} are each independently selected from methyl and
 trideuteromethyl;

10 R^4 is fluoro or chloro; and

R^G is H or D.

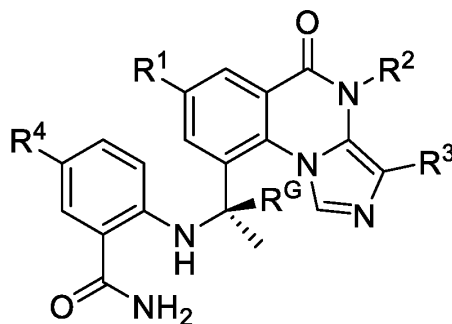
In some embodiments, the compound of Formula I or Formula II is a
 compound of Formula IIa:



15 **IIa**

or a pharmaceutically acceptable salt thereof.

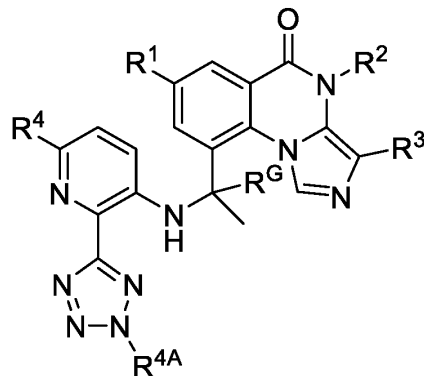
In some embodiments, the compound of Formula I or Formula II is a
 compound of Formula IIb:



20 **IIb**

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula I is a compound of Formula III:

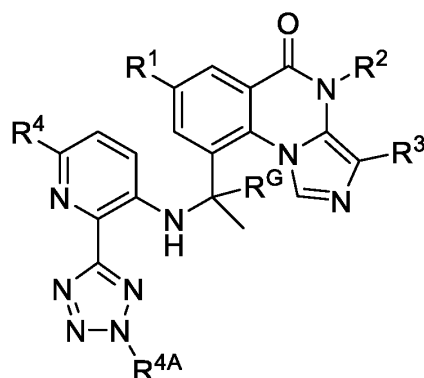


5

III

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula I is a compound of Formula III:



10

III

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is halo or C_{1-3} alkyl;

R^2 is C_{1-3} alkyl;

R^3 is selected from pyrimidinyl, azetidinemethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidinyl, azetidinemethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl,

15

pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

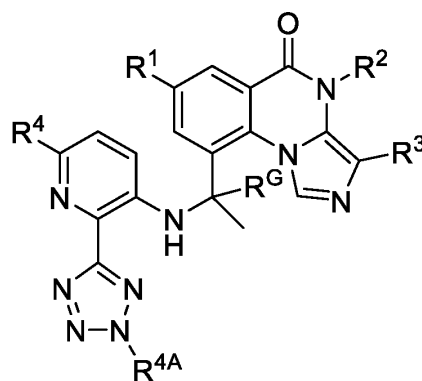
each R^{3A} is independently selected from halo, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxy, oxetanyl, amino, C_{1-3} alkylamino, di(C_{1-3} alkyl)amino, $-C(O)C_{1-3}$ alkyl, $-C(O)C_{1-3}$ hydroxyalkyl, $-C(O)C_{3-6}$ cycloalkyl, and $-S(O)_2C_{1-3}$ alkyl;

R^4 is selected from H, halo, C_{1-3} alkyl, and C_{1-3} alkoxy;

R^{4A} is selected from C_{1-3} alkyl, azetidiny, and piperidinyl, wherein the azetidiny and piperidinyl of R^4 are each optionally substituted with C_{1-3} alkyl; and

R^G is H or D.

In some embodiments, the compound of Formula I is a compound of Formula III:



III

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is halo or C_{1-3} alkyl;

R^2 is C_{1-3} alkyl;

R^3 is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from halo, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxy, oxetanyl, amino, C_{1-3} alkylamino, di(C_{1-3} alkyl)amino, $-C(O)C_{1-3}$ alkyl, $-C(O)C_{1-3}$ hydroxyalkyl, $-C(O)C_{3-6}$ cycloalkyl, and $-S(O)_2C_{1-3}$ alkyl;

R^4 is selected from H, halo, C_{1-3} alkyl, and C_{1-3} alkoxy;

5 R^{4A} is selected from C_{1-3} alkyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^4 are each optionally substituted with C_{1-3} alkyl; and R^G is H or D.

In some embodiments of Formula III, R^1 is chloro or methyl.

In some embodiments of Formula III, R^1 is chloro.

10 In some embodiments of Formula III, R^1 is methyl.

In some embodiments of Formula III, R^2 is methyl or trideuteromethyl.

In some embodiments of Formula III, R^2 is methyl.

In some embodiments of Formula III, R^2 is trideuteromethyl.

In some embodiments of Formula III, R^3 is selected from pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, imidazo[1,5-a]pyridiny, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny of R^3 are each optionally substituted with
20 1 or 2 R^{3A} substituents.

In some embodiments of Formula III, R^3 is selected from pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny, wherein the pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents.

In some embodiments of Formula III, each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl.

In some embodiments of Formula III, R³ is selected from
 (difluoroazetidiny)methyl, oxetanylpiperidinyl, (methylcarbonyl)piperidinyl,
 (isopropylcarbonyl)piperidinyl, (hydroxymethylcarbonyl)piperidinyl,
 (cyclopropylcarbonyl)piperidinyl, (methylsulfonyl)piperidinyl,
 5 (isopropylsulfonyl)piperidinyl, (cyclopropylsulfonyl)piperidinyl, pyrazolyl,
 methylpyrazolyl, (hydroxyethyl)pyrazolyl, pyridinyl, (hydroxymethyl)pyridinyl,
 aminopyridinyl, (amino)(chloro)pyridinyl, (methylamino)pyridinyl,
 (dimethylamino)pyridinyl, aminopyrimidinyl, (hydroxymethyl)pyrimidinyl,
 (amino)(fluoro)pyrimidinyl, (amino)(methyl)pyrimidinyl,
 10 (amino)(methoxy)pyrimidinyl, methyl-2H-pyrazolo[3,4-b]pyridine, pyrazolo[1,5-
 a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl,
 (amino)(fluoro)pyridinyl, methylimidazolyl, aminothiazolyl,
 (amino)(methyl)thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl.

In some embodiments of Formula III, R³ is selected from
 15 (difluoroazetidiny)methyl, oxetanylpiperidinyl, (methylcarbonyl)piperidinyl,
 (isopropylcarbonyl)piperidinyl, (hydroxymethylcarbonyl)piperidinyl,
 (cyclopropylcarbonyl)piperidinyl, (methylsulfonyl)piperidinyl,
 (isopropylsulfonyl)piperidinyl, (cyclopropylsulfonyl)piperidinyl, pyrazolyl,
 methylpyrazolyl, (hydroxyethyl)pyrazolyl, pyridinyl, (hydroxymethyl)pyridinyl,
 20 aminopyridinyl, (amino)(chloro)pyridinyl, (methylamino)pyridinyl,
 (dimethylamino)pyridinyl, aminopyrimidinyl, (hydroxymethyl)pyrimidinyl,
 (amino)(fluoro)pyrimidinyl, (amino)(methyl)pyrimidinyl,
 (amino)(methoxy)pyrimidinyl, methyl-2H-pyrazolo[3,4-b]pyridine, pyrazolo[1,5-
 a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, and imidazo[1,5-a]pyridinyl.

25 In some embodiments of Formula III, R³ is (difluoroazetidiny)methyl.

In some embodiments of Formula III, R³ is selected from oxetanylpiperidinyl.

In some embodiments of Formula III, R³ is (methylcarbonyl)piperidinyl.

In some embodiments of Formula III, R³ is (isopropylcarbonyl)piperidinyl.

In some embodiments of Formula III, R³ is
 30 (hydroxymethylcarbonyl)piperidinyl.

In some embodiments of Formula III, R³ is (cyclopropylcarbonyl)piperidinyl.

In some embodiments of Formula III, R³ is (methylsulfonyl)piperidinyl.

- In some embodiments of Formula III, R³ is (isopropylsulfonyl)piperidinyl.
- In some embodiments of Formula III, R³ is (cyclopropylsulfonyl)piperidinyl.
- In some embodiments of Formula III, R³ is pyrazolyl.
- In some embodiments of Formula III, R³ is methylpyrazolyl.
- 5 In some embodiments of Formula III, R³ is (hydroxyethyl)pyrazolyl.
- In some embodiments of Formula III, R³ is pyridinyl.
- In some embodiments of Formula III, R³ is (hydroxymethyl)pyridinyl.
- In some embodiments of Formula III, R³ is aminopyridinyl.
- In some embodiments of Formula III, R³ is (amino)(chloro)pyridinyl.
- 10 In some embodiments of Formula III, R³ is (methylamino)pyridinyl.
- In some embodiments of Formula III, R³ is (dimethylamino)pyridinyl.
- In some embodiments of Formula III, R³ is aminopyrimidinyl.
- In some embodiments of Formula III, R³ is (hydroxymethyl)pyrimidinyl.
- In some embodiments of Formula III, R³ is (amino)(fluoro)pyrimidinyl.
- 15 In some embodiments of Formula III, R³ is (amino)(methyl)pyrimidinyl.
- In some embodiments of Formula III, R³ is (amino)(methoxy)pyrimidinyl.
- In some embodiments of Formula III, R³ is methyl-2H-pyrazolo[3,4-b]pyridine.
- In some embodiments of Formula III, R³ is pyrazolo[1,5-a]pyridinyl.
- 20 In some embodiments of Formula III, R³ is pyrazolo[1,5-a]pyrimidinyl.
- In some embodiments of Formula III, R³ is imidazo[1,5-a]pyridinyl.
- In some embodiments of Formula III, R³ is (amino)(fluoro)pyridinyl.
- In some embodiments of Formula III, R³ is methylimidazolyl.
- In some embodiments of Formula III, R³ is aminothiazolyl.
- 25 In some embodiments of Formula III, R³ is (amino)(methyl)thiazolyl.
- In some embodiments of Formula III, R³ is 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl.
- In some embodiments of Formula III, R³ is C(O)NR^{c3}R^{d3}.
- In some embodiments of Formula III, R^{c3} and R^{d3} are each independently
- 30 selected from methyl and trideuteromethyl.
- In some embodiments of Formula III, R^{c3} and R^{d3} are each methyl.
- In some embodiments of Formula III, R^{c3} and R^{d3} are each trideuteromethyl.

In some embodiments of Formula III, R^4 is selected from H, fluoro, chloro, methyl, and methoxy.

In some embodiments of Formula III, R^4 is H.

In some embodiments of Formula III, R^4 is fluoro.

5 In some embodiments of Formula III, R^4 is chloro.

In some embodiments of Formula III, R^4 is methyl.

In some embodiments of Formula III, R^4 is methoxy.

In some embodiments of Formula III, R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl.

In some embodiments of Formula III, R^{4A} is selected from methyl, trideuteromethyl, ethyl, methylazetidiny, and methylpiperidiny.

In some embodiments of Formula III, R^{4A} is methyl.

In some embodiments of Formula III, R^{4A} is trideuteromethyl.

15 In some embodiments of Formula III, R^{4A} is ethyl.

In some embodiments of Formula III, R^{4A} is methylazetidiny.

In some embodiments of Formula III, R^{4A} is methylpiperidiny.

In some embodiments of Formula III, R^G is H.

In some embodiments of Formula III, R^G is D.

20 In some embodiments of Formula III:

R^1 is chloro or methyl;

R^2 is methyl or trideuteromethyl;

R^3 is selected from pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, imidazo[1,5-a]pyridiny, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxaziny, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, imidazo[1,5-a]pyridiny, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxaziny of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl,

methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl;

R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

5 R^4 is selected from H, fluoro, chloro, methyl, and methoxy;

R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl; and

R^G is H or D.

10 In some embodiments of Formula III:

R^1 is chloro or methyl;

R^2 is methyl or trideuteromethyl;

R^3 is selected from pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, pyrazolo[1,5-a]pyrimidiny, imidazo[1,5-a]pyridiny, and $C(O)NR^{c3}R^{d3}$,
15 wherein the pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl;

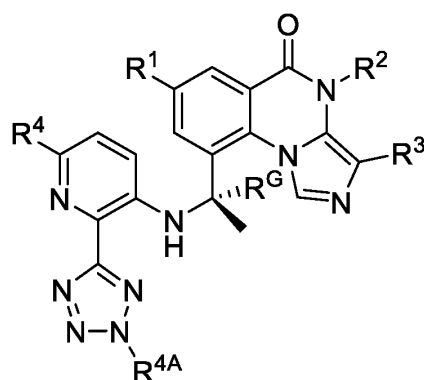
R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

25 R^4 is selected from H, fluoro, chloro, methyl, and methoxy;

R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R^{4A} are each optionally substituted with methyl; and

R^G is H or D.

30 In some embodiments, the compound of Formula III is a compound of Formula IIIa:

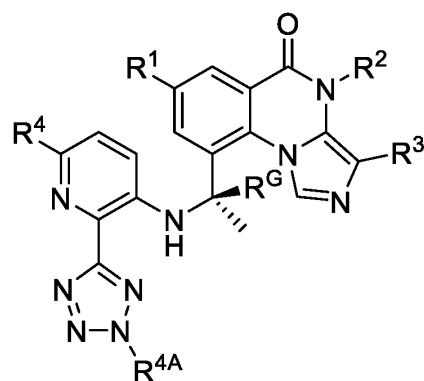


IIIa

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound of Formula III is a compound of

5 Formula IIIb:



IIIb

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound provided herein is selected from:

- 10 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 15 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

5 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

20 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

30 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

2-((1-(3-(1-acetyl piperidin-4-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

5 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

10 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

15 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

20 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4-methyl-N,N-bis(methyl-d₃)-5-oxo-7-(trifluoromethyl)-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(6-(hydroxymethyl)pyridin-3-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

30 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

5 9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(6-(methylamino)pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(dimethylamino)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyethyl)-1H-pyrazol-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

20 9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

25 9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyrimidin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

30 3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(imidazo[1,5-a]pyridin-6-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
5 9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
10 methyl (3-((1-(3-(bis(methyl-d₃)carbamoyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-6-chloropyridin-2-yl)carbamate;
15 9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((4-fluoro-2-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
20 9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
methyl (6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)carbamate;
25 9-(1-((4-fluoro-2-sulfamoylphenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((5-chloroquinolin-8-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
N,N,4,7-tetramethyl-9-(1-((6-methyl-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
30 2-((1-(3-(1-acetylpiperidin-4-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;

2-((1-(3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;
5 2-((1-(4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
5-fluoro-2-((1-(7-methyl-4-(methyl-d₃)-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)benzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
10 2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(oxetan-3-yl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;
15 3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
20 3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-isobutyrylpiperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
25 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropanecarbonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(methylsulfonyl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;
30 one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-
3-(1-(isopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-
one;

5 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-
3-(1-(cyclopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-
5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-methoxy-2-(2-(methyl-d₃)-2H-tetrazol-5-
yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-
5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((6-methyl-2-(2-
(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-
5(4H)-one;

3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((2-(2-(methyl-d₃)-
2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one;

15 9-(1-((6-methoxy-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-
N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)amino)ethyl)-4,7-
dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

20 3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-
yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-
dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-
yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(6-amino-3-pyridyl)-9-[1-[4-fluoro-2-(1-methyltriazol-4-yl)anilino]ethyl]-
4,7-dimethyl-imidazo[1,5-a]quinazolin-5-one;

3-(1-acetylpiperidin-4-yl)-9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-
b][1,4]oxazin-1-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-
one;

30 9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-3-(1-(2-
hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

- 3-(6-aminopyridin-3-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
- 3-(2-aminopyrimidin-5-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
- 5 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;
- 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
- 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 10 *N*,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-*N*-(2-hydroxyethyl)-*N*,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)methyl)carbamate;
- 15 methyl (6-chloro-3-(((3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)pyridin-2-yl)carbamate;
- 9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-*N,N*,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide;
- 20 9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-4,7-dimethyl-5-oxo-*N,N*-bis(trideuteriomethyl)imidazo[1,5-a]quinazoline-3-carboxamide;
- 9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 25 9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-*N,N*,4-tris(methyl-*d*₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
- 30 *a*]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

5 3-(2-aminopyrimidin-5-yl)-9-((6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-((3,3-difluoroazetidin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

methyl (3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)carbamate;

20 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-fluoro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

30 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(pyrimidin-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(4-hydroxypiperidin-1-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

5 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-morpholinopyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,5-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(5-methyl-1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one;

20 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

25 methyl (3-((3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)-6-chloropyridin-2-yl)carbamate;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

30 3-(6-amino-5-chloropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-methylpyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

5 3-(6-amino-5-methoxypyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methoxypyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(2-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyridin-6-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

20 3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-imidazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

30 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminothiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one; and

3-(2-amino-4-methylthiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

5 or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound provided herein is selected from:

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*R*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*S*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

15 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

30 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

5 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 (*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

2-((1-(3-(1-acetylpiperidin-4-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

20 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

25 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

30 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4-methyl-N,N-bis(methyl-d₃)-5-oxo-7-(trifluoromethyl)-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(6-(hydroxymethyl)pyridin-3-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(6-(methylamino)pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(dimethylamino)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyethyl)-1H-pyrazol-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyrimidin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(imidazo[1,5-a]pyridin-6-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

methyl (3-((1-(3-(bis(methyl-d3)carbamoyl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-6-chloropyridin-2-yl)carbamate;

9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

5 9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

10 methyl (6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)carbamate;

9-(1-((4-fluoro-2-sulfamoylphenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((5-chloroquinolin-8-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

15 N,N,4,7-tetramethyl-9-(1-((6-methyl-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

2-((1-(3-(1-acetylpiperidin-4-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;

20 2-((1-(3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;

2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

2-((1-(4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;

25 5-fluoro-2-((1-(7-methyl-4-(methyl-d₃)-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)benzamide;

2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;

30 2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(oxetan-3-yl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-isobutyrylpiperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropanecarbonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(methylsulfonyl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(isopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-methoxy-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((6-methyl-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-methoxy-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

5 9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(6-amino-3-pyridyl)-9-[1-[4-fluoro-2-(1-methyltriazol-4-yl)anilino]ethyl]-4,7-dimethyl-imidazo[1,5-a]quinazolin-5-one;

3-(1-acetylpiperidin-4-yl)-9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

20 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

25 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N-(2-hydroxyethyl)-N,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

30 methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)methyl)carbamate;

methyl (6-chloro-3-(((3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)pyridin-2-yl)carbamate;

9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-*N,N*,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide;

9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-4,7-dimethyl-5-oxo-*N,N*-bis(trideuteriomethyl)imidazo[1,5-a]quinazoline-3-carboxamide;

5 9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-*N,N*,4-tris(methyl- d_3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-*N,N*,4-tris(methyl- d_3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

3-(2-aminopyrimidin-5-yl)-9-((6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-((3,3-difluoroazetidin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1- d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

30 (*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1- d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

5 (*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-10 5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-15 one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

20 (*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-25 5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

30 (*S*)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*R*)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

5 (*S*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

10 (*S*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 (*S*)-2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

(*R*)-2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

20 3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

25 methyl (3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)carbamate;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

30 3-(2-aminopyrimidin-5-yl)-9-(1-((6-fluoro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

5 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(pyrimidin-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(4-hydroxypiperidin-1-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-morpholinopyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,5-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

20 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(5-methyl-1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

25 3-(3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

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methyl (3-(((3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)-6-chloropyridin-2-yl)carbamate;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-
4,7-dimethyl-3-(1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-chloropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-methylpyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-methoxypyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methoxypyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(2-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyridin-6-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-imidazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminothiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one; and

3-(2-amino-4-methylthiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound provided herein is selected from:

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide; and

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound provided herein is selected from:

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one

5 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

10 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one; and

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

15 or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound provided herein is 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide, or a pharmaceutically acceptable salt thereof.

20 In some embodiments, the compound provided herein is (*R*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide, or a pharmaceutically acceptable salt thereof.

25 In some embodiments, the compound provided herein is (*S*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide, or a pharmaceutically acceptable salt thereof.

30 In some embodiments, the compound provided herein is 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one, or a pharmaceutically acceptable salt thereof.

It is further appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, can also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

At various places in the present specification, divalent linking substituents are described. It is specifically intended that each divalent linking substituent include both the forward and backward forms of the linking substituent. For example, -NR(CR'R'')_n- includes both -NR(CR'R'')_n- and -(CR'R'')_nNR-. Where the structure clearly requires a linking group, the Markush variables listed for that group are understood to be linking groups.

The term “n-membered” where n is an integer typically describes the number of ring-forming atoms in a moiety where the number of ring-forming atoms is n. For example, piperidinyl is an example of a 6-membered heterocycloalkyl ring, pyrazolyl is an example of a 5-membered heteroaryl ring, pyridyl is an example of a 6-membered heteroaryl ring, and 1,2,3,4-tetrahydro-naphthalene is an example of a 10-membered cycloalkyl group.

As used herein, the phrase “optionally substituted” means unsubstituted or substituted. The substituents are independently selected, and substitution may be at any chemically accessible position. As used herein, the term “substituted” means that a hydrogen atom is removed and replaced by a substituent. A single divalent substituent, *e.g.*, oxo, can replace two hydrogen atoms. It is to be understood that substitution at a given atom is limited by valency.

As used herein, the phrase “each ‘variable’ is independently selected from” means substantially the same as wherein “at each occurrence ‘variable’ is selected from.”

Throughout the definitions, the terms “C_{n-m}” and “C_{m-n}” indicates a range which includes the endpoints, wherein n and m are integers and indicate the number of carbons. Examples include C₁₋₃, C₁₋₄, C₁₋₆, and the like.

As used herein, the term “C_{n-m} alkyl”, employed alone or in combination with other terms, refers to a saturated hydrocarbon group that may be straight-chain or branched, having n to m carbons. Examples of alkyl moieties include, but are not

limited to, chemical groups such as methyl (Me), ethyl (Et), n-propyl (n-Pr), isopropyl (iPr), n-butyl, tert-butyl, isobutyl, sec-butyl; higher homologs such as 2-methyl-1-butyl, n-pentyl, 3-pentyl, n-hexyl, 1,2,2-trimethylpropyl, and the like. The term “C_{n-m} alkyl” is understood to include deuterated analogs of saturated hydrocarbon groups as defined herein, including but not limited to, groups such as trideuteromethyl (CD₃), pentadeuteroethyl (CD₂CD₃), and the like. In some embodiments, the alkyl group contains from 1 to 6 carbon atoms, from 1 to 4 carbon atoms, from 1 to 3 carbon atoms, from 2 to 6 carbon atoms, from 2 to 4 carbon atoms, from 2 to 3 carbon atoms, or 1 to 2 carbon atoms.

As used herein, “C_{n-m} alkenyl” refers to an alkyl group having one or more double carbon-carbon bonds and having n to m carbons. Example alkenyl groups include, but are not limited to, ethenyl, n-propenyl, isopropenyl, n-butenyl, sec-butenyl, and the like. In some embodiments, the alkenyl moiety contains 2 to 6, 2 to 4, or 2 to 3 carbon atoms.

As used herein, “C_{n-m} alkynyl” refers to an alkyl group having one or more triple carbon-carbon bonds and having n to m carbons. Example alkynyl groups include, but are not limited to, ethynyl, propyn-1-yl, propyn-2-yl, and the like. In some embodiments, the alkynyl moiety contains 2 to 6, 2 to 4, or 2 to 3 carbon atoms.

As used herein, the term “C_{n-m} alkoxy”, employed alone or in combination with other terms, refers to a group of formula -O-alkyl, wherein the alkyl group has n to m carbons. Example alkoxy groups include, but are not limited to, methoxy, ethoxy, propoxy (*e.g.*, n-propoxy and isopropoxy), butoxy (*e.g.*, n-butoxy and tert-butoxy), and the like. In some embodiments, the alkyl group has 1 to 6, 1 to 4, or 1 to 3 carbon atoms.

As used herein, the term “aryl,” employed alone or in combination with other terms, refers to an aromatic hydrocarbon group, which may be monocyclic or polycyclic (*e.g.*, having 2, 3 or 4 fused rings). The term “C_{n-m} aryl” refers to an aryl group having from n to m ring carbon atoms. Aryl groups include, *e.g.*, phenyl, naphthyl, anthracenyl, phenanthrenyl, and the like. In some embodiments, aryl groups have from 5 to 10 carbon atoms. In some embodiments, the aryl group is phenyl or naphthyl. In some embodiments, the aryl is phenyl.

As used herein, “halo” refers to F, Cl, Br, or I. In some embodiments, a halo is F, Cl, or Br. In some embodiments, a halo is F or Cl. In some embodiments, a halo is F. In some embodiments, a halo is Cl.

As used herein, “C_{n-m} haloalkoxy” refers to a group of formula –O-haloalkyl
5 having n to m carbon atoms. Example haloalkoxy groups include OCF₃ and OCHF₂. In some embodiments, the haloalkoxy group is fluorinated only. In some embodiments, the alkyl group has 1 to 6, 1 to 4, or 1 to 3 carbon atoms.

As used herein, the term “C_{n-m} haloalkyl”, employed alone or in combination
10 with other terms, refers to an alkyl group having from one halogen atom to 2s+1 halogen atoms which may be the same or different, where “s” is the number of carbon atoms in the alkyl group, wherein the alkyl group has n to m carbon atoms. In some embodiments, the haloalkyl group is fluorinated only. In some embodiments, the alkyl group has 1 to 6, 1 to 4, or 1 to 3 carbon atoms. Example haloalkyl groups include CF₃, C₂F₅, CHF₂, CH₂F, CCl₃, CHCl₂, C₂Cl₅ and the like.

As used herein, “cycloalkyl” refers to non-aromatic cyclic hydrocarbons
15 including cyclized alkyl and alkenyl groups. Cycloalkyl groups can include mono- or polycyclic (*e.g.*, having 2 fused rings) groups, spirocycles, and bridged rings (*e.g.*, a bridged bicycloalkyl group). Ring-forming carbon atoms of a cycloalkyl group can be optionally substituted by oxo or sulfido (*e.g.*, C(O) or C(S)). Also included in the
20 definition of cycloalkyl are moieties that have one or more aromatic rings fused (*i.e.*, having a bond in common with) to the cycloalkyl ring, for example, benzo or thienyl derivatives of cyclopentane, cyclohexane, and the like. A cycloalkyl group containing a fused aromatic ring can be attached through any ring-forming atom including a ring-forming atom of the fused aromatic ring. Cycloalkyl groups can have 3, 4, 5, 6, 7, 8,
25 9, or 10 ring-forming carbons (*i.e.*, C₃₋₁₀). In some embodiments, the cycloalkyl is a C₃₋₁₀ monocyclic or bicyclic cycloalkyl. In some embodiments, the cycloalkyl is a C₃₋₇ monocyclic cycloalkyl. In some embodiments, the cycloalkyl is a C₄₋₇ monocyclic cycloalkyl. In some embodiments, the cycloalkyl is a C₄₋₁₀ spirocycle or bridged cycloalkyl (*e.g.*, a bridged bicycloalkyl group). Example cycloalkyl groups include
30 cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, cubane, adamantane, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl,

bicyclo[2.2.1]heptanyl, bicyclo[3.1.1]heptanyl, bicyclo[2.2.2]octanyl, spiro[3.3]heptanyl, and the like. In some embodiments, cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

As used herein, “heteroaryl” refers to a monocyclic or polycyclic (*e.g.*, having 2 fused rings) aromatic heterocycle having at least one heteroatom ring member selected from N, O, S and B. In some embodiments, the heteroaryl ring has 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, S and B. In some embodiments, any ring-forming N in a heteroaryl moiety can be an N-oxide. In some embodiments, the heteroaryl is a 5-10 membered monocyclic or bicyclic heteroaryl having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, S, and B. In some embodiments, the heteroaryl is a 5-, 7-, 8-, 9-, or 10-membered monocyclic or bicyclic heteroaryl having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, S, and B. In some embodiments, the heteroaryl is a 5-10 membered monocyclic or bicyclic heteroaryl having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, and S. In some embodiments, the heteroaryl is a 5-, 7-, 8-, 9-, or 10-membered monocyclic or bicyclic heteroaryl having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, and S. In some embodiments, the heteroaryl is a 5-6 membered monocyclic heteroaryl having 1 or 2 heteroatom ring members independently selected from N, O, S, and B. In some embodiments, the heteroaryl is a 5 membered monocyclic heteroaryl having 1 or 2 heteroatom ring members independently selected from N, O, S, and B. In some embodiments, the heteroaryl is a 5 membered monocyclic heteroaryl having 1 or 2 heteroatom ring members independently selected from N, O, and S. In some embodiments, the heteroaryl group contains 5 to 10, 5 to 7, 3 to 7, or 5 to 6 ring-forming atoms. In some embodiments, the heteroaryl group has 1 to 4 ring-forming heteroatoms, 1 to 3 ring-forming heteroatoms, 1 to 2 ring-forming heteroatoms or 1 ring-forming heteroatom. When the heteroaryl group contains more than one heteroatom ring member, the heteroatoms may be the same or different. Example heteroaryl groups include, but are not limited to, thienyl (or thiophenyl), furyl (or furanyl), pyrrolyl, imidazolyl, thiazolyl, oxazolyl, pyrazolyl, isothiazolyl, isoxazolyl, 1,2,3-triazolyl, tetrazolyl, 1,2,3-thiadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-triazolyl, 1,2,4-thiadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-triazolyl, 1,3,4-thiadiazolyl, 1,3,4-oxadiazolyl

and 1,2-dihydro-1,2-azaborine, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, azolyl, triazolyl, thiadiazolyl, quinolinyl, isoquinolinyl, indolyl, benzothiophenyl, benzofuranyl, benzisoxazolyl, imidazo[1, 2-b]thiazolyl, purinyl, triazinyl, thieno[3,2-b]pyridinyl, imidazo[1,2-a]pyridinyl, 1,5-naphthyridinyl, 1H-pyrazolo[4,3-b]pyridinyl, triazolo[4,3-a]pyridinyl, 1H-pyrrolo[3,2-b]pyridinyl, 1H-pyrrolo[2,3-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, indazolyl, and the like.

As used herein, “heterocycloalkyl” refers to monocyclic or polycyclic heterocycles having at least one non-aromatic ring (saturated or partially unsaturated ring), wherein one or more of the ring-forming carbon atoms of the heterocycloalkyl is replaced by a heteroatom selected from N, O, S, and B, and wherein the ring-forming carbon atoms and heteroatoms of a heterocycloalkyl group can be optionally substituted by one or more oxo or sulfido (*e.g.*, C(O), S(O), C(S), or S(O)₂, etc.). When a ring-forming carbon atom or heteroatom of a heterocycloalkyl group is optionally substituted by one or more oxo or sulfide, the O or S of said group is in addition to the number of ring-forming atoms specified herein (*e.g.*, a 1-methyl-6-oxo-1,6-dihydropyridazin-3-yl is a 6-membered heterocycloalkyl group, wherein a ring-forming carbon atom is substituted with an oxo group, and wherein the 6-membered heterocycloalkyl group is further substituted with a methyl group). Heterocycloalkyl groups include monocyclic and polycyclic (*e.g.*, having 2 fused rings) systems. Included in heterocycloalkyl are monocyclic and polycyclic 3 to 10, 4 to 10, 5 to 10, 4 to 7, 5 to 7, or 5 to 6 membered heterocycloalkyl groups. Heterocycloalkyl groups can also include spirocycles and bridged rings (*e.g.*, a 5 to 10 membered bridged biheterocycloalkyl ring having one or more of the ring-forming carbon atoms replaced by a heteroatom independently selected from N, O, S, and B). The heterocycloalkyl group can be attached through a ring-forming carbon atom or a ring-forming heteroatom. In some embodiments, the heterocycloalkyl group contains 0 to 3 double bonds. In some embodiments, the heterocycloalkyl group contains 0 to 2 double bonds.

Also included in the definition of heterocycloalkyl are moieties that have one or more aromatic rings fused (*i.e.*, having a bond in common with) to the non-aromatic heterocyclic ring, for example, benzo or thienyl derivatives of piperidine, morpholine, azepine, etc. A heterocycloalkyl group containing a fused aromatic ring

can be attached through any ring-forming atom including a ring-forming atom of the fused aromatic ring.

In some embodiments, the heterocycloalkyl group contains 3 to 10 ring-forming atoms, 4 to 10 ring-forming atoms, 4 to 8 ring-forming atoms, 3 to 7 ring-forming atoms, or 5 to 6 ring-forming atoms. In some embodiments, the heterocycloalkyl group has 1 to 4 heteroatoms, 1 to 3 heteroatoms, 1 to 2 heteroatoms or 1 heteroatom. In some embodiments, the heterocycloalkyl is a monocyclic 4-6 membered heterocycloalkyl having 1 or 2 heteroatoms independently selected from N, O, S and B and having one or more oxidized ring members. In some embodiments, the heterocycloalkyl is a monocyclic or bicyclic 5-10 membered heterocycloalkyl having 1, 2, 3, or 4 heteroatoms independently selected from N, O, S, and B and having one or more oxidized ring members. In some embodiments, the heterocycloalkyl is a monocyclic or bicyclic 5 to 10 membered heterocycloalkyl having 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S and having one or more oxidized ring members. In some embodiments, the heterocycloalkyl is a monocyclic 5 to 6 membered heterocycloalkyl having 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S and having one or more oxidized ring members.

Example heterocycloalkyl groups include pyrrolidin-2-one (or 2-oxopyrrolidinyl), 1,3-isoxazolidin-2-one, pyranyl, tetrahydropyran, oxetanyl, azetidiny, morpholino, thiomorpholino, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, piperidinyl, pyrrolidinyl, isoxazolidinyl, isothiazolidinyl, pyrazolidinyl, oxazolidinyl, thiazolidinyl, imidazolidinyl, azepanyl, 1,2,3,4-tetrahydroisoquinoline, tetrahydrothiophenyl, tetrahydrothiophenyl 1,1-dioxide, benzazapene, azabicyclo[3.1.0]hexanyl, diazabicyclo[3.1.0]hexanyl, oxobicyclo[2.1.1]hexanyl, azabicyclo[2.2.1]heptanyl, diazabicyclo[2.2.1]heptanyl, azabicyclo[3.1.1]heptanyl, diazabicyclo[3.1.1]heptanyl, azabicyclo[3.2.1]octanyl, diazabicyclo[3.2.1]octanyl, oxobicyclo[2.2.2]octanyl, azabicyclo[2.2.2]octanyl, azaadamantanyl, diazaadamantanyl, oxo-adamantanyl, azaspiro[3.3]heptanyl, 2-azaspiro[3.3]heptanyl, diazaspiro[3.3]heptanyl, azaspiro[3.5]nonanyl, 7-azaspiro[3.5]nonanyl, oxo-azaspiro[3.3]heptanyl, azaspiro[3.4]octanyl, diazaspiro[3.4]octanyl, oxo-azaspiro[3.4]octanyl, azaspiro[2.5]octanyl,

diazaspiro[2.5]octanyl, azaspiro[4.4]nonanyl, diazaspiro[4.4]nonanyl, oxo-
 azaspiro[4.4]nonanyl, azaspiro[4.5]decanyl, diazaspiro[4.5]decanyl,
 diazaspiro[4.4]nonanyl, oxo-diazaspiro[4.4]nonanyl, oxo-dihydropyridazinyl, oxo-
 2,6-diazaspiro[3.4]octanyl, oxohexahydropyrrolo[1,2-a]pyrazinyl, 3-oxopiperazinyl,
 5 oxo-pyrrolidinyl, oxo-pyridinyl, and the like.

As used herein, “C_{o-p} cycloalkyl-C_{n-m} alkyl-” refers to a group of formula
 cycloalkyl-alkylene-, wherein the cycloalkyl has o to p carbon atoms and the alkylene
 linking group has n to m carbon atoms.

As used herein “C_{o-p} aryl-C_{n-m} alkyl-” refers to a group of formula aryl-
 10 alkylene-, wherein the aryl has o to p carbon atoms and the alkylene linking group has
 n to m carbon atoms.

As used herein, “heteroaryl-C_{n-m} alkyl-” refers to a group of formula
 heteroaryl-alkylene-, wherein alkylene linking group has n to m carbon atoms.

As used herein “heterocycloalkyl-C_{n-m} alkyl-” refers to a group of formula
 15 heterocycloalkyl-alkylene-, wherein alkylene linking group has n to m carbon atoms.

As used herein, an “alkyl linking group” or “alkylene linking group” is a
 bivalent straight chain or branched alkyl linking group (“alkylene group”). For
 example, “C_{o-p} cycloalkyl-C_{n-m} alkyl-”, “C_{o-p} aryl-C_{n-m} alkyl-”, “phenyl-C_{n-m} alkyl-”,
 “heteroaryl-C_{n-m} alkyl-”, and “heterocycloalkyl-C_{n-m} alkyl-” contain alkyl linking
 20 groups. Examples of “alkyl linking groups” or “alkylene groups” include methylene,
 ethan-1,1-diyl, ethan-1,2-diyl, propan-1,3-diyl, propan-1,2-diyl, propan-1,1-diyl and
 the like.

As used herein, a “haloalkyl linking group” or “haloalkylene linking group” is
 a bivalent straight chain or branched haloalkyl linking group (“haloalkylene group”).
 25 Example haloalkylene groups include -CF₂-, -C₂F₄-, -CHF-, -CCl₂-, -CHCl-, -C₂Cl₄-,
 and the like.

As used herein, a “cycloalkyl linking group” or “cycloalkylene linking group”
 is a bivalent straight chain or branched cycloalkyl linking group (“cycloalkylene
 group”). Examples of “cycloalkyl linking groups” or “cycloalkylene groups” include
 30 cyclopropyl-1,1-diyl, cyclopropyl-1,2-diyl, cyclobutyl-1,3-diyl, cyclopentyl-1,3-diyl,
 cyclopentyl-1,4-diyl, cyclohexyl-1,2-diyl, cyclohexyl-1,3-diyl, cyclohexyl-1,4-diyl, and the
 like.

As used herein, a “heterocycloalkyl linking group” or “heterocycloalkylene linking group” is a bivalent straight chain or branched heterocycloalkyl linking group (“heterocycloalkylene group”). Examples of “heterocycloalkyl linking groups” or “heterocycloalkylene groups” include azetidin-1,2-diyl, azetidin-1,3-diyl, pyrrolidin-1,2-diyl, pyrrolidin-1,3-diyl, pyrrolidin-2,3-diyl, piperidin-1,2-diyl, piperidin-1,3-diyl, piperidin-1,4-diyl, piperidin-2,3-diyl, piperidin-2,4-diyl, and the like.

As used herein, a “heteroaryl linking group” or “heteroarylene linking group” is a bivalent straight chain or branched heteroaryl linking group (“heteroarylene group”). Examples of “heteroaryl linking groups” or “heteroarylene groups” include pyrazol-1,3-diyl, imidazol-1,2,-diyl, pyridin-2,3-diyl, pyridin-2,4-diyl, pyridin-3,4-diyl, and the like.

At certain places, the definitions or embodiments refer to specific rings (*e.g.*, an azetidine ring, a pyridine ring, etc.). Unless otherwise indicated, these rings can be attached to any ring member provided that the valency of the atom is not exceeded. For example, an azetidine ring may be attached at any position of the ring, whereas a pyridin-3-yl ring is attached at the 3-position.

As used herein, the term “oxo” refers to an oxygen atom (*i.e.*, =O) as a divalent substituent, forming a carbonyl group when attached to a carbon (*e.g.*, C=O or C(O)), or attached to a nitrogen or sulfur heteroatom forming a nitroso, sulfinyl, or sulfonyl group.

As used herein, the term “independently selected from” means that each occurrence of a variable or substituent (*e.g.*, each R^G), are independently selected at each occurrence from the applicable list.

The compounds described herein can be asymmetric (*e.g.*, having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended unless otherwise indicated. Compounds of the present disclosure that contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods on how to prepare optically active forms from optically inactive starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of

the compounds of the present disclosure are described and may be isolated as a mixture of isomers or as separated isomeric forms. In some embodiments, the compound has the (R)-configuration. In some embodiments, the compound has the (S)-configuration. The Formulas (*e.g.*, Formula I, Formula II, etc.) provided herein
5 include stereoisomers of the compounds.

Resolution of racemic mixtures of compounds can be carried out by any of numerous methods known in the art. An example method includes fractional recrystallization using a chiral resolving acid which is an optically active, salt-forming organic acid. Suitable resolving agents for fractional recrystallization methods are, for
10 example, optically active acids, such as the D and L forms of tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid, lactic acid or the various optically active camphorsulfonic acids such as β -camphorsulfonic acid. Other resolving agents suitable for fractional crystallization methods include stereoisomerically pure forms of α -methylbenzylamine (*e.g.*, S and R forms, or
15 diastereomerically pure forms), 2-phenylglycinol, norephedrine, ephedrine, N-methylephedrine, cyclohexylethylamine, 1,2-diaminocyclohexane, and the like.

Resolution of racemic mixtures can also be carried out by elution on a column packed with an optically active resolving agent (*e.g.*, dinitrobenzoylphenylglycine). Suitable elution solvent composition can be determined by one skilled in the art.

20 Compounds provided herein also include tautomeric forms. Tautomeric forms result from the swapping of a single bond with an adjacent double bond together with the concomitant migration of a proton. Tautomeric forms include prototropic tautomers which are isomeric protonation states having the same empirical formula and total charge. Example prototropic tautomers include ketone – enol pairs, amide –
25 imidic acid pairs, lactam – lactim pairs, enamine – imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system, for example, 1H- and 3H-imidazole, 1H-, 2H- and 4H- 1,2,4-triazole, 1H- and 2H-isoindole, 2-hydroxypyridine and 2-pyridone, and 1H- and 2H-pyrazole. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate
30 substitution.

All compounds, and pharmaceutically acceptable salts thereof, can be found together with other substances such as water and solvents (*e.g.* hydrates and solvates) or can be isolated.

5 In some embodiments, preparation of compounds can involve the addition of acids or bases to affect, for example, catalysis of a desired reaction or formation of salt forms such as acid addition salts.

10 In some embodiments, the compounds provided herein, or salts thereof, are substantially isolated. By “substantially isolated” is meant that the compound is at least partially or substantially separated from the environment in which it was formed or detected. Partial separation can include, for example, a composition enriched in the compounds provided herein. Substantial separation can include compositions containing at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 97%, or at least about 99% by weight of the compounds provided herein, or salt thereof.

15 The term “compound” as used herein is meant to include all stereoisomers, geometric isomers, tautomers, and isotopes of the structures depicted. Compounds herein identified by name or structure as one particular tautomeric form are intended to include other tautomeric forms unless otherwise specified.

20 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.

25 The present application also includes pharmaceutically acceptable salts of the compounds described herein. As used herein, “pharmaceutically acceptable salts” refers to derivatives of the disclosed compounds wherein the parent compound is modified by converting an existing acid or base moiety to its salt form. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts of the present disclosure include the conventional non-toxic salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. The pharmaceutically

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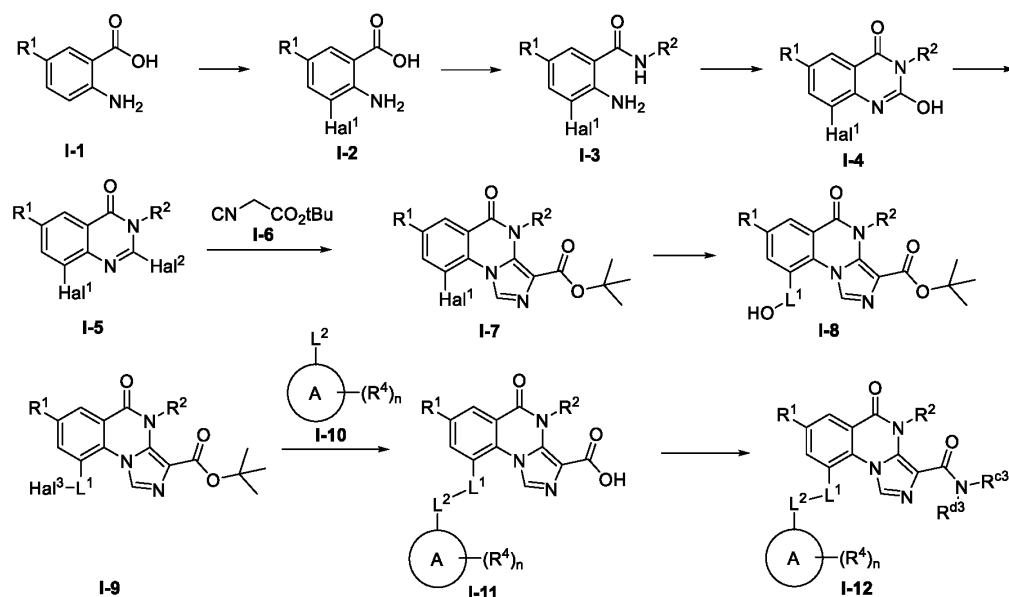
acceptable salts of the present disclosure can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in
5 water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate, alcohols (*e.g.*, methanol, ethanol, iso-propanol, or butanol) or acetonitrile (ACN) are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418 and Journal of Pharmaceutical Science, 66, 2 (1977), each of which
10 is incorporated herein by reference in its entirety.

Synthesis

Compounds of the invention, including salts thereof, can be prepared using known organic synthesis techniques and according to various possible synthetic
15 routes. Example synthetic methods for preparing compounds of the invention are provided in the Schemes below.

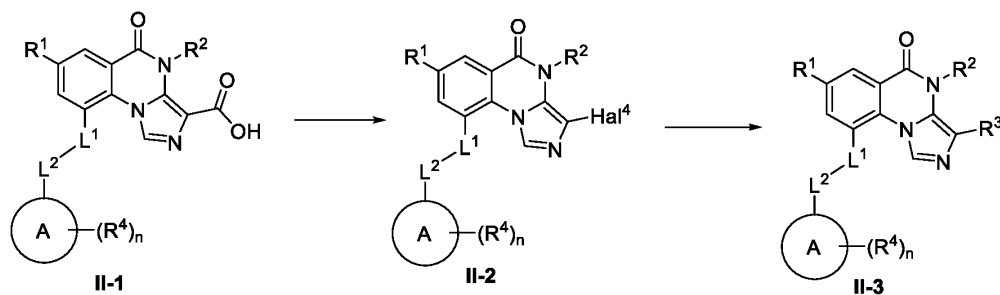
Compounds of formula **I-12** can be synthesized, for example, using a process shown in **Scheme I**. Halogenation of **I-1** with suitable reagent (*e.g.*, N-bromosuccinimide) can afford **I-2**. Compound **I-2** can be converted to **I-3** via amide
20 coupling, which is then converted to **I-4** after treating **I-3** with suitable reagent (*e.g.*, triphosgene). Intermediate **I-5** can be prepared by treating **I-4** with suitable reagent (*e.g.*, POCl₃). Compound **I-7** can be prepared by a process comprising contacting intermediate **I-5** with reagent **I-6**. Compound **I-8** can be prepared from **I-7** via
suitable reactions (*e.g.*, transition metal-catalyzed cross-coupling reactions) followed
25 by a reduction reaction. Intermediate **I-9** can be prepared by treating **I-8** with a suitable reagent (*e.g.*, PBr₃). **I-11** can be obtained via reacting **I-9** with suitable nucleophiles, followed by deprotection. Finally, **I-11** can be converted into **I-12** via amide coupling reaction.

Scheme I.



Compounds of formula **II-3** can be synthesized, for example, using a process shown in **Scheme II**. Compound **II-2** can be prepared via decarboxylative halogenation of **II-1** in the presence of suitable reagent (*e.g.*, N-Iodosuccinimide) under basic conditions. **II-2** can be converted to **II-3** via suitable conditions (*e.g.*, metal-catalyzed cross-coupling reactions).

Scheme II.



The reactions for preparing compounds of the invention can be carried out in suitable solvents which can be readily selected by one of skill in the art of organic synthesis. Suitable solvents can be substantially nonreactive with the starting materials (reactants), the intermediates, or products at the temperatures at which the reactions are carried out, *e.g.*, temperatures which can range from the solvent's freezing temperature to the solvent's boiling temperature. A given reaction can be

carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction step can be selected by the skilled artisan.

Preparation of compounds of the invention can involve the protection and deprotection of various chemical groups. The need for protection and deprotection, and the selection of appropriate protecting groups, can be readily determined by one skilled in the art. The chemistry of protecting groups can be found, for example, in T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 3rd. Ed., Wiley & Sons, Inc., New York (1999), which is incorporated herein by reference in its entirety.

Reactions can be monitored according to any suitable method known in the art. For example, product formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (*e.g.*, ^1H or ^{13}C), infrared spectroscopy, spectrophotometry (*e.g.*, UV-visible), or mass spectrometry, or by chromatography such as high performance liquid chromatography (HPLC) or thin layer chromatography.

The expressions, “ambient temperature,” “room temperature,” and “r.t.,” as used herein, are understood in the art, and refer generally to a temperature, *e.g.* a reaction temperature, that is about the temperature of the room in which the reaction is carried out, for example, a temperature from about 20 °C to about 30 °C.

Methods of Use

The present disclosure provides uses for compounds and compositions described herein. The compounds described herein can inhibit the activity of PI3K α kinase. In some embodiments, provided compounds and compositions are for use in medicine (*e.g.*, as therapy). In some embodiments, provided compounds and compositions are useful in treating a disease, disorder, or condition, wherein an underlying pathology is, wholly or partially, mediated by PI3K α . In some embodiments, provided compounds and compositions are useful in research as, for example, analytical tools and/or control compounds in biological assays.

In some embodiments, the present disclosure provides methods of administering provided compounds or compositions to a subject in need thereof. In

some embodiments, the present disclosure provides methods of administering provided compounds or compositions to a subject suffering from or susceptible to a disease, disorder, or condition associated with PI3K α . In some embodiments, the present disclosure provides methods of administering provided compounds or compositions to a subject suffering from or susceptible to a disease, disorder, or condition, wherein an underlying pathology is, wholly or partially, mediated by PI3K α .

In some embodiments, the compounds provided herein are useful as PI3K α inhibitors. In some embodiments, the present disclosure provides methods of inhibiting PI3K α in a subject comprising administering a provided compound or composition. In some embodiments, the present disclosure provides methods of inhibiting PI3K α in a biological sample comprising contacting the sample with a provided compound or composition.

In some embodiments, the present disclosure provides methods of treating a disease, disorder or condition associated with PI3K α in a subject in need thereof, comprising administering to the subject a compound, salt, or composition of the disclosure. In some embodiments, a disease, disorder or condition is associated with mutation of PI3K α . In some embodiments, the present disclosure provides methods of treating a disease, disorder or condition, wherein an underlying pathology is, wholly or partially, mediated by PI3K α , in a subject in need thereof, comprising administering to the subject a provided compound or composition.

In some embodiments, the present disclosure provides methods of treating a variety of PI3K α -dependent diseases and disorders. In some embodiments, the disease of disorder is a cancer (*e.g.*, breast cancer, brain cancer, prostate cancer, endometrial cancer, gastric cancer, leukemia, lymphoma, sarcoma, colorectal cancer, lung cancer, ovarian cancer, skin cancer, and head and neck cancer). In some embodiments, the disease or disorder associated with PI3K α includes, but is not limited to, CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome), PIK3CA-related overgrowth syndrome (PROS), endometrial cancer, breast cancer, esophageal squamous-cell cancer, cervical squamous-cell carcinoma, cervical adenocarcinoma, colorectal adenocarcinoma, bladder urothelial carcinoma, glioblastoma, ovarian cancer, non-small-cell lung

cancer, esophagogastric cancer, nerve-sheath tumor, head and neck squamous-cell carcinoma, melanoma, esophagogastric adenocarcinoma, soft-tissue sarcoma, prostate cancer, fibrolamellar carcinoma, hepatocellular carcinoma, diffuse glioma, colorectal cancer, pancreatic cancer, cholangiocarcinoma, B-cell lymphoma, mesothelioma, 5 adrenocortical carcinoma, renal non-clear-cell carcinoma, renal clear-cell carcinoma, germ-cell carcinoma, thymic tumor, pheochromocytoma, miscellaneous neuroepithelial tumor, thyroid cancer, leukemia, and encapsulated glioma. In some embodiments, the cancer is breast cancer.

In some embodiments, provided herein is a method of increasing survival or 10 progression-free survival in a patient, comprising administering a compound provided herein to the patient. In some embodiments, the patient has cancer. In some embodiments, the patient has a disease or disorder described herein. As used herein, progression-free survival refers to the length of time during and after the treatment of a solid tumor that a patient lives with the disease but it does not get worse.

15 Progression-free survival can refer to the length of time from first administering the compound until the earlier of death or progression of the disease. Progression of the disease can be defined by RECIST v. 1.1 (Response Evaluation Criteria in Solid Tumors), as assessed by an independent centralized radiological review committee. In some embodiments, administering of the compound results in a progression free 20 survival that is greater than about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 8 months, about 9 months, about 12 months, about 16 months, or about 24 months. In some embodiments, the administering of the compound results in a progression free survival that is at least about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, 25 about 6 months, about 8 months, about 9 months, or about 12 months; and less than about 24 months, about 16 months, about 12 months, about 9 months, about 8 months, about 6 months, about 5 months, about 4 months, about 3 months, or about 2 months. In some embodiments, the administering of the compound results in an increase of progression free survival that is at least about 1 month, about 2 months, about 3 30 months, about 4 months, about 5 months, about 6 months, about 8 months, about 9 months, or about 12 months; and less than about 24 months, about 16 months, about

12 months, about 9 months, about 8 months, about 6 months, about 5 months, about 4 months, about 3 months, or about 2 months.

The present disclosure further provides a compound described herein, or a pharmaceutically acceptable salt thereof, for use in any of the methods described
5 herein.

The present disclosure further provides use of a compound described herein, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for use in any of the methods described herein.

As used herein, the term “cell” is meant to refer to a cell that is *in vitro*, *ex vivo* or *in vivo*. In some embodiments, an *ex vivo* cell can be part of a tissue sample excised from an organism such as a mammal. In some embodiments, an *in vitro* cell
10 can be a cell in a cell culture. In some embodiments, an *in vivo* cell is a cell living in an organism such as a mammal.

As used herein, the term “contacting” refers to the bringing together of indicated moieties in an *in vitro* system or an *in vivo* system. For example,
15 “contacting” a PI3K α kinase with a compound described herein includes the administration of a compound described herein to an individual or patient, such as a human, having a PI3K α kinase, as well as, for example, introducing a compound described herein into a sample containing a cellular or purified preparation containing
20 the PI3K α kinase.

As used herein, the term “individual” or “patient,” used interchangeably, refers to any animal, including mammals, preferably mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, and most preferably humans.

As used herein, the phrase “therapeutically effective amount” refers to the
25 amount of active compound or pharmaceutical agent such as an amount of any of the solid forms or salts thereof as disclosed herein that elicits the biological or medicinal response in a tissue, system, animal, individual or human that is being sought by a researcher, veterinarian, medical doctor or other clinician. An appropriate “effective” amount in any individual case may be determined using techniques known to a person
30 skilled in the art.

The phrase “pharmaceutically acceptable” is used 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, immunogenicity or other problem or complication, commensurate with a reasonable benefit/risk ratio.

5 As used herein, the phrase “pharmaceutically acceptable carrier or excipient” refers to a pharmaceutically-acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, solvent, or encapsulating material. Excipients or carriers are generally safe, non-toxic and neither biologically nor otherwise undesirable and include excipients or carriers that are acceptable for veterinary use as well as human
10 pharmaceutical use. In one embodiment, each component is “pharmaceutically acceptable” as defined herein. See, *e.g.*, *Remington: The Science and Practice of Pharmacy*, 21st ed.; Lippincott Williams & Wilkins: Philadelphia, Pa., 2005; *Handbook of Pharmaceutical Excipients*, 6th ed.; Rowe et al., Eds.; The Pharmaceutical Press and the American Pharmaceutical Association: 2009; *Handbook*
15 *of Pharmaceutical Additives*, 3rd ed.; Ash and Ash Eds.; Gower Publishing Company: 2007; *Pharmaceutical Preformulation and Formulation*, 2nd ed.; Gibson Ed.; CRC Press LLC: Boca Raton, Fla., 2009.

 As used herein, the term “treating” or “treatment” refers to inhibiting the disease; for example, inhibiting a disease, condition or disorder in an individual who
20 is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (*i.e.*, arresting further development of the pathology and/or symptomatology) or ameliorating the disease; for example, ameliorating a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (*i.e.*, reversing the pathology
25 and/or symptomatology) such as decreasing the severity of disease.

 In some embodiments, the compounds of the invention are useful in preventing or reducing the risk of developing any of the diseases referred to herein; *e.g.*, preventing or reducing the risk of developing a disease, condition or disorder in an individual who may be predisposed to the disease, condition or disorder but does
30 not yet experience or display the pathology or symptomatology of the disease.

 It is appreciated that certain features of the disclosure, which are, for clarity, described in the context of separate embodiments, can also be provided in

combination in a single embodiment (while the embodiments are intended to be combined as if written in multiply dependent form). Conversely, various features of the disclosure which are, for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

5

Combination Therapy

One or more additional therapeutic agents such as, for example, chemotherapeutics or other anti-cancer agents, anti-inflammatory agents, steroids, immunosuppressants, anesthetics (*e.g.*, for use in combination with a surgical
10 procedure), or other agents useful for treating diseases associated with PI3K α can be used in combination with the compounds and salts provided herein. The agents can be combined with the present compounds in a single dosage form, or the agents can be administered simultaneously or sequentially as separate dosage forms.

Compounds described herein can be used in combination with one or more
15 other kinase inhibitors for the treatment of diseases, such as cancer, that are impacted by multiple signaling pathways. For example, a combination can include one or more inhibitors of the following kinases for the treatment of cancer: Akt1, Akt2, Akt3, TGF- β R, Pim, PKA, PKG, PKC, CaM-kinase, phosphorylase kinase, CDK4/6, MEKK, ERK, MAPK, mTOR, EGFR, HER2, HER3, HER4, INS-R, IGF-1R, IR-R,
20 PDGF α R, PDGF β R, CSFIR, KIT, FLK-II, KDR/FLK-1, FLK-4, flt-1, FGFR1, FGFR2, FGFR3, FGFR4, c-Met, Ron, Sea, TRKA, TRKB, TRKC, FLT3, VEGFR/Flt2, Flt4, EphA1, EphA2, EphA3, EphB2, EphB4, Tie2, Src, Fyn, Lck, Fgr, Btk, Fak, SYK, FRK, JAK, ABL, ALK and B-Raf. Additionally, the solid forms of the inhibitor as described herein can be combined with inhibitors of kinases associated
25 with the PIK3/Akt/mTOR signaling pathway, such as PI3K, Akt (including Akt1, Akt2 and Akt3) and mTOR kinases.

For treating cancer and other proliferative diseases, compounds described herein can be used in combination with targeted therapies, including JAK kinase inhibitors (ruxolitinib, additional JAK1/2 and JAK1-selective, baricitinib or
30 itacitinib), Pim kinase inhibitors (*e.g.*, LGH447, INCB053914 and SGI-1776), PI3 kinase inhibitors including PI3K-delta selective and broad spectrum PI3K inhibitors (*e.g.*, piasclisib and INCB50797), PI3K-gamma inhibitors such as PI3K-gamma

selective inhibitors, MEK inhibitors, CSF1R inhibitors (*e.g.*, PLX3397 and LY3022855), TAM receptor tyrosine kinases inhibitors (Tyr-3, Axl, and Mer; *e.g.*, INCB81776), angiogenesis inhibitors, interleukin receptor inhibitors, Cyclin Dependent kinase inhibitors (*e.g.*, palbociclib, ribociclib, and abemaciclib), BRAF inhibitors, mTOR inhibitors, proteasome inhibitors (Bortezomib, Carfilzomib), HDAC-inhibitors (panobinostat, vorinostat), DNA methyl transferase inhibitors, dexamethasone, bromo and extra terminal family members inhibitors (for example, bromodomain inhibitors or BET inhibitors, such as OTX015, CPI-0610, INCB54329 or INCB57643), LSD1 inhibitors (*e.g.*, GSK2979552, INCB59872 and INCB60003), estrogen receptor modulators (*e.g.*, fulvestrant), androgen receptor modulators (*e.g.*, enzalutamide), BCL2 inhibitors (*e.g.*, venetoclax), hypoxia-inducible factor-2 alpha inhibitors (*e.g.*, belzutifan), exportin-1 (XPO-1) inhibitors (*e.g.*, selinexor), KRAS inhibitors (*e.g.*, sotorasib), arginase inhibitors (*e.g.*, INCB1158), indoleamine 2,3-dioxygenase inhibitors (*e.g.*, epacadostat, NLG919 or BMS-986205), PARP inhibitors (*e.g.*, olaparib or rucaparib), and inhibitors of BTK such as ibrutinib.

For treating cancer and other proliferative diseases, compounds described herein can be used in combination with chemotherapeutic agents, agonists or antagonists of nuclear receptors, or other anti-proliferative agents. Compounds described herein can also be used in combination with a medical therapy such as surgery or radiotherapy, *e.g.*, gamma-radiation, neutron beam radiotherapy, electron beam radiotherapy, proton therapy, brachytherapy, and systemic radioactive isotopes.

Examples of suitable chemotherapeutic agents include any of: abarelix, abiraterone, afatinib, aflibercept, aldesleukin, alemtuzumab, alitretinoin, allopurinol, altretamine, amidox, amsacrine, anastrozole, aphidicolon, arsenic trioxide, asparaginase, axitinib, azacitidine, bevacizumab, bexarotene, baricitinib, bendamustine, bicalutamide, bleomycin, bortezomib, bortezomib, brivanib, buparlisib, busulfan intravenous, busulfan oral, calusterone, camptosar, capecitabine, carboplatin, carmustine, cediranib, cetuximab, chlorambucil, cisplatin, cladribine, clofarabine, crizotinib, cyclophosphamide, cytarabine, dacarbazine, dacomitinib, dactinomycin, dalteparin sodium, dasatinib, dactinomycin, daunorubicin, decitabine, degarelix, denileukin, denileukin diftitox, deoxycoformycin, dexrazoxane, didox, docetaxel, doxorubicin, droloxafine, dromostanolone propionate, eculizumab,

enzalutamide, epidophyllotoxin, epirubicin, epothilones, erlotinib, estramustine, etoposide phosphate, etoposide, exemestane, fentanyl citrate, filgrastim, floxuridine, fludarabine, fluorouracil, flutamide, fulvestrant, gefitinib, gemcitabine, gemtuzumab ozogamicin, goserelin acetate, histrelin acetate, ibritumomab tiuxetan, idarubicin, idelalisib, ifosfamide, imatinib mesylate, interferon alfa 2a, irinotecan, lapatinib ditosylate, lenalidomide, letrozole, leucovorin, leuprolide acetate, levamisole, lonafarnib, lomustine, mecllorethamine, megestrol acetate, melphalan, mercaptopurine, methotrexate, methoxsalen, mithramycin, mitomycin C, mitotane, mitoxantrone, nandrolone phenpropionate, navelbene, necitumumab, nelarabine, neratinib, nilotinib, nilutamide, niraparib, nofetumomab, oserelin, oxaliplatin, paclitaxel, pamidronate, panitumumab, panobinostat, pazopanib, pegaspargase, pegfilgrastim, pemetrexed disodium, pentostatin, pilaralisib, pipobroman, plicamycin, ponatinib, porfimer, prednisone, procarbazine, quinacrine, ranibizumab, rasburicase, regorafenib, reloxafine, revlimid, rituximab, rucaparib, ruxolitinib, sorafenib, streptozocin, sunitinib, sunitinib maleate, tamoxifen, tegafur, temozolomide, teniposide, testolactone, tezacitabine, thalidomide, thioguanine, thiotepa, tipifarnib, topotecan, toremifene, tositumomab, trastuzumab, tretinoin, triapine, trimidox, triptorelin, uracil mustard, valrubicin, vandetanib, vinblastine, vincristine, vindesine, vinorelbine, vorinostat, veliparib, talazoparib, and zoledronate.

Methods for the safe and effective administration of most of these chemotherapeutic agents are known to those skilled in the art. In addition, their administration is described in the standard literature. For example, the administration of many of the chemotherapeutic agents is described in the “Physicians’ Desk Reference” (PDR, *e.g.*, 1996 edition, Medical Economics Company, Montvale, NJ), the disclosure of which is incorporated herein by reference as if set forth in its entirety.

Example anti-inflammatory agents include, but are not limited to, aspirin, choline salicylates, celecoxib, diclofenac potassium, diclofenac sodium, diclofenac sodium with misoprostol, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, ketoprofen, meclofenamate sodium, mefenamic acid, nabumetone, naproxen, naproxen sodium, oxaprozin, piroxicam, rofecoxib, salsalate, sodium salicylate, sulindac, tolmetin sodium, and valdecoxib.

Example steroids include, but are not limited to, corticosteroids such as cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, and prednisone.

Example immunosuppressants include, but are not limited to, azathioprine, chlorambucil, cyclophosphamide, cyclosporine, daclizumab, infliximab, methotrexate, and tacrolimus.

Example anesthetics include, but are not limited, to local anesthetics (*e.g.*, lidocaine, procain, ropivacaine) and general anesthetics (*e.g.*, desflurane, enflurane, halothane, isoflurane, methoxyflurane, nitrous oxide, sevoflurane, mmobarbital, methohexital, thiamylal, thiopental, diazepam, lorazepam, midazolam, etomidate, ketamine, propofol, alfentanil, fentanyl, remifentanyl, buprenorphine, butorphanol, hydromorphone levorphanol, meperidine, methadone, morphine, nalbuphine, oxymorphone, pentazocine).

In some embodiments, the additional therapeutic agent is administered simultaneously with a compound or salt provided herein. In some embodiments, the additional therapeutic agent is administered after administration of the compound or salt provided herein. In some embodiments, the additional therapeutic agent is administered prior to administration of the compound or salt provided herein. In some embodiments, the compound or salt provided herein is administered during a surgical procedure. In some embodiments, the compound or salt provided herein is administered in combination with an additional therapeutic agent during a surgical procedure.

As provided herein, the additional compounds, inhibitors, agents, etc. can be combined with the compounds provided herein in a single or continuous dosage form, or they can be administered simultaneously or sequentially as separate dosage forms.

Pharmaceutical Formulations and Dosage Forms

When employed as pharmaceuticals, the compounds of the invention can be administered in the form of pharmaceutical compositions which refers to a combination of a compound of the invention, or its pharmaceutically acceptable salt, and at least one pharmaceutically acceptable carrier. These compositions can be prepared in a manner well known in the pharmaceutical art, and can be administered

by a variety of routes, depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic and to mucous membranes including intranasal, vaginal and rectal delivery), pulmonary (*e.g.*, by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal), ocular, oral or parenteral. Methods for ocular delivery can include topical administration (eye drops), subconjunctival, periocular or intravitreal injection or introduction by balloon catheter or ophthalmic inserts surgically placed in the conjunctival sac. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal, or intramuscular injection or infusion; or intracranial, *e.g.*, intrathecal or intraventricular, administration. Parenteral administration can be in the form of a single bolus dose, or may be, for example, by a continuous perfusion pump. Pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable.

This invention also includes pharmaceutical compositions which contain, as the active ingredient, one or more of the compounds of the invention above in combination with one or more pharmaceutically acceptable carriers. In making the compositions of the invention, the active ingredient is typically mixed with an excipient, diluted by an excipient or enclosed within such a carrier in the form of, for example, a capsule, sachet, paper, or other container. When the excipient serves as a diluent, it can be a solid, semi-solid, or liquid material, which acts as a vehicle, carrier or medium for the active ingredient. Thus, the compositions can be in the form of tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols (as a solid or in a liquid medium), ointments containing, for example, up to 10 % by weight of the active compound, soft and hard gelatin capsules, suppositories, sterile injectable solutions, and sterile packaged powders.

In preparing a formulation, the active compound can be milled to provide the appropriate particle size prior to combining with the other ingredients. If the active compound is substantially insoluble, it can be milled to a particle size of less than 200 mesh. If the active compound is substantially water soluble, the particle size can be

adjusted by milling to provide a substantially uniform distribution in the formulation, *e.g.* about 40 mesh.

The active compound can be effective over a wide dosage range and is generally administered in a pharmaceutically effective amount. It will be understood, however, that the amount of the compound actually administered will usually be determined by a physician, according to the relevant circumstances, including the condition to be treated, the chosen route of administration, the actual compound administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

For preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutical excipient to form a solid pre-formulation composition containing a homogeneous mixture of a compound of the present invention. When referring to these pre-formulation compositions as homogeneous, the active ingredient is typically dispersed evenly throughout the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid pre-formulation is then subdivided into unit dosage forms of the type described above.

The tablets or pills of the present invention can be coated or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an enteric layer which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release.

The liquid forms in which the compounds and compositions of the present invention can be incorporated for administration orally or by injection include aqueous solutions, suitably flavored syrups, aqueous or oil suspensions, and flavored emulsions with edible oils.

The compositions for inhalation or insufflation include solutions and suspensions in pharmaceutically acceptable, aqueous or organic solvents, or mixtures thereof, and powders. The liquid or solid compositions may contain suitable pharmaceutically acceptable excipients as described *supra*. In some embodiments, the

compositions are administered by the oral or nasal respiratory route for local or systemic effect. Compositions in can be nebulized by use of inert gases. Nebulized solutions may be breathed directly from the nebulizing device or the nebulizing device can be attached to a face masks tent, or intermittent positive pressure breathing machine. Solution, suspension, or powder compositions can be administered orally or nasally from devices which deliver the formulation in an appropriate manner

The amount of compound or composition administered to a patient will vary depending upon what is being administered, the purpose of the administration, such as prophylaxis or therapy, the state of the patient, the manner of administration, and the like. In therapeutic applications, compositions can be administered to a patient already suffering from a disease in an amount sufficient to cure or at least partially arrest the symptoms of the disease and its complications. Effective doses will depend on the disease condition being treated as well as by the judgment of the attending clinician depending upon factors such as the severity of the disease, the age, weight and general condition of the patient, and the like.

The compositions administered to a patient can be in the form of pharmaceutical compositions described above. These compositions can be sterilized by conventional sterilization techniques, or may be sterile filtered. Aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the compound preparations typically will be between 3 and 11, more preferably from 5 to 9 and most preferably from 7 to 8. It will be understood that use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of pharmaceutical salts.

The therapeutic dosage of the compounds of the present invention can vary according to, for example, the particular use for which the treatment is made, the manner of administration of the compound, the health and condition of the patient, and the judgment of the prescribing physician. The proportion or concentration of a compound of the invention in a pharmaceutical composition can vary depending upon a number of factors including dosage, chemical characteristics (*e.g.*, hydrophobicity), and the route of administration. The dosage is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status

of the particular patient, the relative biological efficacy of the compound selected, formulation of the excipient, and its route of administration. Effective doses can be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

5 The compositions of the disclosure can further include one or more additional pharmaceutical agents such as a chemotherapeutic, steroid, anti-inflammatory compound, or immunosuppressant, examples of which are provided herein..

Labeled Compounds and Assay Methods

10 Another aspect of the present invention relates to fluorescent dye, spin label, heavy metal or radio-labeled compounds of the invention that would be useful not only in imaging but also in assays, both *in vitro* and *in vivo*, for localizing and quantitating the PI3K α enzyme in tissue samples, including human, and for identifying PI3K α enzyme ligands by inhibition binding of a labeled compound.
15 Accordingly, the present invention includes PI3K α enzyme assays that contain such labeled compounds.

 The present invention further includes isotopically-labeled compounds of the invention. An “isotopically” or “radio-labeled” compound is a compound of the invention where one or more atoms are replaced or substituted by an atom having an
20 atomic mass or mass number different from the atomic mass or mass number typically found in nature (*i.e.*, naturally occurring). Suitable radionuclides that may be incorporated in compounds of the present invention include but are not limited to ^2H (also written as D for deuterium), ^3H (also written as T for tritium), ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{18}F , ^{35}S , ^{36}Cl , ^{82}Br , ^{75}Br , ^{76}Br , ^{77}Br , ^{123}I , ^{124}I , ^{125}I and ^{131}I . The
25 radionuclide that is incorporated in the instant radio-labeled compounds will depend on the specific application of that radio-labeled compound. For example, for *in vitro* FGFR enzyme labeling and competition assays, compounds that incorporate ^3H , ^{14}C , ^{82}Br , ^{125}I , ^{131}I , or ^{35}S will generally be most useful. For radio-imaging applications
 ^{11}C , ^{18}F , ^{125}I , ^{123}I , ^{124}I , ^{131}I , ^{75}Br , ^{76}Br or ^{77}Br will generally be most useful.

30 One or more constituent atoms of the compounds presented herein can be replaced or substituted with isotopes of the atoms in natural or non-natural abundance. In some embodiments, one or more atoms are replaced or substituted by deuterium.

For example, one or more hydrogen atoms in a compound of the present disclosure can be replaced by deuterium atoms (*e.g.*, one or more hydrogen atoms of a C₁₋₆ alkyl group of Formula I can be optionally substituted with deuterium atoms, such as -CD₃ being substituted for -CH₃). In some embodiments, alkyl groups of the disclosed Formulas (*e.g.*, the compound of any of Formulas I-VIIa) can be perdeuterated.

In some embodiments, the compound provided herein (*e.g.*, the compound of any of Formulas I-IIIb), or a pharmaceutically acceptable salt thereof, comprises at least one deuterium atom.

In some embodiments, the compound provided herein (*e.g.*, the compound of any of Formulas I-IIIb), or a pharmaceutically acceptable salt thereof, comprises two or more deuterium atoms.

In some embodiments, the compound provided herein (*e.g.*, the compound of any of Formulas I-IIIb), or a pharmaceutically acceptable salt thereof, comprises three or more deuterium atoms.

In some embodiments, for a compound provided herein (*e.g.*, the compound of any of Formulas I-IIIb), or a pharmaceutically acceptable salt thereof, all of the hydrogen atoms are replaced by deuterium atoms (*i.e.*, the compound is “perdeuterated”).

It is understood that a “radio-labeled ” or “labeled compound” is a compound that has incorporated at least one radionuclide. In some embodiments the radionuclide is selected from the group consisting of ³H, ¹⁴C, ¹²⁵I, ³⁵S and ⁸²Br.

Synthetic methods for including isotopes into organic compounds are known in the art (Deuterium Labeling in Organic Chemistry by Alan F. Thomas (New York, N.Y., Appleton-Century-Crofts, 1971; The Renaissance of H/D Exchange by Jens Atzrodt, Volker Derdau, Thorsten Fey and Jochen Zimmermann, Angew. Chem. Int. Ed. 2007, 7744-7765; The Organic Chemistry of Isotopic Labelling by James R. Hanson, Royal Society of Chemistry, 2011). Isotopically labeled compounds can be used in various studies such as NMR spectroscopy, metabolism experiments, and/or assays.

Substitution with heavier isotopes, such as deuterium, may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be

preferred in some circumstances. (see *e.g.*, A. Kerekes et. al. *J. Med. Chem.* 2011, 54, 201-210; R. Xu et. al. *J. Label Compd. Radiopharm.* 2015, 58, 308-312). In particular, substitution at one or more metabolism sites may afford one or more of the therapeutic advantages.

5 A radio-labeled compound of the invention can be used in a screening assay to identify/evaluate compounds. In general terms, a newly synthesized or identified compound (*i.e.*, test compound) can be evaluated for its ability to reduce binding of the radio-labeled compound of the invention to the PI3K α enzyme. Accordingly, the ability of a test compound to compete with the radio-labeled compound for binding to
10 the PI3K α enzyme directly correlates to its binding affinity.

Kits

 The present invention also includes pharmaceutical kits useful, for example, in the treatment or prevention of PI3K α -associated diseases or disorders referred to
15 herein which include one or more containers containing a pharmaceutical composition comprising a therapeutically effective amount of a compound of the invention. Such kits can further include, if desired, one or more of various conventional pharmaceutical kit components, such as, for example, containers with one or more pharmaceutically acceptable carriers, additional containers, etc., as will be readily
20 apparent to those skilled in the art. Instructions, either as inserts or as labels, indicating quantities of the components to be administered, guidelines for administration, and/or guidelines for mixing the components, can also be included in the kit.

 The invention will be described in greater detail by way of specific examples.
25 The following examples are offered for illustrative purposes, and are not intended to limit the invention in any manner. Those of skill in the art will readily recognize a variety of non-critical parameters which can be changed or modified to yield essentially the same results. The compounds of the Examples were found to be inhibitors of PI3K α as described below.

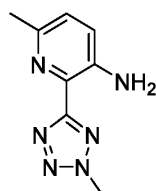
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EXAMPLES

Experimental procedures for compounds of the invention are provided below. Preparatory LC-MS purifications of some of the compounds prepared were performed on Waters mass directed fractionation systems. The basic equipment setup, protocols, and control software for the operation of these systems have been described in detail
5 in the literature. See e.g. "Two-Pump At Column Dilution Configuration for Preparative LC-MS", K. Blom, *J. Combi. Chem.*, 4, 295 (2002); "Optimizing Preparative LC-MS Configurations and Methods for Parallel Synthesis Purification", K. Blom, R. Sparks, J. Doughty, G. Everlof, T. Haque, A. Combs, *J. Combi. Chem.*, 5, 670 (2003); and "Preparative LC-MS Purification: Improved Compound Specific
10 Method Optimization", K. Blom, B. Glass, R. Sparks, A. Combs, *J. Combi. Chem.*, 6, 874-883 (2004). The compounds separated were typically subjected to analytical liquid chromatography mass spectrometry (LCMS) for purity check.

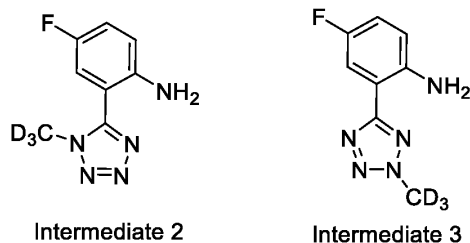
Some of the compounds prepared were also separated on a preparative scale by reverse-phase high performance liquid chromatography (RP-HPLC) with MS
15 detector or flash chromatography (silica gel) as indicated in the Examples.

Intermediate 1. 6-Methyl-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine

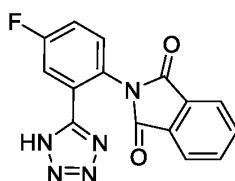


A solution of 6-chloro-2-(2-methyltetrazol-5-yl)pyridin-3-amine (Example 8,
20 step 4) (55.0 mg, 0.26 mmol), tetrakis(triphenylphosphine)palladium(0) (60.4 mg, 0.05 mmol), K₃PO₄ (166.3 mg, 0.78 mmol) and methylboronic acid (31.3 mg, 0.52 mmol) in 3 mL dioxane/H₂O (5:1) was bubbled with N₂ for 1 min. The resulting reaction mixture was stirred at 100 °C for 2h. LCMS analysis indicated the reaction was complete. The mixture was diluted with water and extracted with EtOAc. The
25 combined organics were washed with sat. NaCl, dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and EtOAc (0 to 100%) to provide the desired product as a white solid. LCMS calculated for C₈H₁₁N₆ (M+H)⁺ m/z = 191.1; found 191.1.

**Intermediates 2-3. 4-Fluoro-2-(1-(methyl-d3)-1H-tetrazol-5-yl)aniline
(Intermediate 2) & 4-fluoro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)aniline
(Intermediate 3)**



5 *Step 1: 2-(4-fluoro-2-(1H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione*

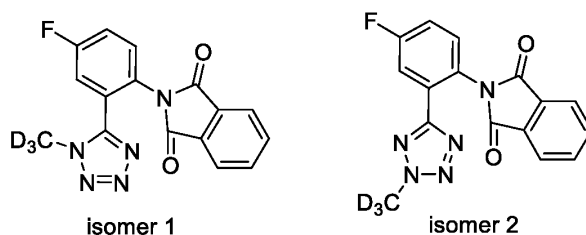


The titled intermediate was prepared using similar procedures as described for *Example 8* with 2-amino-5-fluorobenzonitrile replacing 3-amino-6-chloro-pyridine-2-carbonitrile in step 1. The reaction mixture was diluted with water and adjusted the pH to 2 by adding 10 % HCl. The precipitate was collected by filtration to give product as a brown solid. LCMS calculated for $C_{15}H_9FN_5O_2$ ($M+H$)⁺ m/z = 310.1; found 310.1.

10

*Step 2: 2-(4-fluoro-2-(1-(methyl-d3)-1H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione
and 2-(4-fluoro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione*

15



To a solution of 2-(4-fluoro-2-(1H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione (2.49 g, 8.05 mmol) in 10 mL of DMF was added CD_3I (0.70 mL, 11.27 mmol) and K_2CO_3 (3.34 g, 24.15 mmol). After stirring at rt. for 2h, the mixture was diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced

20

pressure. The resulting mixture was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the 2 products, isomer 1 and isomer 2. LCMS calculated for $C_{16}H_8D_3FN_5O_2$ (M+H)⁺ m/z = 327.1; found 327.1

5 *Step 3: 4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)aniline*

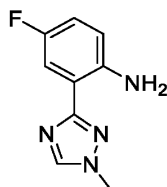
The mixture of 2-(4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione (0.13 g, 0.40 mmol) in 1 mL hydrazine monohydrate was stirred at 45 °C for 2 h, then cooled to rt and diluted with water. The precipitate was collected by filtration and washed with water to give the product as white solid.

10 LCMS calculated for $C_8H_6D_3FN_5$ (M+H)⁺ m/z = 197.1; found 197.1.

Step 4: 4-fluoro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)aniline

The titled intermediate was prepared using similar procedures as described in step 3 with 2-(4-fluoro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione replacing 2-(4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)isoindoline-1,3-dione. LCMS calculated for $C_8H_6D_3FN_5$ (M+H)⁺ m/z = 197.1; found 197.1.

Intermediate 4. 4-Fluoro-2-(1-methyl-1,2,4-triazol-3-yl)aniline

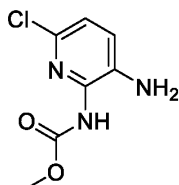


20 A solution of 4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.0 g, 4.22 mmol), 3-bromo-1-methyl-1,2,4-triazole (683.3 mg, 4.22 mmol), K_3PO_4 (2686 mg, 12.65 mmol) and [2-(2-aminophenyl)phenyl]-chloro-palladium;dicyclohexyl-[2-(2,4,6-triisopropylphenyl)phenyl]phosphane (663.8 mg, 0.84 mmol) in 15 mL dioxane/ H_2O (5:1) was bubbled with N_2 for 1 min. The

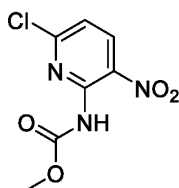
25 resulting reaction mixture was stirred at 90 °C for 2h. LCMS analysis indicated the reaction was complete. The mixture was diluted with water and extracted with EtOAc. The combined organics were washed with sat. NaCl, dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and EtOAc (0 to 100%) to

provide the desired product as a white solid. LCMS calculated for $C_9H_{10}FN_4$ ($M+H$)⁺ m/z = 193.1; found 193.1.

Intermediate 5. Methyl (3-amino-6-chloropyridin-2-yl)carbamate



Step 1. methyl (6-chloro-3-nitropyridin-2-yl)carbamate

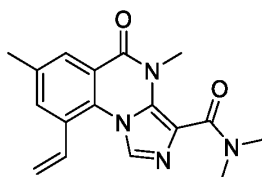


To the suspension of 6-chloro-3-nitropyridin-2-amine (5.00 g, 28.81 mmol) in DCM was added *N,N*-diisopropylethylamine (24 mL, 172.85 mmol) followed by addition of methyl chloroformate (26.8 mL, 345.71 mmol) dropwise. The resulting mixture was heated at 45 °C for 1 hour. The reaction was cooled to rt. The reaction mixture was concentrated under vacuum and loaded onto silica gel (20 g), eluted with 0-50% ethyl acetate in hexanes to give the desired product (1.14 g, 17.1 %) as a yellow solid. LCMS calculated for $C_7H_7ClN_3O_4$ ($M+H$)⁺ m/z = 232.0; found 232.0.

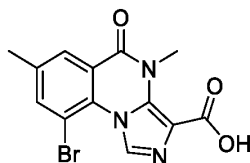
Step 2. methyl (3-amino-6-chloropyridin-2-yl) carbamate

To the solution of methyl N-(6-chloro-3-nitro-2-pyridyl) carbamate (1.11 g, 4.79 mmol) in 5 to 1 mixture of ethanol and water was added iron (0.94 g, 16.78 mmol) and ammonium chloride (0.90 g, 16.78 mmol) at rt. The resulting mixture was heated at 60 °C for 1 hour. Upon completion of reaction, the mixture was cooled to room temperature, filtered through a celite pad and concentrated. The residue was purified with silica gel chromatography, eluting with 0-100% ethyl acetate in dichloromethane to give the desired product (0.33 g, 34.2 %) as yellow solid. LCMS calculated for $C_7H_9ClN_3O_2$ ($M+H$)⁺ m/z = 202.0; found 202.0.

Intermediate 6. N,N,4,7-Tetramethyl-5-oxo-9-vinyl-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



Step 1. 9-bromo-4,7-dimethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxylic acid



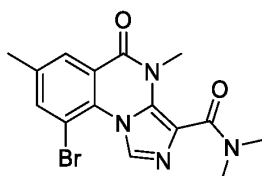
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The solid of tert-butyl 9-bromo-4,7-dimethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxylate (Example 1, step 6) (4.00 g, 10.20 mmol) was treated with TFA (20 mL) at rt. The resulting mixture was stirred at rt for 2 h. Upon completion, the solvent was removed under reduced pressure. The residue was azeotrope with toluene (20 mL) 3 times to give the crude product, which was used in the next step directly. LCMS calculated for $C_{13}H_{11}BrN_3O_3$ ($M+H$)⁺ m/z = 336.0; found 336.0.

10

Step 2. 9-bromo-N,N,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide

15



To the solution of 9-bromo-4,7-dimethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxylic acid (3.43 g, 10.20 mmol) in DMF (20 mL) was added [dimethylamino(triazolo[4,5-b]pyridin-3-yloxy)methylene]-dimethylammonium;hexafluorophosphate (5.82 g, 15.31 mmol), N-ethyl-N-isopropyl-propan-2-amine (17.8 mL, 102.04 mmol) and dimethylamine (2M THF, 6.1 mL, 12.24 mmol) at rt. The resulting mixture was stirred at rt for 1 h. Upon completion, the mixture was diluted with water (50 mL) extracted with ethyl acetate (100 mL), the organic layer

20

was washed with water (50 mL x 3). The combined organic layer was dried with sodium sulfate, concentrated under reduced pressure. The residue was purified with silica gel chromatography to give the desired product (2.54 g, 68.5 %) as a light yellow solid. LCMS calculated for $C_{15}H_{16}BrN_4O_2$ (M+H)⁺ m/z = 363.0; found 363.0.

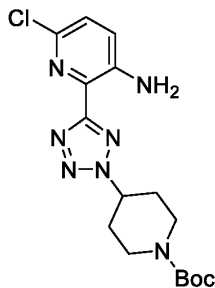
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Step 3. N,N,4,7-tetramethyl-5-oxo-9-vinyl-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

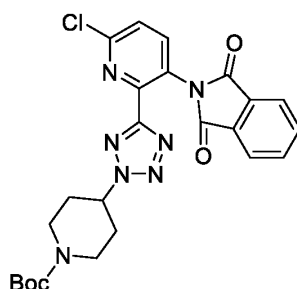
To a 5 to 1 mixture of THF and water (25 mL) was added 9-bromo-N,N,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide (0.94 g, 2.59 mmol),
10 [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (211 mg, 0.26 mmol), potassium trifluoro(vinyl)boranuide (1.04 g, 7.76 mmol) and K_2CO_3 (1.07 g, 7.76 mmol) at rt. The resulting mixture was heated at 70 °C for 4 h. Upon cooling to rt, the reaction mixture was diluted with DCM (50 mL), washed with water (20 mL). The combined organic layer was dried with sodium
15 sulfate, concentrated, and purified with silica gel chromatography to give the desired product (0.50 g, 62.3 %) as a yellow solid. LCMS calculated for $C_{17}H_{19}N_4O_2$ (M+H)⁺ m/z = 311.2; found 311.2.

Intermediate 7. tert-Butyl 4-(5-(3-amino-6-chloropyridin-2-yl)-2H-tetrazol-2-yl)piperidine-1-carboxylate

20



Step 1. tert-butyl 4-(5-(6-chloro-3-(1,3-dioxoisindolin-2-yl)pyridin-2-yl)-2H-tetrazol-2-yl)piperidine-1-carboxylate

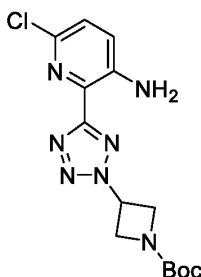


To the suspension of 2-(6-chloro-2-(2H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione (Example 8, step 1) (100 mg, 0.31 mmol) in DMF was added K_2CO_3 (63 mg, 0.46 mmol) and tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (171 mg, 0.61 mmol). The resulting mixture was heated at 80 °C overnight. The reaction was cooled to rt. The reaction mixture was concentrated under vacuum purified with silica gel chromatography to afford the desired product. LCMS calculated for $C_{24}H_{25}ClN_7O_4$ ($M+H$)⁺ m/z = 510.2; found 510.2.

Step 2. tert-butyl 4-(5-(3-amino-6-chloropyridin-2-yl)-2H-tetrazol-2-yl)piperidine-1-carboxylate

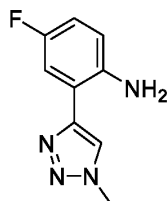
The mixture of tert-butyl 4-(5-(6-chloro-3-(1,3-dioxoisindolin-2-yl)pyridin-2-yl)-2H-tetrazol-2-yl)piperidine-1-carboxylate (30 mg, 0.06 mmol) in 0.5 mL of hydrazine monohydrate was stirred at 45 °C for 2 h, then cooled to rt and concentrated under vacuum. The residue was purified with silica gel chromatography to afford the desired product. LCMS calculated for $C_{16}H_{23}ClN_7O_2$ ($M+H$)⁺ m/z = 380.2; found 380.2.

Intermediate 8. tert-Butyl 3-(5-(3-amino-6-chloropyridin-2-yl)-2H-tetrazol-2-yl)azetidine-1-carboxylate



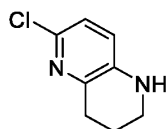
The titled intermediate was prepared using similar procedures as described in Intermediate 7 with tert-butyl 3-((methylsulfonyl)oxy)azetidine-1-carboxylate replacing tert-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate in step 1. LCMS calculated for $C_{14}H_{19}ClN_7O_2$ ($M+H$)⁺ m/z = 352.1; found 352.1.

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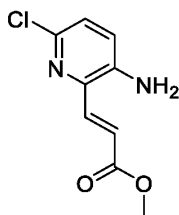
Intermediate 9. 4-Fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)aniline

The titled compound was prepared using similar procedures as described for Intermediate 4 with 4-bromo-1-methyl-1H-1,2,3-triazole replacing 3-bromo-1-methyl-1,2,4-triazole. The residue was purified by silica gel column chromatography, eluted with DCM and EtOAc (0 to 100%) to provide the desired product as a white solid. LCMS calculated for $C_9H_{10}FN_4$ ($M+H$)⁺ m/z = 193.1; found 193.1.

10

Intermediate 10. 6-Chloro-1,2,3,4-tetrahydro-1,5-naphthyridine

15

Step 1. methyl (E)-3-(3-amino-6-chloro-2-pyridyl)prop-2-enoate

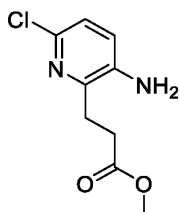
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To the solution of 6-chloro-2-iodo-pyridin-3-amine (1.00 g, 3.93 mmol) in anhydrous DMF (3.33 mL) was added $Pd(OAc)_2$ (88 mg, 0.39 mmol), tris-o-tolylphosphane (84 mg, 0.28 mmol), methyl prop-2-enoate (605.43 μ L, 6.68 mmol) and N-ethyl-N-isopropyl-propan-2-amine (2.05 mL, 11.79 mmol) at rt. The mixture was deoxygenated by three vacuum–nitrogen cycles. The resulting mixture was heated at 100 °C for 16 h. Upon completion of reaction, the reaction mixture was

cooled to rt, diluted with water (20 mL), extracted with ethyl acetate (20 mL x 3). The combined organic layers were dried with sodium sulfate. Solvent was removed under reduced pressure. The residue was purified with silica gel chromatography, eluting from 0-100% EA in DCM to give desired product (740 mg, 88.6 %) as a yellow solid.

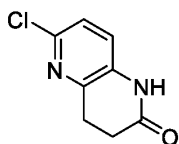
5 LCMS calculated for $C_9H_{10}ClN_2O_2$ (M+H)⁺ m/z = 213.0; found 213.0.

Step 2. Methyl 3-(3-amino-6-chloro-2-pyridyl)propanoate



To a dry vial was charged diacetoxycopper (55 mg, 0.30 mmol) and (2-
10 diphenylphosphanylphenyl)-diphenyl-phosphane (13 mg, 0.03 mmol) in 2-
methylpropan-2-ol (857 uL, 9.03 mmol) and anhydrous toluene (2.0 mL), the
resulting mixture was stirred at rt for 20 min under nitrogen, followed by addition of
polymethylhydrosiloxane (557 uL) via syringe, the solution changed from blue into
dark yellow in about 5 min; then methyl (E)-3-(3-amino-6-chloro-2-pyridyl)prop-2-
15 enoate (640 mg, 3.01 mmol) was added in one portion. The resulting mixture was
stirred at rt for 2 days before diluted with DCM, then washed with water, organic
layer was separated, dried with Na₂SO₄, solvent was then removed under reduced
pressure. The residue was charged with DCM, precipitate was collected by filtration,
Filtrate was loaded onto silica gel, purified with silica gel, eluting from 0-100%
20 DCM/EA followed by 0-30% MeOH/EA to give desired product (362 mg, 56.1 %) as
a white solid. LCMS calculated for $C_9H_{12}ClN_2O_2$ (M+H)⁺ m/z = 215.1; found 215.1.

Step 3. 6-chloro-3,4-dihydro-1H-1,5-naphthyridin-2-one



25 To methyl 3-(3-amino-6-chloro-2-pyridyl)propanoate (362 mg, 1.69 mmol)
was added a 10 to 1 mixture of ethanol and acetic acid (10 mL) at rt. The resulting

mixture was heated at 70 °C overnight. The solvent was removed under reduced pressure. The residue was azeotrope with EA/DCM for 2 times to give desired crude material as a yellow solid, which was used in the next step directly. LCMS calculated for $C_8H_8ClN_2O$ ($M+H$)⁺ m/z = 183.0; found 183.0.

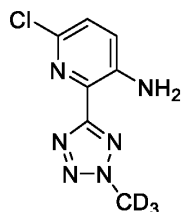
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Step 4. 6-chloro-1,2,3,4-tetrahydro-1,5-naphthyridine

To the solution of 6-chloro-3,4-dihydro-1H-1,5-naphthyridin-2-one (512 mg, 2.80 mmol) in anhydrous THF (5.6 mL) was added LAH (THF solution, 5.61 mL, 5.61 mmol) at 0 °C. The resulting mixture was heated at 60 °C for 14 hours. The reaction was quenched with ice water, extracted with EA twice. The organic layer was then dried with sodium sulfate, concentrated under reduced pressure. The residue was purified with silica gel chromatography to give the desired product (296 mg, 62.6 % over 2 steps) as a white solid. LCMS calculated for $C_8H_{10}ClN_2$ ($M+H$)⁺ m/z = 169.1; found 169.1.

15

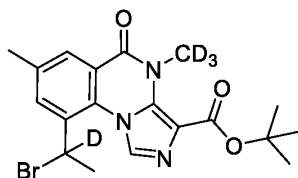
Intermediate 11. 6-Chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-amine



The titled compound was prepared using similar procedures as described for *Example 8* with iodomethane-d₃ replacing iodomethane in step 3. LCMS calculated for $C_7H_5D_3ClN_6$ ($M+H$)⁺ m/z = 214.1; found 214.1.

20

Intermediate 12. tert-Butyl 9-(1-bromoethyl-1-d)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate

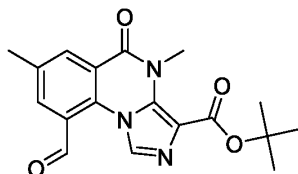


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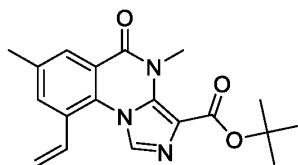
The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-3-bromo-5-methyl-N-(methyl-d₃)benzamide (*Example 4*,

step 1) replacing 2-amino-3-bromo-N,5-dimethylbenzamide in step 4, and NaBD₄ replacing NaBH₄ in step 8. LCMS calculated for C₁₉H₁₉D₄BrN₃O₃ (M+H)⁺ m/z = 424.1; found 424.1.

5 **Intermediate 13. tert-Butyl 9-formyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate**



Step 1: tert-butyl 4,7-dimethyl-5-oxo-9-vinyl-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



10

To the mixture of tert-butyl 9-bromo-4,7-dimethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxylate (Example 1, step 6) (2.00 g, 5.10 mmol) in a 5 to 1 mixture of THF and water (75 mL) was added [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with
15 dichloromethane (416.4 mg, 0.51 mmol), potassium carbonate (2.11 g, 15.30 mmol) and potassium vinyltrifluoroborate (2.05 g, 15.30 mmol) at rt. The resulting mixture was degassed with nitrogen for 1 minute. The mixture was heated at 70 °C for 4 hours then cooled to rt and diluted with DCM (250 mL), washed with water (100 mL). The organic layer was then separated, dried with sodium sulfate. Solvent was removed
20 under reduced pressure. The residue was purified with silica gel chromatography to give the desired product (1.21 g, 69.9 %) as a yellow solid. LCMS calculated for C₁₉H₂₂N₃O₃ (M+H)⁺ m/z = 340.2; found 340.2.

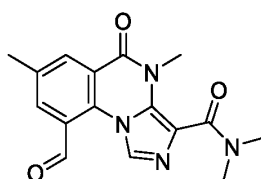
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Step 2: tert-butyl 9-formyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate

To the 5 to 1 mixture of THF and water was charged *tert*-butyl 4,7-dimethyl-5-oxo-9-vinyl-imidazo[1,5-a]quinazoline-3-carboxylate (1.21 g, 3.57 mmol), OsO₄

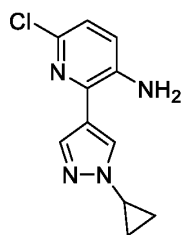
(4% water solution, 679 uL, 0.11 mmol), 2,6-dimethylpyridine (826 uL, 7.13 mmol) and sodium periodate (3.05 g, 14.26 mmol) successively. The resulting mixture was heated at 45 °C for 2 hours. The reaction mixture was cooled to room temperature, diluted with DCM (15 mL), washed with water (10 mL x 2). The organic layer was then separated, dried with sodium sulfate. The solvent was then removed under reduced pressure, the residue was used in the next step directly. LCMS calculated for $C_{18}H_{20}N_3O_4$ ($M+H$)⁺ m/z = 342.1; found 342.1.

Intermediate 14. 9-Formyl-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



The titled compound was prepared using similar procedures as described for Intermediate 13 with N,N,4,7-tetramethyl-5-oxo-9-vinyl-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (Intermediate 6) replacing *tert*-butyl 4,7-dimethyl-5-oxo-9-vinyl-imidazo[1,5-a]quinazoline-3-carboxylate in step 2. LCMS calculated for $C_{16}H_{17}N_4O_3$ ($M+H$)⁺ m/z = 313.1; found 313.1.

Intermediate 15. 6-Chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-amine



To a solution of 2-bromo-6-chloropyridin-3-amine (300 mg, 1.5 mmol) in 2.5 mL of dioxane and 0.5 mL of water was added 1-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole (230 mg, 1.8 mmol), potassium carbonate (400 mg, 2.9 mmol) and tetrakis(triphenylphosphine)palladium (220 mg, 0.2 mmol) under nitrogen. After stirring at 85 °C for 1 h, the mixture was diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with

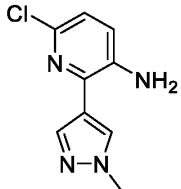
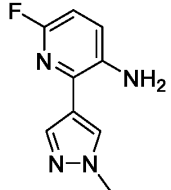
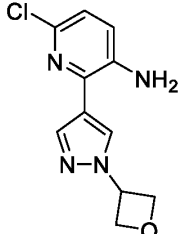
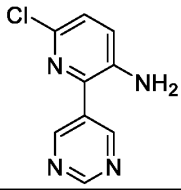
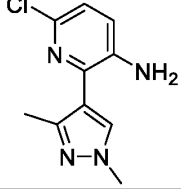
anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a yellow solid. LCMS calculated for $C_{11}H_{12}ClN_4$ ($M+H$)⁺ m/z = 235.1; found 235.1.

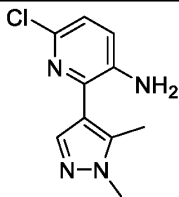
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Intermediates 16-21.

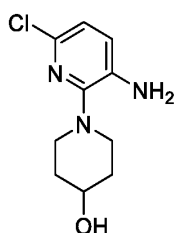
The following intermediates in Table I-1 were prepared similarly according to the procedures described for Intermediate 15.

Table I-1.

Intermediate #	Chemical Name	Structure	LCMS m/z ($M+H$) ⁺
16	6-chloro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-amine		209.1
17	6-fluoro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-amine		193.1
18	6-chloro-2-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-3-amine		251.1
19	6-chloro-2-(pyrimidin-5-yl)pyridin-3-amine		207.1
20	6-chloro-2-(1,3-dimethyl-1H-pyrazol-4-yl)pyridin-3-amine		223.1

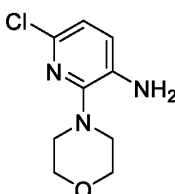
Intermediate #	Chemical Name	Structure	LCMS m/z (M+H) ⁺
21	6-chloro-2-(1,5-dimethyl-1H-pyrazol-4-yl)pyridin-3-amine		223.1

Intermediate 22. 1-(3-Amino-6-chloropyridin-2-yl)piperidin-4-ol

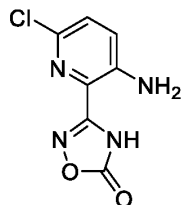


To a solution of 6-chloro-2-fluoro-3-nitro-pyridine (100 mg, 0.57 mmol) in 3 mL of EtOH was added piperidin-4-ol (57.3 mg, 0.57 mmol). The reaction mixture was stirred at 45 °C for 1 h. To this mixture was added potassium tert-butoxide (127 mg, 1.13 mmol) and 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (432 mg, 1.70 mmol). After stirring at 80 °C overnight, the mixture was cooled to rt, diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a yellow solid (90 mg, 70%). LCMS calculated for C₁₀H₁₅ClN₃O (M+H)⁺ m/z = 228.1; found 228.1.

Intermediate 23. 6-Chloro-2-morpholinopyridin-3-amine



The titled compound was prepared using similar procedures as described for Intermediate 22 with morpholine replacing piperidin-4-ol. LCMS calculated for C₉H₁₃ClN₃O (M+H)⁺ m/z = 214.1; found 214.1.

Intermediate 24: 3-(3-amino-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one*Step 1: 3-amino-6-chloro-N-hydroxypicolinimidamide*

5 The mixture of 3-amino-6-chloropyridonitrile (5.0 g, 32.5 mmol) and 50% aqueous hydroxylamine (2 mL, 32.5 mmol) in MeOH (100 mL) was stirred at rt. for 1 h. Then the mixture was poured into water (500 mL). The resulting solid was collected via filtration, washed with water (100 mL), and dried to afford the desired product as a brown solid (5.1 g, 84% yield). LCMS calculated for C₆H₈ClN₄O

10 (M+H)⁺ m/z = 187.0; found 187.0.

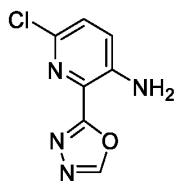
Step 2: 3-(3-amino-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one

To a solution of 3-amino-6-chloro-N-hydroxypicolinimidamide (5.1 g, 27.3 mmol) in THF (100 mL) was added 1,1'-carbonyldiimidazole (4.87 g, 30 mmol) and

15 1,8-diazabicyclo[5.4.0]undec-7-ene (16.6 mL, 109 mmol) at 0 °C. After stirring for 4 h at rt., the mixture was diluted with 500 mL of water. The aqueous phase was washed with 50mL ethyl acetate 3 times, then adjusted pH to 7 with 3N HCl. The resulting solid was collected via filtration, washed with water (100 mL), and dried to afford the desired product as a brown solid (4.9 g, 84% yield). LCMS calculated for

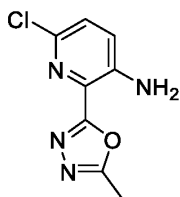
20 C₇H₆ClN₄O₂ (M+H)⁺ m/z = 213.0; found 213.0.

Intermediate 25. 6-Chloro-2-(1,3,4-oxadiazol-2-yl)pyridin-3-amine



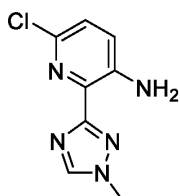
To a solution of 3-amino-6-chloropicolinic acid (100 mg, 0.58 mmol) in 2 mL of DCM was added (N-isocyanoimino)triphenylphosphorane (175 mg, 0.58 mmol). After stirring at r.t. for overnight, the mixture was diluted with water and extracted with DCM. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a yellow solid (84 mg, 74%). LCMS calculated for $C_7H_6ClN_4O$ (M+H)⁺ m/z = 197.0; found 197.0.

Intermediate 26. 6-Chloro-2-(5-methyl-1,3,4-oxadiazol-2-yl)pyridin-3-amine

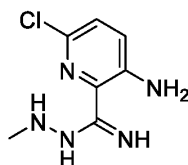


A solution of 6-chloro-2-(1H-tetrazol-5-yl)pyridin-3-amine (Example 8, step 1) (500 mg, 2.55 mmol) in 2 mL of acetic anhydride was stirred at 110 °C overnight, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a brown solid (187 mg, 35%). LCMS calculated for $C_8H_8ClN_4O$ (M+H)⁺ m/z = 211.0; found 211.0.

Intermediate 27. 6-Chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-amine



Step 1: 3-amino-6-chloro-N'-methylpicolinimidohydrazide

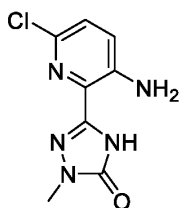


To a solution of 3-amino-6-chloro-pyridine-2-carbonitrile (500 mg, 3.26 mmol) in 10 mL of EtOH was added methylhydrazine (1.03 mL, 19.54 mmol) at r.t. After stirring at 100 °C for 24 h, the solvent was removed under vacuum to provide the desired product as a yellow solid (600 mg, 92%). LCMS calculated for $C_7H_{11}ClN_5$ (M+H)⁺ m/z = 200.1; found 200.1.

Step 2: 6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-amine

A solution of 3-amino-6-chloro-N¹-methylpicolinimidohydrazide (600 mg, 3 mmol) in 5 mL of formic acid was stirred at 105 °C for overnight. After cooling to rt, the solvent was removed under vacuum. Then to the residue was added 5 mL of ammonium hydroxide solution in water and EtOH, the mixture was stirred for overnight at 100 °C. The mixture was diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was triturated with ether, filtered and washed with ether to provide the desired product as a yellow solid (420 mg, 67%). LCMS calculated for $C_8H_9ClN_5$ (M+H)⁺ m/z = 210.1; found 210.1.

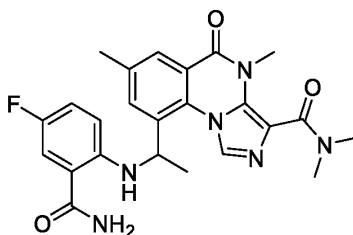
Intermediate 28. 5-(3-Amino-6-chloropyridin-2-yl)-2-methyl-2,4-dihydro-3H-1,2,4-triazol-3-one



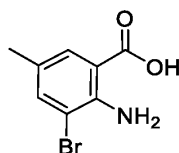
To a solution of 3-amino-6-chloro-N¹-methylpicolinimidohydrazide (intermediate 27, step 1) (200 mg, 1.3 mmol) in 2 mL of THF was added CDI (230 mg, 1.43 mmol) followed by slow addition of DBU (0.58 mL, 3.9 mmol). The resulting mixture was stirred at rt. The mixture was then diluted with water and

extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a brown solid. LCMS calculated for $C_8H_9ClN_5O$ ($M+H$)⁺ m/z = 226.0; found 226.0.

Example 1. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

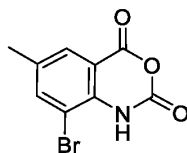


Step 1: 2-amino-3-bromo-5-methylbenzoic acid



To a mixture of 2-amino-5-methylbenzoic acid (100 g, 660 mmol) in DMF (300 mL) was added NBS (117 g, 660 mmol) at 0 °C under nitrogen atmosphere. The reaction mixture was then slowly warmed to rt and stirred for 1 h. After completion, the reaction was diluted with ice water while stirred. The resulting solid was collected to afford the desired product as a light brown solid (127 g, 85%) which was used in the next step without further purification. LCMS calculated for $C_8H_9BrNO_2$ ($M+H$)⁺ m/z = 230.0; found 230.1.

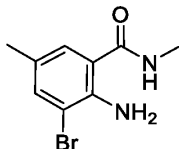
Step 2: 8-bromo-6-methyl-2H-benzo[d][1,3]oxazine-2,4(1H)-dione



To a mixture of 2-amino-3-bromo-5-methylbenzoic acid (110 g, 480 mmol) in dioxane (1000 mL) was added triphosgene (57 g, 192 mmol) at 0 °C. The resulting

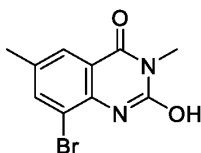
mixture was stirred at 100 °C for 2h. Upon cooling to room temperature, the resulting solid was collected to afford the desired product as a white solid, which was used in the next step without further purification.

5 *Step 3: 2-amino-3-bromo-N,5-dimethylbenzamide*



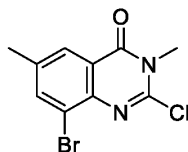
To a mixture of 8-bromo-6-methyl-2H-benzo[d][1,3]oxazine-2,4(1H)-dione (90 g, 354 mmol) in THF (900 mL) was added methylamine (175 mL, 2 M solution in THF) at 0 °C. The resulting mixture was warmed to rt, and then stirred for 1h. The
10 solvent was removed, and the crude product was used in the next step without further purification.

Step 4: 8-bromo-2-hydroxy-3,6-dimethylquinazolin-4(3H)-one



To the solid from *Step 3* was added THF (700 mL) and triphosgene (70 g, 237 mmol) at rt. The resulting mixture was heated at 70 °C for 2h, upon cooling to room temperature, half of the solvent was removed under vacuum, the resulting solid was collected. The solid product was then washed with 4:1 hexanes and ethyl acetate, then dried under vacuum overnight to afford pure product as a white solid, which was used
20 in the next step without further purification.

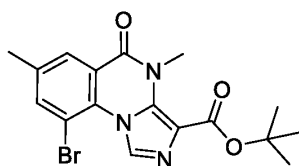
Step 5: 8-bromo-2-chloro-3,6-dimethylquinazolin-4(3H)-one



To a mixture of 8-bromo-2-hydroxy-3,6-dimethylquinazolin-4(3H)-one (72 g, 269 mmol) in POCl₃ (374 mL) was added DIEA (182 mL, 1.1 mmol) at 0 °C. The
25

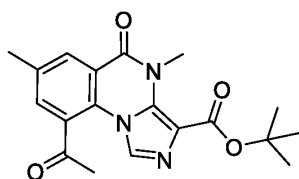
resulting mixture was stirred at 120 °C for 12h in a pressure vessel. Upon cooling to room temperature, the mixture was slowly poured onto 4000 mL ice carefully. After 2h, the resulting solid was collected to afford a light brown solid, which was washed with water, sat NaHCO₃ then water. The solid was dried under vacuum to afford the
 5 desired product as light brown solid (62.5 g, 82%).

Step 6: tert-butyl 9-bromo-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



10 To a mixture of KO^tBu (29 g, 260 mmol) in dry DMF (700 mL) under nitrogen was added tert-butyl 2-isocyanoacetate (27 mL, 191.3 mmol) at 0 °C dropwise. The resulting mixture was stirred at 0 °C for 10 min then 8-bromo-2-chloro-3,6-dimethylquinazolin-4(3H)-one (50 g, 173 mmol) was added in one portion. The resulting mixture was warmed to rt and stirred for 2h. After completion, the
 15 reaction mixture was poured into 1000 mL sat. NH₄Cl solution, then diluted with 800 mL water. The resulting solid was collected by filtration, washed with water then dried under vacuum to provide the desired product as a beige solid (59 g, 90%).
 LCMS calculated for C₁₇H₁₉BrN₃O₃ (M+H)⁺ m/z = 392.1; found 392.1.

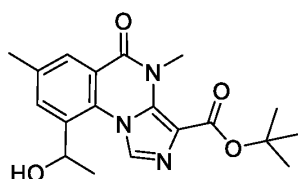
20 *Step 7: tert-butyl 9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate*



The mixture of tert-butyl 9-bromo-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (22.8 g, 58.1 mmol), PdCl₂(PPh₃)₂ (4.1 g, 5.8 mmol), and tributyl(1-ethoxyvinyl)stannane (25 g, 69.9 mmol) in dioxane
 25 (750 mL) was heated at 100 °C for 8 h under nitrogen atmosphere. Upon cooling to room temperature, 2 N HCl was added to the reaction mixture then stirred for 4 h. The

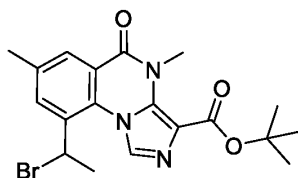
mixture was diluted with water and extracted with EtOAc. The combined organics were washed with sat. NaCl, dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. After most of solvent was removed, hexanes and EtOAc 4:1 mixture was added. The mixture was stirred for 2h, the precipitate solid was collected via filtration, which was washed with 4:1 hexanes and EtOAc mixture to provide the desired product as a brown solid (17 g, 84%). LCMS calculated for $C_{19}H_{22}N_3O_4$ ($M+H$)⁺ m/z = 356.2; found 356.2.

Step 8: *tert*-butyl 9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate



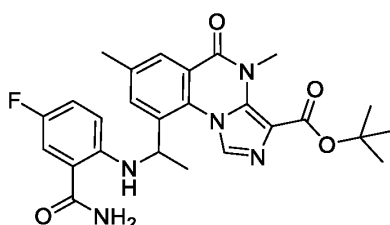
tert-Butyl 9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate (7 g, 19.6 mmol) was dissolved in MeOH (200 mL) and DCM (200 mL) then NaBH₄ (771.4 mg, 20.4 mmol) was added at 0 °C in three portions under nitrogen. The resulting mixture was stirred at same temperature for 10 min before quenched with sat. NH₄Cl. The mixture was diluted with water and extracted with DCM. The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and MeOH (0 to 4%) to provide the desired product as a light yellow solid (5.3 g 75%). LCMS calculated for $C_{19}H_{24}N_3O_4$ ($M+H$)⁺ m/z = 358.2; found 358.2.

Step 9: *tert*-butyl 9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate



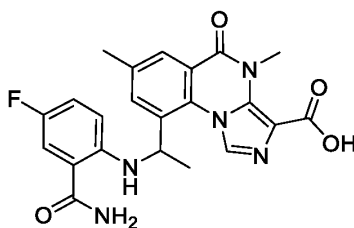
To a mixture of tert-butyl 9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (4.0 g, 11.2 mmol) in THF (300 mL) was added pyridine (1.7 g, 22 mmol) and PBr₃ (1.26 mL, 13.3 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for 2 h. The mixture was then quenched with sat. NaHCO₃ and extracted with DCM (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification.

Step 10: tert-butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



To the solution of tert-butyl 9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (1.6 g, 3.8 mmol) in DMF (50 mL) was added 2-amino-5-fluorobenzamide (770 mg, 5 mmol). The mixture was heated to 80 °C for 2 h. Upon cooling to room temperature, the mixture was diluted with water and extracted with ethyl acetate (3X). The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with hexanes and EtOAc (0 to 100%) to provide the desired product as a light yellow solid (1.5 g, 80%). LCMS calculated for C₂₆H₂₉FN₅O₄ (M+H)⁺ m/z = 494.2; found 494.2.

Step 11: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid

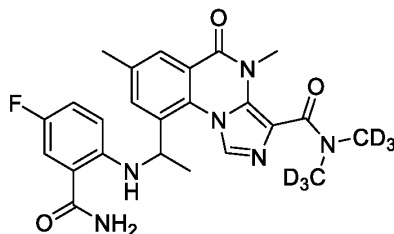


tert-Butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (1.5 g, 3.0 mmol) was dissolved in TFA (20 mL). The mixture was stirred for 3 h at rt. After completion, TFA was removed under vacuum. EtOAc (100 mL) and hexanes (100 mL) were added to the reaction residue while stirring. After stirring for 20 min, the resulting solid was collected to afford a white solid, which was washed with hexanes/EtOAc (1:1). The solid was dried under vacuum to provide the pure product (1.1 g, 83%). LCMS calculated for $C_{22}H_{21}FN_5O_4$ (M+H)⁺ m/z = 438.2; found 438.2.

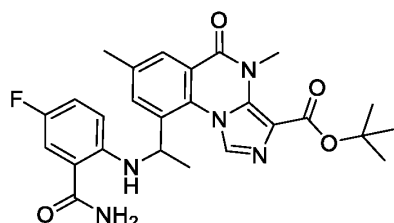
Step 12: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

To a mixture of 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (20 mg, 0.045 mmol) in DMF (0.5 mL) was added HATU (22 mg, 0.06 mmol), dimethylamine (30 uL, 2M THF solution), and DIEA (10 uL, 0.06 mmol). After stirring for 1 h, the reaction was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{24}H_{26}FN_6O_3$ (M+H)⁺ m/z = 465.2; found 465.2. ¹H NMR (400 MHz, DMSO-d₆) δ 8.64 (s, 1H), 8.37 (s, 1H), 8.09–7.97 (bs, 2H), 7.78 (s, 1H), 7.53 (dd, J = 10.1, 3.0 Hz, 1H), 7.44 (s, 1H), 7.03 (td, J = 8.6, 3.0 Hz, 1H), 6.36 (dd, J = 9.2, 4.6 Hz, 1H), 5.27 (q, J = 6.5 Hz, 1H), 3.48 (s, 3H), 3.06 (s, 3H), 3.03 (s, 3H), 2.36 (s, 3H), 1.60 (d, J = 6.3 Hz, 3H).

Example 2. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (Peak 1)



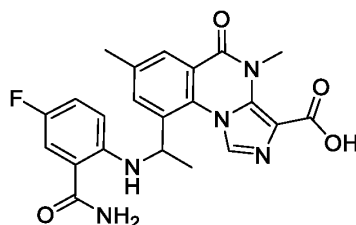
5 *Step 1: tert-butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate*



The titled racemic compound (Example 1, step 10) was separated by chiral HPLC to afford 2 enantiomers, the peak 1 was taken into the next step.

10

Step 2: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (peak 1)



The peak 1 of above tert-butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (60 mg, 0.12 mmol) was added in a 2 dram reaction vial. To the reaction vial was added 0.5 mL of neat TFA, the reaction was stirred for 1 h at rt. After completion, TFA was removed under vacuum. 1 mL of EtOAc and 1 mL of hexanes were added to the reaction vial while stirring. After stirring for 20 min, the resulting solid was collected to afford a white solid, which was washed with

20

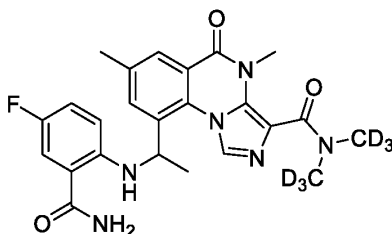
hexanes/EtOAc (1:1). The solid was dried under vacuum to provide the pure product (48 mg, 91%). LCMS calculated for $C_{22}H_{21}FN_5O_4$ ($M+H$)⁺ m/z = 438.2; found 438.2.

Step 3: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (peak 1)

To a mixture of 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (peak 1) (20 mg, 0.045 mmol) in DMF (0.5 mL) was added HATU (22 mg, 0.06 mmol), bis(methyl-d₃)amine HCl salt (5 mg, 0.06 mmol), and DIEA (20 μ L, 0.12 mmol).

After stirring for 1 h, the reaction was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{24}H_{20}D_6FN_6O_3$ ($M+H$)⁺ m/z = 471.2; found 471.2.

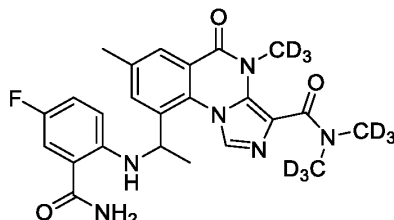
Example 3. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (peak 2)



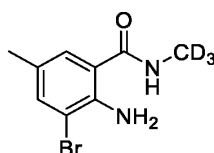
The titled compound was prepared using similar procedures as described for *Example 2* with tert-butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (*Example 2*, Step 1, peak 2) replacing tert-butyl 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (peak 1) in step 2. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were

collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{24}H_{20}D_6FN_6O_3$ ($M+H$)⁺ m/z = 471.2; found 471.2.

Example 4. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

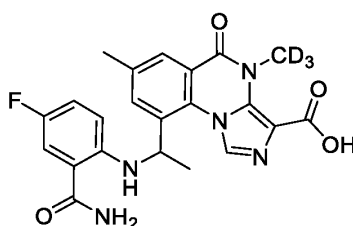


Step 1: 2-amino-3-bromo-5-methyl-N-(methyl-d3)benzamide



To a mixture of 2-amino-3-bromo-5-methylbenzoic acid (6.90 g, 30 mmol) in DMF (80 mL) was added HATU (14.83 g, 39 mmol), methan-d₃-amine HCl salt (2.33 g, 33 mmol), and DIEA (20.96 mL, 120 mmol) at 0 °C. After stirring at rt for 3 h, the mixture was poured in 1000 mL ice water. The resulting solid was collected to afford a light brown solid, which was washed with water and dried under vacuum to afford the desired product as a light brown solid. LCMS calculated for $C_9H_9D_3BrN_2O$ ($M+H$)⁺ m/z = 246.0; found 246.0.

Step 2: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-3-bromo-5-methyl-N-(methyl-d₃)benzamide replacing 2-

amino-3-bromo-N,5-dimethylbenzamide in step 4. LCMS calculated for $C_{22}H_{18}D_3FN_5O_4$ (M+H)⁺ m/z = 441.2; found 441.2.

Step 3: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

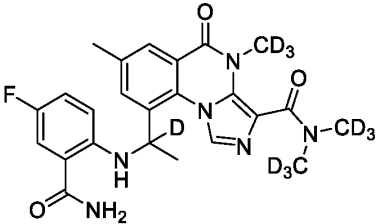
To a mixture of 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (20 mg, 0.045 mmol) in DMF (0.5 mL) was added HATU (22 mg, 0.06 mmol), bis(methyl-d₃)amine HCl salt (10 mg, 0.25 mmol), and DIEA (100 uL, 0.6 mmol). After stirring for 1 h, the reaction was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{24}H_{17}D_9FN_6O_3$ (M+H)⁺ m/z = 474.3; found 474.3.

Examples 5-7.

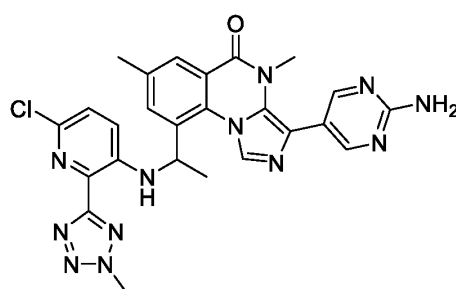
The following compounds in Table 1 were prepared similarly according to the procedures described for Example 1 using appropriate intermediates.

Table 1.

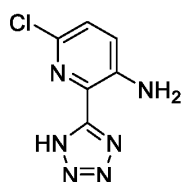
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
5	9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		468.2
6	9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-1-d-4,7-dimethyl-N,N-bis(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		472.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
7	9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		475.3

Example 8. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

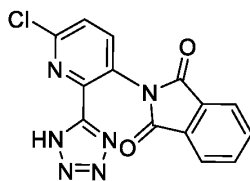


5 *Step 1: 6-chloro-2-(1H-tetrazol-5-yl)pyridin-3-amine*



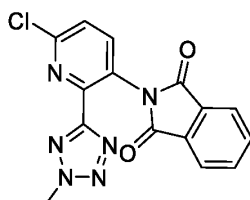
To a solution of 3-amino-6-chloro-pyridine-2-carbonitrile (1.54 g, 10.00 mmol) in 20 mL DMF was added sodium azide (1.3 g, 20.00 mmol) and ammonia hydrochloride (1.7 g, 20.00 mmol) in one portion. After stirring at 120 °C for 12h, the solvent was removed under vacuum. The residue was dissolved in water and adjusted the pH to 2 by adding 10 % HCl. The precipitate was collected by filtration to give product as white solid (1.8 g, 92%). LCMS calculated for C₆H₆ClN₆ (M+H)⁺ m/z = 197.0; found 197.0.

15 *Step 2: 2-(6-chloro-2-(1H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione*



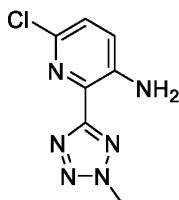
To a solution of 6-chloro-2-(1H-tetrazol-5-yl)pyridin-3-amine (1.8 g, 9.16 mmol) in 10 mL acetic acid was added isobenzofuran-1,3-dione (3.4 g, 22.89 mmol) at r.t. After stirring at 120 °C overnight, the solvent was removed under vacuum to provide the desired product as a yellow solid (2.9 g, 97%). LCMS calculated for $C_{14}H_8ClN_6O_2$ (M+H)⁺ m/z = 327.0; found 327.0.

Step 3: 2-(6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione



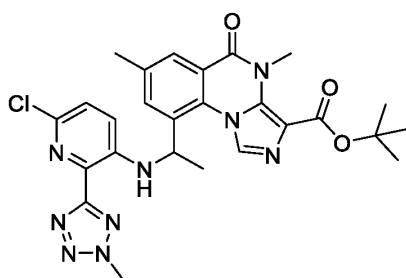
To a solution of 2-[6-chloro-2-(1H-tetrazol-5-yl)-3-pyridyl]isoindoline-1,3-dione (3.00 g, 9.18 mmol) in 10 mL DMF was added iodomethane (0.86 mL, 1.96 g, 13.77 mmol) and potassium carbonate (3.81 g, 27.55 mmol). The reaction mixture was stirred at r.t. for 2h, then diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography, eluted with hexanes and ethyl acetate to provide the desired product as a yellow solid (540 mg, 17%) and another regioisomer as a yellow solid (570 mg, 18%). LCMS calculated for $C_{15}H_{10}ClN_6O_2$ (M+H)⁺ m/z = 341.1; found 341.1.

Step 4: 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine



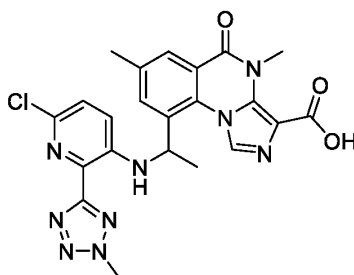
The mixture of 2-(6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione (540 mg, 1.58 mmol) in 10 mL of hydrazine monohydrate was stirred at 45 °C for 2 h, then cooled to room temperature and the resulting precipitate was collected by filtration and washed with water to give the product as white solid (330 mg, 100 %). LCMS calculated for $C_7H_8ClN_6$ ($M+H$)⁺ m/z = 211.0; found 211.0.

Step 5: tert-butyl 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



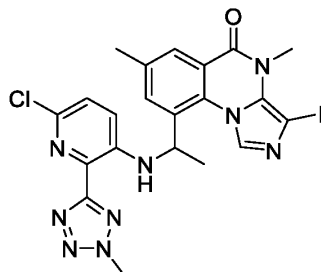
To the solution of tert-butyl 9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (Example 1, step 9) (3.2 g, 7.6 mmol) in DMF (70 mL) was added 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine (1.8 g, 8.5 mmol). The mixture was heated to 70 °C for 3 h. Upon cooling to rt, the mixture was diluted with water and extracted with ethyl acetate (3X). The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to provide the desired product as a light yellow solid (1.25 g, 30%). LCMS calculated for $C_{26}H_{29}ClN_9O_3$ ($M+H$)⁺ m/z = 550.2; found 550.2.

Step 6: 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



tert-Butyl 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (1.25 g, 2.27 mmol) was dissolved in TFA (10 mL). The mixture was stirred for 3 h at rt. After completion, TFA was removed under vacuum. EtOAc (20 mL) and hexanes (20 mL) were added to the reaction residue while stirring. After stirring for 20 min, the resulting solid was collected to afford a white solid, which was washed with hexanes/EtOAc (1:1). The solid was dried under vacuum to provide the pure product (1.0 g, 90%). LCMS calculated for $C_{22}H_{21}ClN_9O_3$ ($M+H$)⁺ m/z = 494.1; found 494.2.

Step 7: 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



To a mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (1.0 g, 1.05 mmol) in DMF (10 mL) under nitrogen was added $NaHCO_3$ (336 mg, 4 mmol) at 0 °C, after stirring for 5 min, NIS (234 mg, 1.05 mmol) was added in one portion. The resulting mixture was warmed to rt and stirred for 2h under vacuum. After completion, the reaction mixture was quenched with sat. $Na_2S_2O_3$ and diluted with water. The resulting solid was collected as a brown solid by filtration which was purified by silica gel column chromatography, eluted with DCM

and EtOAc to provide the desired product as a white solid (470 mg, 78%). LCMS calculated for $C_{21}H_{20}ClN_9O$ ($M+H$)⁺ m/z = 576.1; found 576.1.

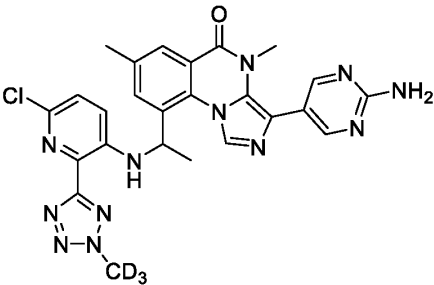
Step 8: 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

The mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (47 mg, 0.08 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (27 mg, 0.12 mmol), K_3PO_4 (52 mg, 0.24 mmol) and $Pd(PPh_3)_4$ (19 mg, 0.02 mmol) in dioxane (3.0 mL) and water (0.6 mL) was heated at 80 °C for 8h under nitrogen atmosphere. The solvent was removed under vacuum and the residue was purified by silica gel column chromatography (0 – 95% EA in DCM, then 0-20% MeOH in DCM) to provide the crude product. The product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a light yellow solid. LCMS calculated for $C_{25}H_{24}ClN_{12}O$ ($M+H$)⁺ m/z = 543.2; found 543.2.

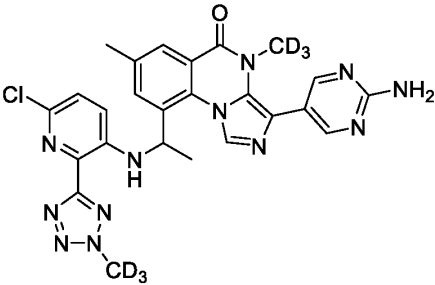
Examples 9-14.

The following compounds in Table 2 were prepared similarly according to the procedures described for Example 8 using appropriate intermediates.

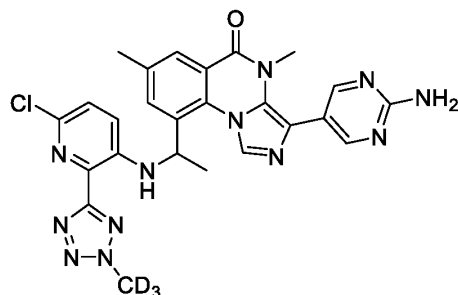
Table 2.

Example #	Chemical name	Structure	LCMS m/z ($M+H$) ⁺
9	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		546.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
10	3-(2-aminopyrimidin-5-yl)-9-(1-(((6-chloro-2-(2-methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		547.2
11	3-(2-aminopyrimidin-5-yl)-9-(1-(((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		544.2
12	3-(2-aminopyrimidin-5-yl)-9-(1-(((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		547.2
13	3-(2-aminopyrimidin-5-yl)-9-(1-(((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		546.2

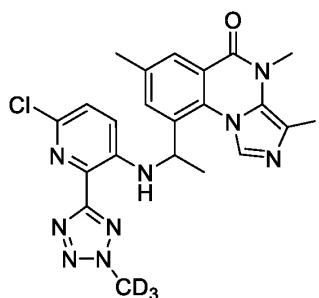
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
14	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		549.2

Example 15. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (peak 1)



5

Step 1: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



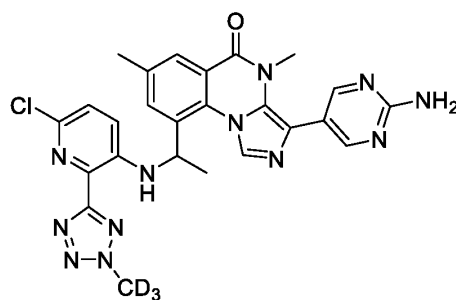
The titled compound was prepared using similar procedures as described for
 10 *Example 8* with 6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-amine (Intermediate 11) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in Step 5. LCMS calculated for C₂₁H₁₇D₃ClIN₉O (M+H)⁺ m/z = 579.1; found 579.1.

The racemic compound was separated by chiral HPLC to afford 2 enantiomers, the peak 1 was taken into next step.

Step 2: 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (peak 1)

The mixture of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (peak 1) (47 mg, 0.08mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (27 mg, 0.12 mmol), K₃PO₄ (52 mg, 0.24 mmol) and Pd(PPh₃)₄ (19 mg, 0.02 mmol) in dioxane (3.0 mL) and water (0.6 mL) was heated at 80 °C for 8h under nitrogen atmosphere. The solvent was removed under reduced vacuum and the residue was purified by silica gel column chromatography (0 – 95% EA in DCM, then 0-20% MeOH in DCM) to provide the crude product. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a light yellow. LCMS calculated for C₂₅H₂₁D₃ClN₁₂O (M+H)⁺ m/z = 546.2; found 546.2.

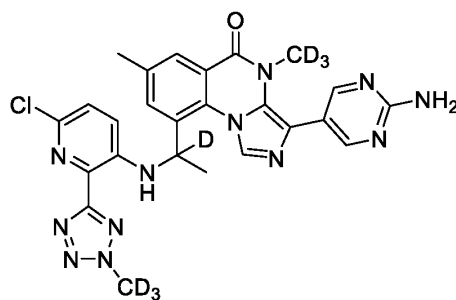
Example 16. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (peak 2)



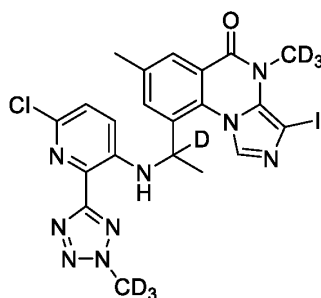
The titled compound was prepared using similar procedures as described for Example 15 with 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (Example

15, Step 1, peak 2) replacing 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (peak 1) in Step 2. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a light yellow solid. LCMS calculated for C₂₅H₂₁D₃ClN₁₂O (M+H)⁺ m/z = 546.2; found 546.2.

10 **Example 17. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one**



15 *Step 1: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-iodo-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one*



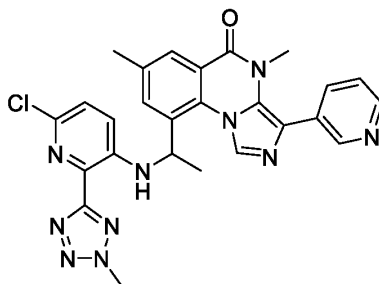
The titled compound was prepared using similar procedures as described for *Example 8* with tert-butyl 9-(1-bromoethyl-1-d)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (Intermediate 12) replacing tert-butyl 9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate and 6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-amine

(Intermediate 11) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in Step 5. LCMS calculated for $C_{21}H_{13}D_7ClIN_9O$ ($M+H$)⁺ m/z = 583.1; found 583.1.

Step 2: 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1- d)-7-methyl-4-(methyl- d_3)imidazo[1,5- a]quinazolin-5(4H)-one

The mixture of 9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1- d)-3-iodo-7-methyl-4-(methyl- d_3)imidazo[1,5- a]quinazolin-5(4H)-one (200 mg, 0.34 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (62.0 mg, 0.45 mmol), K_3PO_4 (218.5 mg, 1.03 mmol) and $Pd(PPh_3)_4$ (39.7 mg, 0.03 mmol) in dioxane (6.0 mL) and water (1.2 mL) was heated at 80 °C for 8h under nitrogen atmosphere. The solvent was removed under vacuum and the residue was purified by silica gel column chromatography (0 – 95% EA in DCM, then 0-20% MeOH in DCM) to provide the crude product. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a light yellow. LCMS calculated for $C_{25}H_{17}D_7ClIN_{12}O$ ($M+H$)⁺ m/z = 550.2; found 550.2.

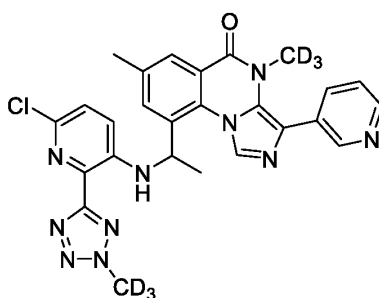
Example 18. 9-(1-((6-Chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5- a]quinazolin-5(4H)-one



The mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5- a]quinazolin-5(4H)-one (Example 8, Step 7) (10 mg, 0.02mmol), pyridin-3-ylboronic acid (5 mg, 0.04 moml), K_3PO_4 (10 mg, 0.05 mmol) and $Pd(PPh_3)_4$ (2 mg, 0.002 mmol) in dioxane (0.5 mL) and water

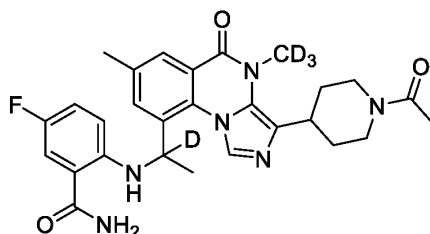
(0.1 mL) was heated at 100 °C for 20 min under nitrogen atmosphere. After cooling to room temperature, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₄ClN₁₀O (M+H)⁺ m/z = 527.2; found 527.2.

Example 19. 9-(1-((6-Chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one

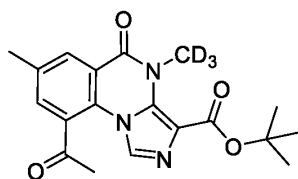


The titled compound was prepared using similar procedures as described for *Example 18*. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₁₈D₆ClN₁₀O (M+H)⁺ m/z = 533.2; found 533.2.

Example 20. 2-((1-(3-(1-Acetylpiperidin-4-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide

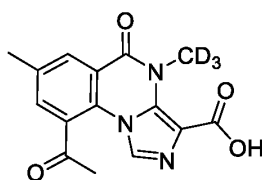


Step 1: tert-butyl 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



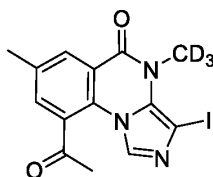
The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-3-bromo-5-methyl-N-(methyl-d₃)benzamide (*Example 4*, Step 1) replacing 2-amino-3-bromo-N,5-dimethylbenzamide in Step 4. LCMS
 5 calculated for C₁₉H₁₉D₃N₃O₄ (M+H)⁺ m/z = 359.2; found 359.2.

Step 2: 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



10 tert-Butyl 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (2.0 g, 5.5 mmol) was dissolved in TFA (20 mL). The mixture was stirred for 3 h at rt. After completion, TFA was removed under vacuum. EtOAc (50 mL) and hexanes (50 mL) were added to the reaction residue while stirring. After stirring for 20 min, the resulting solid was collected to afford a white
 15 solid, which was washed with hexanes/EtOAc (1:1). The solid was dried under vacuum to provide the pure product (1.5 g, 90%). LCMS calculated for C₁₅H₁₁D₃N₃O₄ (M+H)⁺ m/z = 303.1; found 303.1.

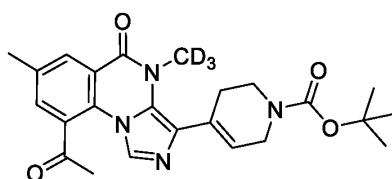
Step 3: 9-acetyl-3-iodo-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



20 To a mixture of 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (1.5 g, 4.9 mmol) in DMF (20 mL) under nitrogen was added NaHCO₃ (1.68 g, 20 mmol) at 0 °C, after stirring for 5

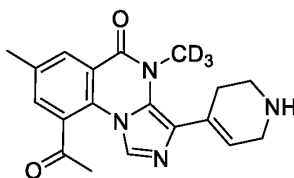
min, NIS (1.1 g, 5 mmol) was added in one portion. The resulting mixture was warmed to rt and stirred for 2h under vacuum. After completion, the reaction mixture was quenched with sat. Na₂S₂O₃ and diluted with water. The crude product was collected as a brown solid by filtration which was purified by silica gel column chromatography, eluted with DCM and EtOAc to provide the desired product as a white solid (1.5 g, 84%). LCMS calculated for C₁₄H₁₀D₃IN₃O₂ (M+H)⁺ m/z = 385.0; found 385.0.

Step 4: tert-butyl 4-(9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate



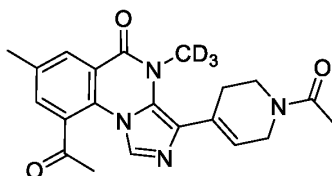
The mixture of 9-acetyl-3-iodo-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (1.5 g, 3.91 mmol), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (1.29 g, 4.2 mmol), K₃PO₄ (1.5 g, 7 mmol) and Xphos-PdG2 (306 mg, 0.39 mmol) in dioxane (50 mL) and water (5 mL) was heated at 100 °C for 1h under nitrogen atmosphere. The mixture was diluted with water and extracted with ethyl acetate (3X). The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to provide the desired product as a light yellow solid (1.2 g, 70%). LCMS calculated for C₂₄H₂₆D₃N₄O₄ (M+H)⁺ m/z = 440.2; found 440.2.

Step 5: 9-acetyl-7-methyl-4-(methyl-d₃)-3-(1,2,3,6-tetrahydropyridin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one



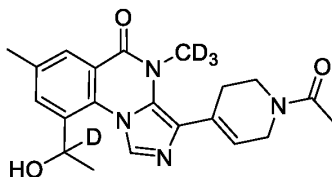
tert-Butyl 4-(9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate (1.2 g, 2.7 mmol) was dissolved in TFA (10 mL). The mixture was stirred for 3 h at rt. After completion, TFA was removed under vacuum. The residue was quenched with sat. NaHCO₃, the mixture was extracted with DCM/IPA (3:1). The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification. LCMS calculated for C₁₉H₁₈D₃N₄O₂ (M+H)⁺ m/z = 340.2; found 340.2.

Step 6: 9-acetyl-3-(1-acetyl-1,2,3,6-tetrahydropyridin-4-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



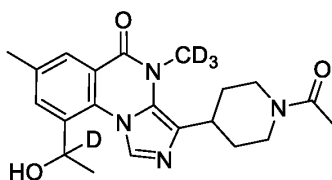
9-Acetyl-7-methyl-4-(methyl-d₃)-3-(1,2,3,6-tetrahydropyridin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one (920 mg, 2.4 mmol) was dissolved in DCM (50 mL), then acetyl chloride (218 mg, 2.8 mmol) was added at 0 °C followed by adding DIEA (619 mg, 4.8 mmol). The resulting mixture was stirred at the same temperature for 20 min before diluted with sat. NaHCO₃. The mixture was diluted with water and extracted with DCM. The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification. LCMS calculated for C₂₁H₂₀D₃N₄O₃ (M+H)⁺ m/z = 382.2; found 382.2.

Step 7: 3-(1-acetyl-1,2,3,6-tetrahydropyridin-4-yl)-9-(1-hydroxyethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



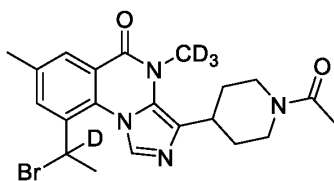
9-Acetyl-3-(1-acetyl-1,2,3,6-tetrahydropyridin-4-yl)-7-methyl-4-(methyl-
d₃)imidazo[1,5-a]quinazolin-5(4H)-one (910 mg, 2.34 mmol) was dissolved in MeOH
(30 mL) and DCM (30 mL) then NaBD₄ (107 mg, 2.5 mmol) was added at 0 °C in
three portions under nitrogen. The resulting mixture was stirred at same temperature
for 10 min before quenched with sat. NH₄Cl. The mixture was diluted with water and
extracted with DCM. The combined organics were washed with sat. NaCl, and dried
with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure.
The residue was purified by silica gel column chromatography, eluted with DCM and
MeOH (0 to 4%) to provide the desired product as a light brown solid (781 mg 87%).
LCMS calculated for C₂₁H₂₁D₄N₄O₃ (M+H)⁺ m/z = 385.2; found 385.3.

*Step 8: 3-(1-acetylpiperidin-4-yl)-9-(1-hydroxyethyl-1-d)-7-methyl-4-(methyl-
d₃)imidazo[1,5-a]quinazolin-5(4H)-one*



3-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)-9-(1-hydroxyethyl-1-d)-7-methyl-
4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (781 mg, 2.03 mmol), Pd/C (212
mg, 10 wt%, 0.2 mmol), and ammonium formate (1.2 g, 20 mmol) were dissolved in
MeOH (30 mL) and 0.5 mL of AcOH. The reaction vial was purged with nitrogen gas
and the mixture was stirred at 60 °C overnight. After completion, the reaction mixture
was filtrated, and the solvent was removed under reduced pressure. The residue was
purified by silica gel column chromatography, eluted with DCM and MeOH (0 to 8%)
to provide the desired product as a pale solid (631 mg 81%). LCMS calculated for
C₂₁H₂₃D₄N₄O₃ (M+H)⁺ m/z = 387.2; found 387.3.

*Step 9: 3-(1-acetylpiperidin-4-yl)-9-(1-bromoethyl-1-d)-7-methyl-4-(methyl-
d₃)imidazo[1,5-a]quinazolin-5(4H)-one*

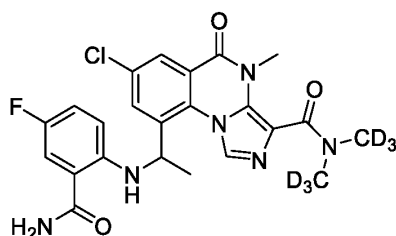


To a mixture of 3-(1-acetylpiperidin-4-yl)-9-(1-hydroxyethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (631 mg, 1.63 mmol) in DCM (100 mL) was added PBr₃ (0.33 mL, 3.2 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for 2 h. The mixture was then quenched with sat. NaHCO₃ and extracted with DCM (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification.

Step 10: 2-((1-(3-(1-acetylpiperidin-4-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide

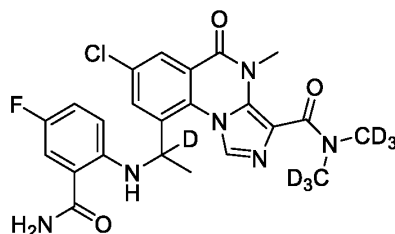
To the solution of 3-(1-acetylpiperidin-4-yl)-9-(1-bromoethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (20 mg, 0.04 mmol) in DMF (0.5 mL) was added 2-amino-5-fluorobenzamide (20 mg, 0.13 mmol). The mixture was heated to 80 °C for 2 h. Upon cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₈H₂₈D₄FN₆O₃ (M+H)⁺ m/z = 523.3; found 523.3.

Example 21. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



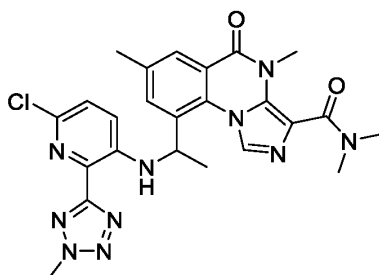
The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-5-chlorobenzoic acid replacing 2-amino-5-methylbenzoic acid in step 1, and bis(methyl-d₃)amine HCl salt replacing dimethylamine in step 12. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₃H₁₇D₆ClFN₆O₃ (M+H)⁺ m/z = 491.2; found 491.2.

Example 22. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-5-chlorobenzoic acid replacing 2-amino-5-methylbenzoic acid in step 1, NaBD₄ replacing NaBH₄ in step 8, and bis(methyl-d₃)amine HCl salt replacing dimethylamine in step 12. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₃H₁₆D₇ClFN₆O₃ (M+H)⁺ m/z = 492.2; found 492.2.

Example 23. 9-(1-((6-Chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



To a mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (Example 8, step 6) (20 mg, 0.04 mmol) in DMF (0.5 mL) was added
 5 HATU (22 mg, 0.06 mmol), dimethylamine (30 uL, 2M THF solution), and DIEA (10 uL, 0.06 mmol). After stirring for 1 h, the reaction mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of
 10 the desired product as a white solid. LCMS calculated for C₂₄H₂₆ClN₁₀O₂ (M+H)⁺ m/z = 521.2; found 521.2.

Examples 24-27.

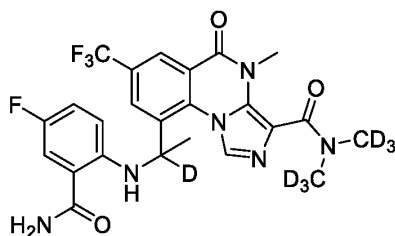
The following compounds in Table 3 were prepared similarly according to the
 15 procedures described for Example 23 using appropriate intermediates.

Table 3.

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
24	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		527.2

Example #	Chemical name	Structure	LCMS m/z (M+H)⁺
25	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,N,7-trimethyl-4-(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		524.2
26	9-(1-(((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl))-N,N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		524.2
27	9-(1-(((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-1-d)-7-methyl-N,N,4-tris(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		534.3

Example 28. 9-(1-((2-Carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4-methyl-N-bis(methyl-d₃)-5-oxo-7-(trifluoromethyl)-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



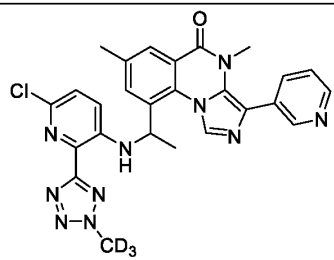
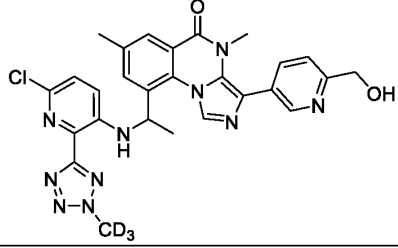
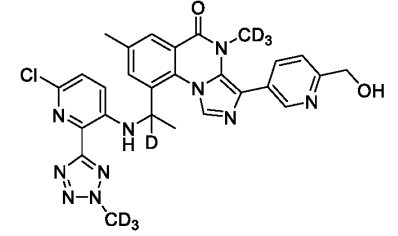
The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-5-(trifluoromethyl)benzoic acid replacing 2-amino-5-methylbenzoic acid in step 1, NaBD₄ replacing NaBH₄ in step 8, and bis(methyl-d₃)amine HCl salt replacing dimethylamine in step 12. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₄H₁₆D₇F₄N₆O₃ (M+H)⁺ m/z = 526.2; found 526.2.

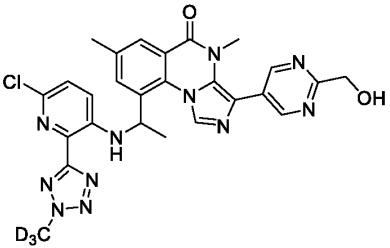
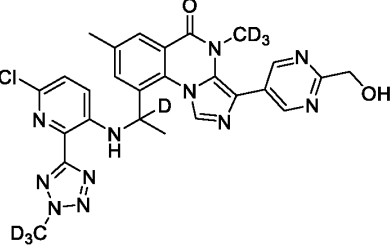
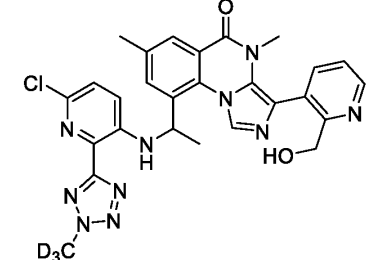
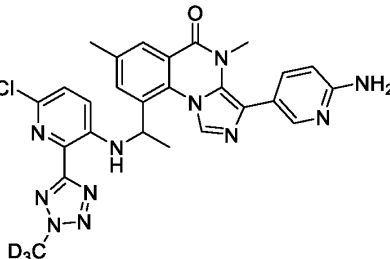
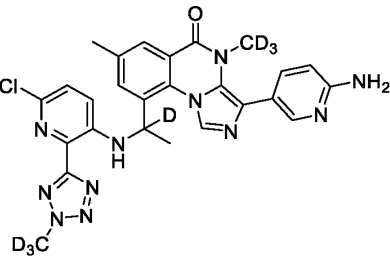
10

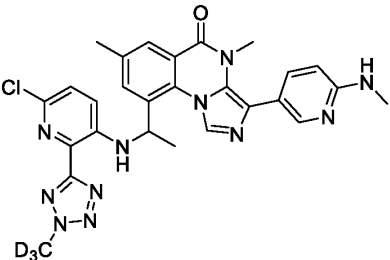
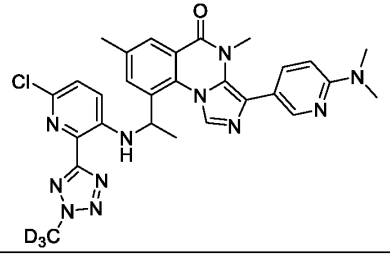
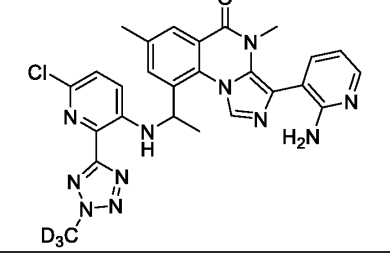
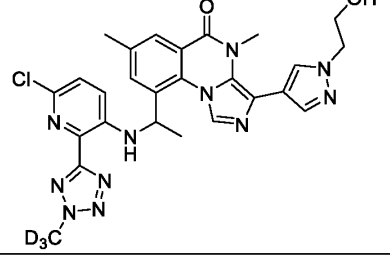
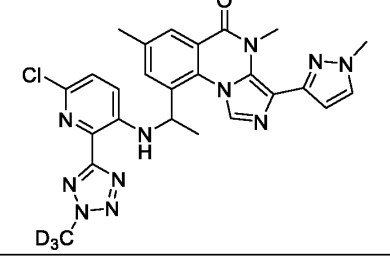
Examples 29-46.

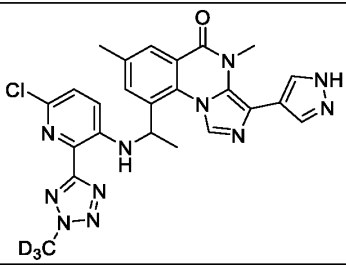
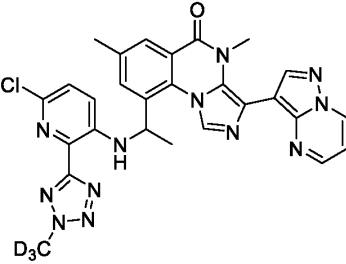
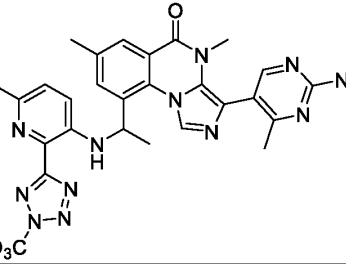
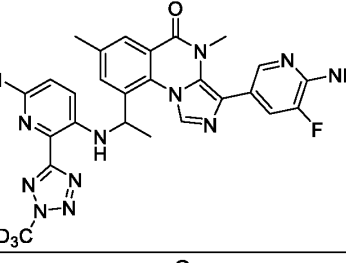
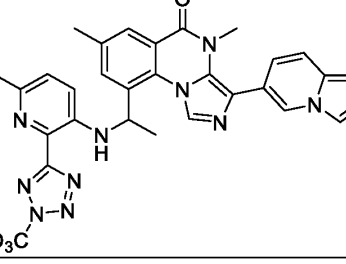
The following compounds in Table 4 were prepared similarly according to the procedures described for Example 8 using appropriate intermediates.

Table 4.

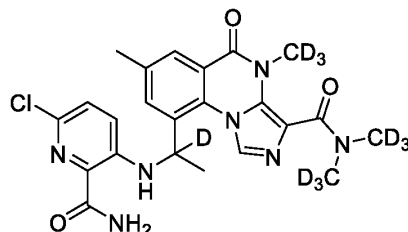
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
29	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one		530.2
30	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		560.2
31	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(6-(hydroxymethyl)pyridin-3-yl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		564.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
32	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		561.2
33	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one		565.2
34	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		560.2
35	3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		545.2
36	3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one		549.2

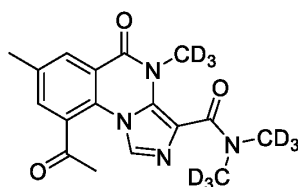
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
37	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(6-(methylamino)pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one		559.2
38	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(dimethylamino)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		573.2
39	3-(2-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		545.2
40	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyethyl)-1H-pyrazol-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		563.2
41	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one		533.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
42	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one		519.2
43	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyrimidin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one		570.2
44	3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		560.2
45	3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		563.2
46	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(imidazo[1,5-a]pyridin-6-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		569.2

Example 47. 9-(1-((2-Carbamoyl-6-chloropyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

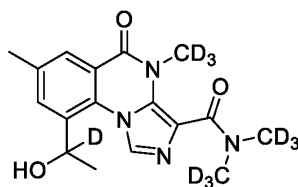


5 *Step 1: 9-acetyl-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide*



To a mixture of 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (Example 20, step 2) (1.4 g, 4.63 mmol) in DMF (10 mL) was added HATU (1900 mg, 5.0 mmol), bis(methyl-d₃)amine HCl salt (435 mg, 5.0 mmol), and DIEA (1.8 mL, 10 mmol). After stirring for 1 h, the reaction mixture was diluted with ice water and the resulting solid was collected to afford the desired product as a white solid, which was used in the next step without further purification LCMS calculated for C₁₇H₁₀D₉N₄O₃ (M+H)⁺ m/z = 336.2; found 336.2.

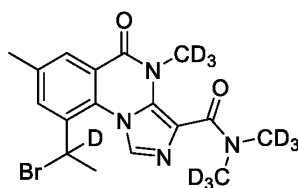
Step 2: 9-(1-hydroxyethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



20 9-Acetyl-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (1.2 g, 3.5 mmol) was dissolved in MeOH (40 mL) and DCM (40 mL) then NaBD₄ (160 mg, 4 mmol) was added at 0 °C under nitrogen. The

resulting mixture was stirred at same temperature for 10 min before quenched with 0.3 mL of sat. NH_4Cl . The mixture was dried over MgSO_4 , filtered, and concentrated under reduced pressure. The resulting solid was collected to afford the desired product as a beige solid, which was used in the next step without further purification. LCMS calculated for $\text{C}_{17}\text{H}_{11}\text{D}_{10}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$ $m/z = 339.2$; found 339.2.

Step 3: 9-(1-bromoethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

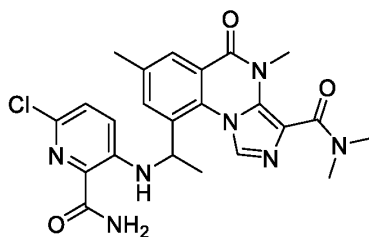


To a mixture of 9-(1-hydroxyethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (1.0 g, 2.96 mmol) in DCM (200 mL) was added PBr_3 (0.33 mL, 3.2 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for 2 h. The mixture was then quenched with sat. NaHCO_3 and extracted with DCM (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification.

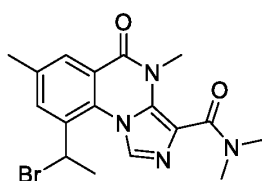
Step 4: 9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

To the solution of 9-(1-bromoethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (20 mg, 0.05 mmol) in DMF (0.3 mL) was added 3-amino-6-chloropyridin-2-ylamine (17 mg, 0.1 mmol). The mixture was heated to 80 °C for 2 h. Upon cooling to room temperature, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μm ; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $\text{C}_{23}\text{H}_{15}\text{D}_{10}\text{ClN}_7\text{O}_3$ ($\text{M}+\text{H}$) $^+$ $m/z = 492.2$; found 492.2.

Example 48. 9-(1-((2-Carbamoyl-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



Step 1: 9-(1-bromoethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



The titled compound was prepared using similar procedures as described for *Example 47* with 9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid replacing 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid, dimethyl amine replacing bis(methyl-d₃)amine in step 1, and NaBH₄ replacing NaBD₄ in step 2. LCMS calculated for C₁₇H₂₀BrN₄O₂ (M+H)⁺ m/z = 391.1; found 391.1.

Step 2: 9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

To the solution of 9-(1-bromoethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (20 mg, 0.05 mmol) in DMF (0.3 mL) was added 3-amino-6-chloropicolinamide (17 mg, 0.1 mmol). The mixture was heated to 80 °C for 2 h. Upon cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₃H₂₅ClN₇O₃ (M+H)⁺ m/z = 482.2; found 482.2.

Examples 49-59.

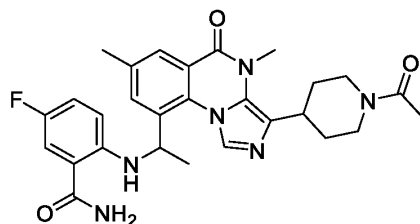
The following compounds in Table 5 were prepared similarly according to the procedures described for Example 47 or Example 48 using appropriate intermediates.

Table 5.

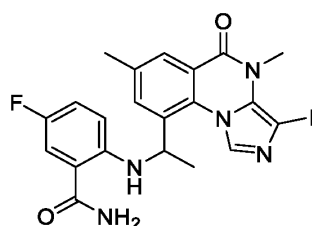
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
49	9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		491.2
50	9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		555.3
51	methyl (3-((1-(3-(bis(methyl-d3)carbamoyl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-6-chloropyridin-2-yl)carbamate		522.2
52	9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		481.2
53	9-(1-((4-fluoro-2-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		504.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
54	9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		545.2
55	9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		503.2
56	methyl (6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)carbamate		512.2
57	9-(1-((4-fluoro-2-sulfamoylphenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		501.2
58	9-(1-((5-chloroquinolin-8-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		489.2
59	N,N,4,7-tetramethyl-9-(1-((6-methyl-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		501.2

Example 60. 2-((1-(3-(1-Acetylpiperidin-4-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide

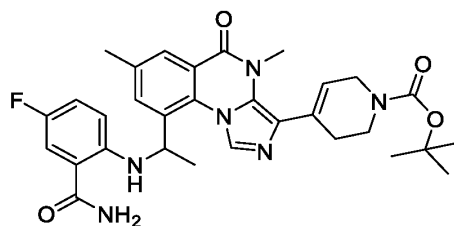


Step 1: 5-fluoro-2-((1-(3-(1-iodo-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)benzamide



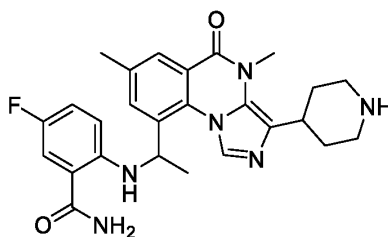
To a mixture of 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid (Example 1, step 11) (1.00 g, 2.29 mmol) in DMF (10 mL) under nitrogen was added NaHCO₃ (768 mg, 9.14 mmol) at 0 °C, after stirring for 5 min, 1-iodopyrrolidine-2,5-dione (617 mg, 2.74 mmol) was added in one portion. The resulting mixture was warmed to rt and stirred for 2 h. After completion, the reaction was quenched with aq. sat. Na₂S₂O₃ and diluted with water. The mixture was then extracted with EtOAc. The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with hexanes and EtOAc (0 to 30%) to provide the desired product as a white solid. LCMS calculated for C₂₁H₂₀FIN₅O₂ (M+H)⁺ m/z = 520.1; found 520.1.

Step 2: tert-butyl 4-(9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate



A solution of 5-fluoro-2-((1-(3-iodo-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)benzamide (15 mg, 0.03 mmol), K_3PO_4 (18 mg, 0.09 mmol), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (18 mg, 0.06 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (5 mg, 0.01 mmol) in 1 mL dioxane/ H_2O (5:1) was bubbled with N_2 for 1 min. The resulting reaction mixture was stirred at 90 °C for 30 min. The reaction mixture was diluted with 1 mL water and extracted with EtOAc. The organic layer was concentrated to dryness. The residue was purified by silica gel column chromatography to provide the desired product. LCMS calculated for $C_{31}H_{36}FN_6O_4$ ($M+H$)⁺ m/z = 575.3; found 575.2.

Step 3: 2-((1-(4,7-dimethyl-5-oxo-3-(piperidin-4-yl)-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide



To a solution of *tert*-butyl 4-(9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (5.0 mg, 0.01 mmol) and palladium on activated carbon 10% (1.1 mg, 0.001 mmol) in 1 mL MeOH was added ammonium acetate (2.4 mg, 0.03 mmol) and the resulting mixture was stirred at 60 °C for 12h. The reaction mixture was filtered through celite, and the filtrate was concentrated to dryness. 2 mL 4M HCl in dioxane was then added to the residue and the resulting mixture was stirred at rt for 2h. The reaction mixture was concentrated under reduced

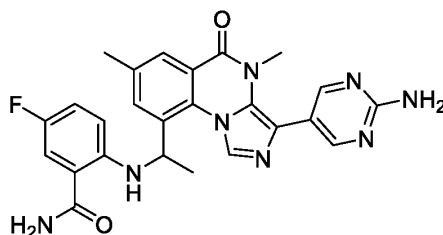
pressure. The residue was used directly in the next step without further purification.

LCMS calculated for $C_{26}H_{30}FN_6O_2$ ($M+H$)⁺ m/z = 477.2; found 477.2.

Step 4: 2-((1-(3-(1-acetylpiperidin-4-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-
a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide

To a stirred solution of 2-((1-(4,7-dimethyl-5-oxo-3-(piperidin-4-yl)-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide (10.0 mg, 0.02 mmol) in DCM was added *N,N*-diethylethanamine (4.3 mg, 0.04 mmol) and acetyl chloride (2.0 mg, 0.03 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 10 min and diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{28}H_{32}FN_6O_3$ ($M+H$)⁺ m/z = 519.2; found 519.2.

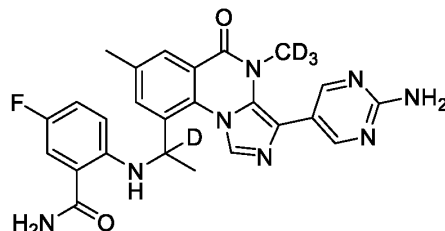
Example 61. 2-((1-(3-(2-Aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide



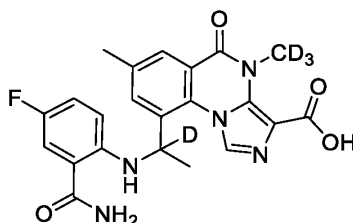
The mixture of 5-fluoro-2-((1-(3-iodo-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)benzamide (Example 60, step 1) (18.0 mg, 0.03 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (15.3 mg, 0.07 mmol), K_3PO_4 (22.1 mg, 0.10 mmol) and XPhos Pd G2 (5.5 mg, 0.01 mmol) in dioxane (0.5 mL) and water (0.1 mL) was heated at 90 °C for 20 min under nitrogen atmosphere. After cooled to room temperature, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the

TFA salt of the desired product as a white solid. LCMS calculated for $C_{25}H_{24}FN_8O_2$
 $(M+H)^+$ $m/z = 487.2$; found 487.2.

Example 62. 2-((1-(3-(2-Aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-
dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide

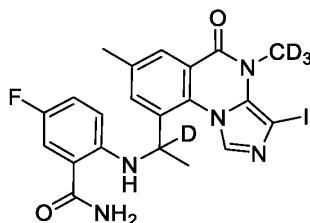


Step 1: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



The titled compound was prepared using similar procedures as described
Example 1 with 2-amino-3-bromo-5-methyl-N-(methyl-d₃)benzamide (Example 4,
 step 1) replacing 2-amino-3-bromo-N,5-dimethylbenzamide in step 4, and NaBD₄
 replacing NaBH₄ in step 8. After completion, the resulting solid was collected to
 afford the desired product as a light grey solid. LCMS calculated for $C_{22}H_{17}D_4FN_5O_4$
 $(M+H)^+$ $m/z = 442.2$; found 442.2.

Step 2: 5-fluoro-2-((1-(3-iodo-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-
a]quinazolin-9-yl)ethyl-1-d)amino)benzamide

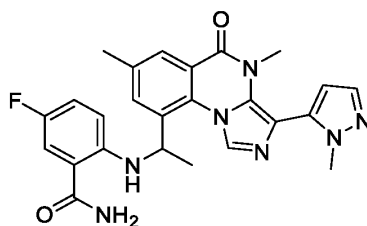


The titled compound was prepared using similar procedures as described for *Example 60* with 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid replacing 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid in step 1. The residue was purified by silica gel column chromatography, eluted with hexanes and EtOAc (0 to 30%) to provide the desired product as a white solid. LCMS calculated for C₂₁H₁₆D₄FN₅O₂ (M+H)⁺ m/z = 524.1; found 524.1.

Step 3: 2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide

The mixture of 5-fluoro-2-((1-(3-iodo-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)benzamide (18.0 mg, 0.03 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (15.3 mg, 0.07 mmol), K₃PO₄ (22.1 mg, 0.10 mmol) and XPhos Pd G2 (5.5 mg, 0.01 mmol) in dioxane (0.5 mL) and water (0.1 mL) was heated at 90 °C for 20 min under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₅H₂₀D₄FN₈O₂ (M+H)⁺ m/z = 491.2; found 491.2.

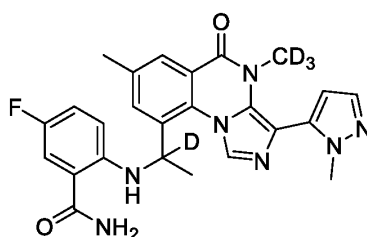
Example 63. 2-((1-(4,7-Dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide



The titled compound was prepared using similar procedures as described for *Example 61* with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole

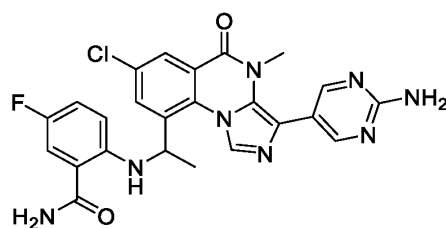
replacing 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine. The mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₅H₂₅FN₇O₂ (M+H)⁺ m/z = 474.2; found 474.2.

Example 64. 5-Fluoro-2-((1-(7-methyl-4-(methyl-d3)-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)benzamide

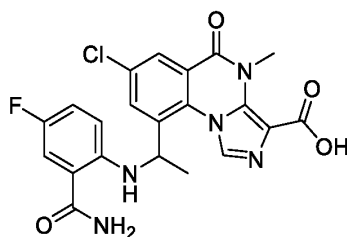


The titled compound was prepared using similar procedures as described for *Example 62* with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrazole replacing 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine in step 3. The mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₅H₂₁D₄FN₇O₂ (M+H)⁺ m/z = 478.2; found 478.2.

Example 65. 2-((1-(3-(2-Aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide



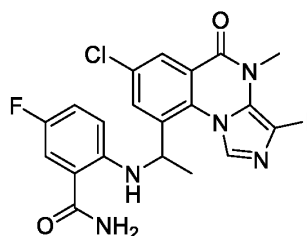
Step 1: 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



The titled compound was prepared using similar procedures as described for *Example 1* with 2-amino-5-chlorobenzamide replacing 2-amino-5-methylbenzamide in step 1. LCMS calculated for $C_{21}H_{18}ClFN_5O_4$ ($M+H$)⁺ m/z = 458.1; found 458.1.

5

Step 2: 2-((1-(7-chloro-3-iodo-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide



The titled compound was prepared using similar procedures as described for *Example 60* with 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid replacing 9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid in step 1. LCMS calculated for $C_{20}H_{17}ClFIN_5O_2$ ($M+H$)⁺ m/z = 540.0; found 540.1.

15

Step 3: 2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide

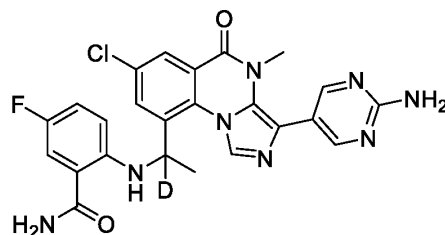
The mixture of 2-((1-(7-chloro-3-iodo-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide (20.0 mg, 0.03 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (15 mg, 0.07 mmol), K_3PO_4 (22 mg, 0.10 mmol) and XPhos Pd G2 (4 mg, 0.01 mmol) in dioxane (0.5 mL) and water (0.1 mL) was heated at 80 °C for 20 min under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A:

20

water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{24}H_{21}ClFN_8O_2$ ($M+H$)⁺ m/z = 507.1; found 507.2.

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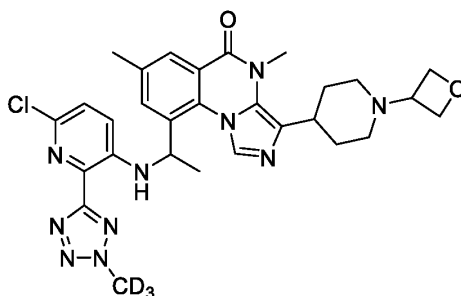
Example 66. 2-((1-(3-(2-Aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide



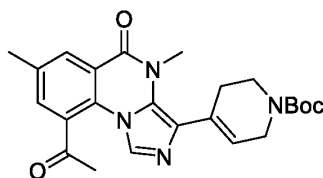
The titled compound was prepared using similar procedures as described for
 10 *Example 65*. LCMS calculated for $C_{24}H_{20}DClFN_8O_2$ ($M+H$)⁺ m/z = 508.1; found 508.2.

Example 67. 9-(1-((6-Chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(oxetan-3-yl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one

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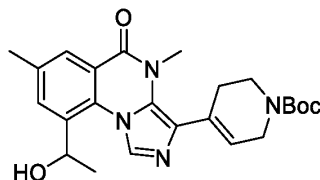


Step 1: tert-Butyl 4-(9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate



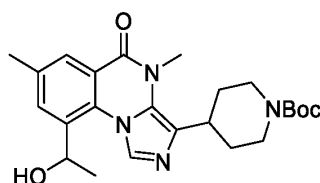
The titled compound was prepared using similar procedures as described for Example 20, Step 4.

Step 2: *tert*-butyl 4-(9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-
a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate



tert-Butyl 4-(9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-
a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate (1.6 g, 3.67 mmol) was
dissolved in MeOH (30 mL) and DCM (30 mL) then NaBH₄ (208 mg, 5.50 mmol)
was added at 0 °C in three portions under nitrogen. The resulting mixture was stirred
at same temperature for 10 min before quenched with sat. NH₄Cl. The mixture was
diluted with water and extracted with DCM. The combined organics were washed
with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated
under reduced pressure. The residue was purified by silica gel column
chromatography, eluted with DCM and EA (0 to 95%) to provide the desired product
as a white solid (1.4 g, 87%). LCMS calculated for C₂₄H₃₁N₄O₄ (M+H)⁺ m/z = 439.2;
found 439.2.

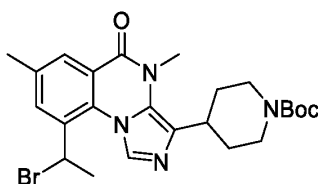
Step 3: *tert*-butyl 4-(9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-
a]quinazolin-3-yl)piperidine-1-carboxylate



The mixture of *tert*-butyl 4-(9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-
dihydroimidazo[1,5-a]quinazolin-3-yl)-3,6-dihydropyridine-1(2H)-carboxylate (1.4 g,
3.19 mmol), ammonia chloride (1.21 g, 19.2 mmol) and 10% palladium on carbon
(300 mg) was added into a 40 ml vial. Then methanol (15.0 mL) and acetic acid (1
mL) were added. The resulting mixture was heated at 50 °C for 16 hours under

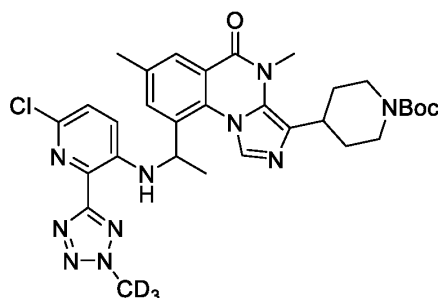
nitrogen atmosphere. The resulting mixture was filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography, eluted with DCM and EtOAc (0 to 95%) to provide the desired product as a white solid (1.15 g, 82%). LCMS calculated for $C_{24}H_{33}N_4O_4$ ($M+H$)⁺ m/z = 441.2; found 441.2.

Step 4: tert-butyl 4-(9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)piperidine-1-carboxylate



To a mixture of tert-butyl 4-(9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)piperidine-1-carboxylate (300 mg, 0.68 mmol) in THF (20 mL) was added pyridine (0.22 mL, 2.72 mmol) and PBr_3 (0.13 mL, 1.36 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for 2 h. The mixture was then quenched with sat. $NaHCO_3$ and extracted with EtOAc (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification.

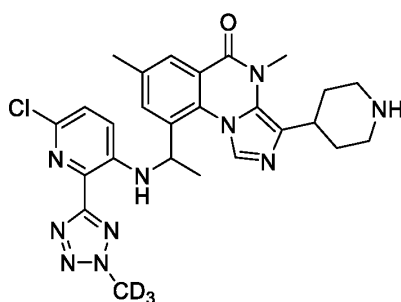
Step 5: tert-butyl 4-(9-(1-((6-chloro-2-(2-(methyl- d_3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)piperidine-1-carboxylate



To the solution of tert-butyl 4-(9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)piperidine-1-carboxylate (300 mg, 0.60 mmol)

in DMF (2 mL) was added 6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-amine (Intermediate 11) (254 mg, 1.2 mmol). The mixture was heated to 80 °C for 2 h. The mixture was diluted with water and extracted with EtOAc (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography, eluted with DCM and EtOAc (0 to 95%) to provide the desired product as a white solid (42 mg, 11%). LCMS calculated for C₃₁H₃₅D₃ClN₁₀O₃ (M+H)⁺ m/z = 636.3; found 636.3.

Step 6: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one



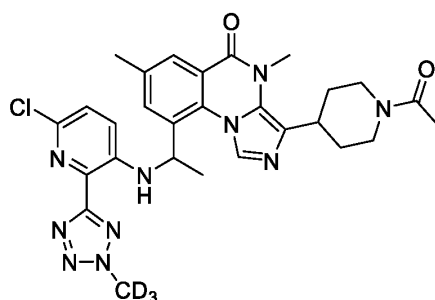
tert-Butyl 4-(9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)piperidine-1-carboxylate (42 mg, 0.066 mmol) was dissolved in 4M HCl in dioxane (2 mL). The resulting solution was stirred at room temperature for 2 hours. The solvent was removed under reduced pressure and the product used directly in the next step without further purification. LCMS calculated for C₂₆H₂₇D₃ClN₁₀O (M+H)⁺ m/z = 536.2; found 536.2.

Step 7: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(oxetan-3-yl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one

To the solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one (10 mg, 0.02 mmol) in MeOH (1 mL) and acetic acid (0.5 mL) was added oxetan-3-one (6.7 mg, 0.1 mmol). The resulting mixture was heated at 50 °C for 2 hours. Upon cooling to room temperature, NaBH₃CN (2.34 mg, 0.04 mmol) was added, and the

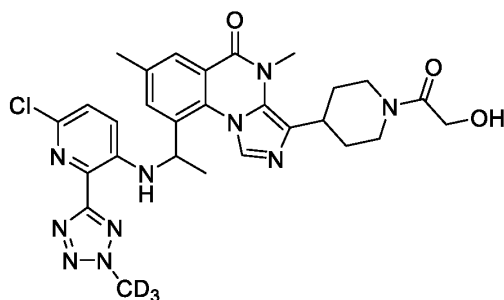
mixture was stirred for 30 min. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₉H₃₁D₃ClN₁₀O₂ (M+H)⁺ m/z = 592.3; found 592.3.

Example 68. 3-(1-Acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



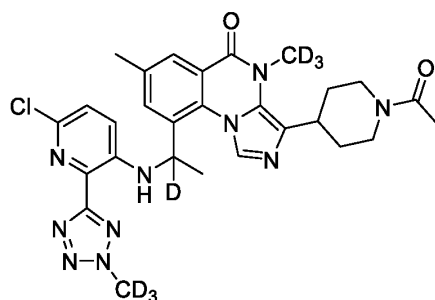
To a solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one (Example 67, step 6) (8 mg, 0.01 mmol) in DCM (1 mL) was added triethylamine (3.0 mg, 0.03 mmol) and acetyl chloride (1.8 mg, 0.02 mmol). The resulting mixture was stirred at room temperature for 30 minutes. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₈H₂₉D₃ClN₁₀O₂ (M+H)⁺ m/z = 578.3; found 578.3.

Example 69. 9-(1-((6-Chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



To a solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one (Example 67, step 6) (8 mg, 0.01 mmol) in DMF (0.5 mL) was added 2-hydroxyacetic acid (2.3 mg, 0.03 mmol), HATU (8.5 mg, 0.02 mmol) and *N,N*-diisopropylethylamine (13 uL, 0.07 mmol). The resulting mixture was stirred at room temperature for 30 minutes then diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₈H₂₉D₃ClN₁₀O₃ (M+H)⁺ m/z = 594.3; found 594.3.

Example 70. 3-(1-Acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



The titled compound was prepared using similar procedures as described for *Example 68*. The reaction mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a

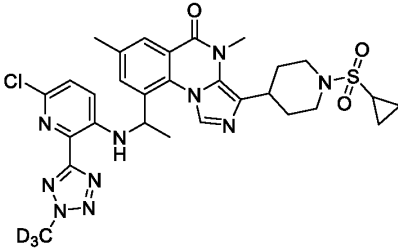
white solid. LCMS calculated for $C_{28}H_{23}D_7ClN_{10}O_2$ (M+H)⁺ m/z = 582.3; found 582.3.

Examples 71-75.

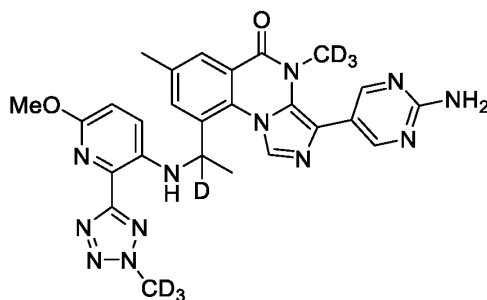
5 The following compounds in Table 6 were prepared similarly according to the procedures described for Example 68 using appropriate intermediates.

Table 6.

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
71	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-isobutylpiperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		606.3
72	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropanecarbonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		604.3
73	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(methylsulfonyl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one		614.2
74	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(isopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		642.3

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
75	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		640.2

Example 76. 3-(2-Aminopyrimidin-5-yl)-9-(1-(((6-methoxy-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one

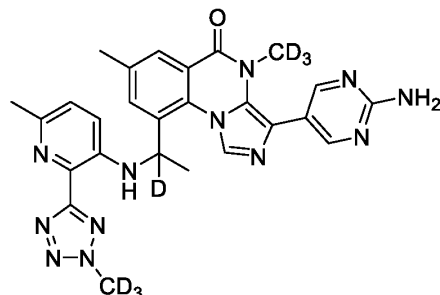


5

The mixture of 3-(2-aminopyrimidin-5-yl)-9-(1-(((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (Example 17) (15.0 mg, 0.03 mmol), [2-(2-aminophenyl)phenyl]-methylsulfonyloxy-palladium;ditert-butyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (4.7 mg, 0.01 mmol), sodium tert-butoxide (7.9 mg, 0.08 mmol) in dioxane (1 mL) and MeOH (0.2 mL) was heated at 100 °C for 1h under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₀D₇N₁₂O₂ (M+H)⁺ m/z = 546.3; found 546.2.

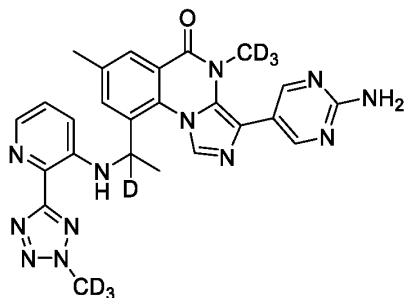
15

Example 77. 3-(2-Aminopyrimidin-5-yl)-7-methyl-4-(methyl-d3)-9-(1-((6-methyl-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one



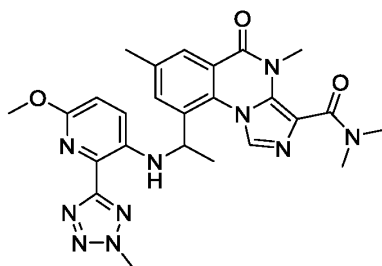
5 The mixture of 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one (Example 17) (12.00 mg, 0.02 mmol), [2-(2-aminophenyl)phenyl]-chloro-palladium;dicyclohexyl-[2-(2,4,6-triisopropylphenyl)phenyl]phosphane (3.4 mg, 0.001 mmol), K₃PO₄ (13.9 mg, 0.07 mmol) and methyl boronic acid (2.0 mg, 0.03 mmol) in dioxane (0.5 mL) and water (0.1 mL) was heated at 90 °C for 1 h under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and
10 lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₀D₇N₁₂O (M+H)⁺ m/z = 530.3; found 530.3.

Example 78. 3-(2-Aminopyrimidin-5-yl)-7-methyl-4-(methyl-d3)-9-(1-((2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one



A solution of ammonium formate (4.13 mg, 0.07 mmol) in 1 mL MeOH was added to 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one (Example 17) (12.00 mg, 0.02 mmol) and palladium on activated carbon (2.3 mg, 0.002 mmol) in a sealed tube filled with nitrogen. The reaction mixture was stirred at 60 °C for 3h. After cooling to rt, the reaction mixture was filtered through celite, and the filtrate was concentrated to dryness. The residue was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₅H₁₈D₇N₁₂O (M+H)⁺ m/z = 516.2; found 516.3.

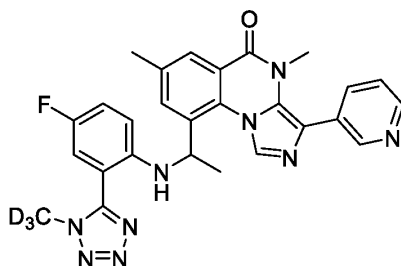
Example 79. 9-(1-((6-Methoxy-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



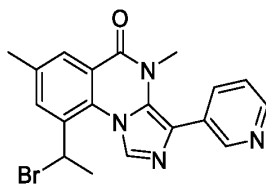
The mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (Example 23) (12.5 mg, 0.02 mmol), [2-(2-aminophenyl)phenyl]-methylsulfonyloxy-palladium;ditert-butyl-[3,6-dimethoxy-2-(2,4,6-triisopropylphenyl)phenyl]phosphane (4.1 mg, 0.001 mmol) and sodium tert-butoxide (6.9 mg, 0.07 mmol) in dioxane (1 mL) and MeOH (0.2 mL) was heated at 100 °C for 1 h under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA

salt of the desired product as a white solid. LCMS calculated for $C_{25}H_{29}N_{10}O_3$
 $(M+H)^+$ $m/z = 517.2$; found 517.2.

Example 80. 9-(1-((4-Fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one



Step 1: 9-(1-bromoethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one



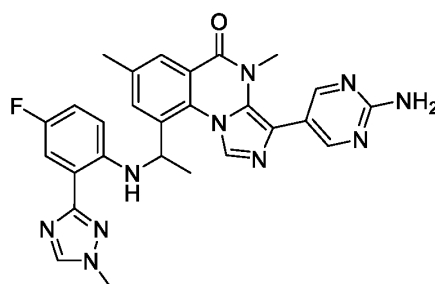
The titled compound was prepared using similar procedures as described for *Example 20* with tert-butyl 9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate replacing tert-butyl 9-acetyl-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate in step 2, pyridin-3-ylboronic acid replacing tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate in step 4, and NaBH₄ replacing NaBD₄ in step 7. LCMS calculated for $C_{19}H_{18}BrN_4O$ $(M+H)^+$ $m/z = 397.1$; found 397.1.

Step 2: 9-(1-((4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one

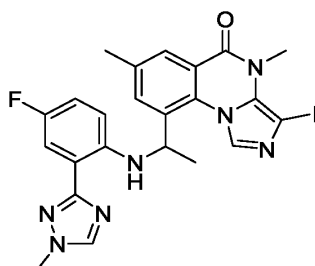
To the solution of 9-(1-bromoethyl)-4,7-dimethyl-3-(3-pyridyl)imidazo[1,5-a]quinazolin-5-one (18.0 mg, 0.05 mmol) in DMF (0.7 mL) was added 4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)aniline (Intermediate 2) (13.3 mg, 0.07 mmol). The mixture was heated to 80 °C for 3 h. After cooling to rt, the mixture was diluted with

MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₇H₂₂D₃FN₉O (M+H)⁺ m/z = 513.2; found 513.2.

Example 81. 3-(2-Aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



Step 1: 9-[1-[4-fluoro-2-(1-methyl-1,2,4-triazol-3-yl)anilino]ethyl]-3-iodo-4,7-dimethyl-imidazo[1,5-a]quinazolin-5-one



The titled compound was prepared using similar procedures as described for *Example 8* with 4-fluoro-2-(1-methyl-1,2,4-triazol-3-yl)aniline (Intermediate 4) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in step 5. LCMS calculated for C₂₃H₂₂FIN₇O (M+H)⁺ m/z = 558.1; found 558.1.

Step 2: 3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

The mixture of 9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (18

mg, 0.03 mmol), 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (10.7 mg, 0.05 mmol), K₃PO₄ (20.57 mg, 0.10 mmol) and XPhos Pd G2 (5 mg, 0.01 mmol) in dioxane (0.5 mL) and water (0.1 mL) was heated at 90 °C for 20 min under nitrogen atmosphere. After cooling to rt, the mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₇H₂₆FN₁₀O (M+H)⁺ m/z = 525.2; found 525.2.

10

Examples 82-84.

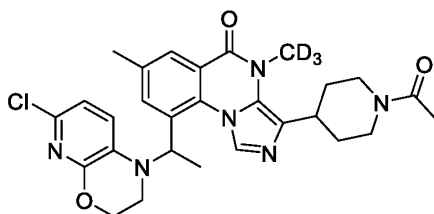
The following compounds in Table 7 were prepared similarly according to the procedures described for Example 81 using appropriate intermediates.

Table 7.

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
82	9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one		512.2
83	3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		525.2

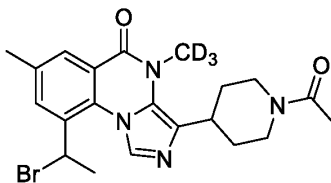
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
84	3-(6-amino-3-pyridyl)-9-[1-[4-fluoro-2-(1-methyltriazol-4-yl)anilino]ethyl]-4,7-dimethyl-imidazo[1,5-a]quinazolin-5-one		524.2

Example 85. 3-(1-Acetylpiperidin-4-yl)-9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



5

Step 1: 3-(1-acetylpiperidin-4-yl)-9-(1-bromoethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one



10

The titled compound was prepared using similar procedures as described in *Example 20* with NaBH₄ replacing NaBD₄ in step 7. LCMS calculated for C₂₁H₂₃D₃BrN₄O₂ (M+H)⁺: m/z = 448.1; found: 448.1;

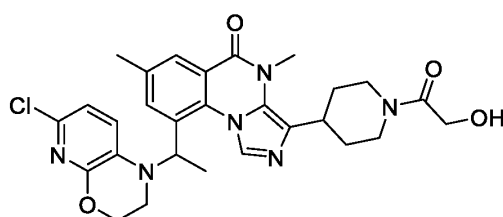
Step 2: 3-(1-acetylpiperidin-4-yl)-9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one

15

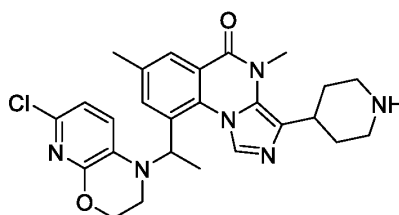
To the solution of 3-(1-acetylpiperidin-4-yl)-9-(1-bromoethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one (43 mg, 0.10 mmol) in DMF (0.1 mL) was added 6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine (24 mg, 0.14 mmol) at rt. The resulting mixture was heated at 80 °C for 4 hours. Upon completion,

the mixture was cooled to rt. The crude material was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₈H₂₉D₃ClN₆O₃ (M+H)⁺ m/z = 538.2; found 538.2.

Example 86. 9-(1-(6-Chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



Step 1: 9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one



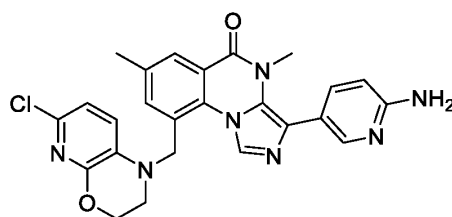
The titled compound was prepared using similar procedures as described in *Example 67* with 6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine replacing 6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-amine in step 5. LCMS calculated for C₂₆H₃₀ClN₆O₂ (M+H)⁺: m/z = 493.2; found: 493.2;

Step 2: 9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

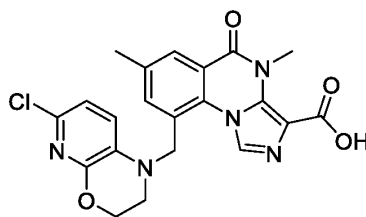
To the solution of 9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-4,7-dimethyl-3-(piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one (40 mg, 0.08 mmol) in DMF was added HATU (40.1 mg, 0.11 mmol), *N*-ethyl-*N*-isopropylpropan-2-amine (141 μ L, 0.81 mmol) and 2-hydroxyacetic acid (6.2 mg, 0.08

mmol) at 0 °C. The resulting mixture was stirred at rt for 30 min, then the reaction mixture was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{28}H_{32}ClN_6O_4$ (M+H)⁺ m/z = 551.2; found 551.2.

Example 87. 3-(6-Aminopyridin-3-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

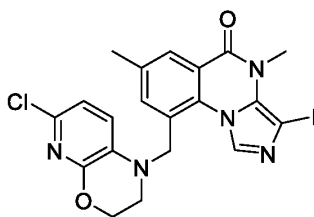


Step 1: 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



The titled compound was prepared using similar procedures as described in *Example 1* with tert-butyl 9-formyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (Intermediate 13) replacing tert-butyl 9-acetyl-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate in step 8, 6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine replacing 2-amino-5-fluorobenzamide in step 10. LCMS calculated for $C_{21}H_{19}ClN_5O_4$ (M+H)⁺ m/z = 440.1; found 440.1.

Step 2: 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



The titled compound was prepared using similar procedures as described in *Example 8* with 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid replacing 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid in step 7. LCMS calculated for $C_{20}H_{18}ClIN_5O_2$ ($M+H$)⁺ m/z = 522.0; found 522.0.

Step 3: 3-(6-aminopyridin-3-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

To a mixture of 9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (11 mg, 0.02 mmol) in dioxane (0.8 mL), water (0.2 mL) was added potassium phosphate (13 mg, 0.06 mmol), $Pd(PPh_3)_4$ (5 mg, 0.001 mmol), and (6-amino-3-pyridyl)boronic acid (4 mg, 0.03 mmol) at rt. The resulting mixture was deoxygenated by three vacuum–nitrogen cycles. The mixture was heated at 80 °C for 1 hour before diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $C_{25}H_{23}ClIN_7O_2$ ($M+H$)⁺ m/z = 488.2; found 488.2.

Examples 88-90.

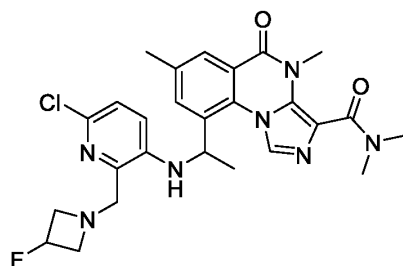
The following compounds in Table 8 were prepared similarly according to the procedures described for Example 87 using appropriate intermediates.

Table 8.

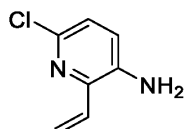
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
88	3-(2-aminopyrimidin-5-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		489.2
89	9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one		476.2
90	9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		504.2

Example 91. 9-(1-((6-Chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

5

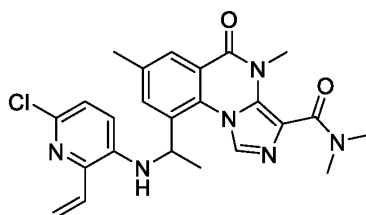


Step 1: 6-chloro-2-vinylpyridin-3-amine



To the 5 to 1 mixture of tetrahydrofuran and water (120 mL) was added 2-bromo-6-chloro-pyridin-3-amine (5.00 g, 24.10 mmol), tetrakis(triphenylphosphine)palladium(0) (2.79 g, 2.41 mmol), potassium vinyltrifluoroborate (9.69 g, 72.30 mmol) and potassium carbonate (9.99 g, 72.30 mmol) at rt. The resulting mixture was purged with nitrogen for 5 minutes. The mixture was then heated at 80 °C for 8 hours. Upon completion of reaction, the reaction mixture was cooled to room temperature. The solvent was removed under reduced pressure, the residue was diluted with ethyl acetate, washed with water twice. The organic layer was then dried with sodium sulfate. The crude product was purified with silica gel chromatography, eluting with ethyl acetate in dichloromethane from 0-50% to give the desired product (3.16 g, 84.8 %). LCMS calculated for C₇H₈ClN₂ (M+H)⁺ m/z = 155.0; found 155.0.

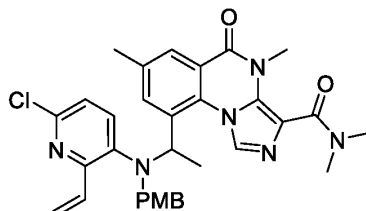
Step 2: 9-(1-((6-chloro-2-vinylpyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



The titled compound was prepared using similar procedures as described in Example 48 with 6-chloro-2-vinylpyridin-3-amine replacing 3-amino-6-

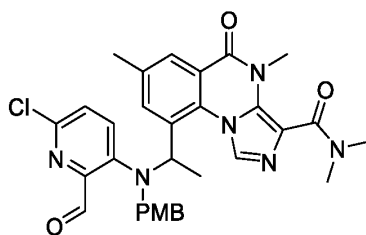
chloropicolinamide in step 2. LCMS calculated for $C_{24}H_{26}ClN_6O_2$ (M+H)⁺ m/z = 465.2; found 465.2.

Step 3: 9-(1-((6-chloro-2-vinylpyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



To the solution of 9-(1-((6-chloro-2-vinylpyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (326 mg, 0.70 mmol) in anhydrous DMF was added sodium hydride (56 mg, 1.40 mmol) at 0 °C. After the mixture was stirred for 30 min, 1-(bromomethyl)-4-methoxy-benzene (202 μ L, 1.40 mmol) was added at the same temperature. The resulting mixture was stirred at rt for 1 h. Upon completion, the reaction mixture was diluted with 10% MeOH in DCM, washed with water (3 $\times$). The organic layers were combined, and the solvent was removed under reduced pressure. The residue was purified with silica gel chromatography to give the desired product as a yellow solid (310 mg, 75.5 %). LCMS calculated for $C_{32}H_{34}ClN_6O_3$ (M+H)⁺ m/z = 585.2; found 585.2.

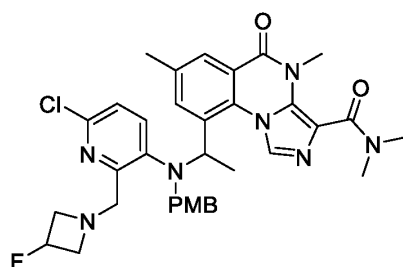
Step 4: 9-(1-((6-chloro-2-formylpyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



To the 5 to 1 solution of tetrahydrofuran and water was added 9-(1-((6-chloro-2-vinylpyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (540 mg, 0.92 mmol), OsO_4 (4% water solution, 586 μ L, 0.09 mmol), 2,6-dimethylpyridine (213 μ L, 1.85 mmol) and

sodium periodate (987 mg, 4.61 mmol) successively at rt. The resulting mixture was heated at 45 °C for 4 h. Upon completion of reaction, the mixture was cooled to rt. The mixture was diluted with dichloromethane. The organic layer was washed with water twice, dried with sodium sulfate. The solvent was removed under reduced pressure. The residue was used in the next step directly. LCMS calculated for $C_{31}H_{32}ClN_6O_4$ ($M+H$)⁺ m/z = 587.2; found 587.2.

Step 5: 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



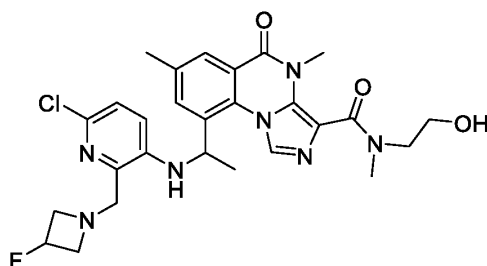
To the solution of 9-(1-((6-chloro-2-formylpyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (50 mg, 85.17 μ mol) in DCM (2 mL) was added 3-fluoroazetidine hydrochloride (12 mg, 0.11 mmol) and sodium triacetoxyborohydride (36 mg, 0.17 mmol) at rt successively. The resulting mixture was stirred for 1 h. Upon completion, the reaction was diluted with 10% MeOH/DCM, washed with water. The organic layer was separated, dried with sodium sulfate and dried under reduced pressure. The residue was used in the next step directly. LCMS calculated for $C_{34}H_{38}ClFN_7O_3$ ($M+H$)⁺ m/z = 646.3; found 646.3.

Step 6: 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

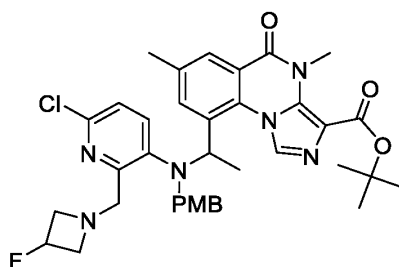
9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (10 mg, 0.015 mmol) in a 2 dram vial was treated with trifluoroacetic acid at rt. After stirring for 2h, the reaction mixture was diluted with methanol, purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm,

5 μm ; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for $\text{C}_{26}\text{H}_{30}\text{ClFN}_7\text{O}_2$ ($\text{M}+\text{H}$)⁺ $m/z = 526.2$; found 526.2.

Example 92. 9-(1-((6-Chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N-(2-hydroxyethyl)-N,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



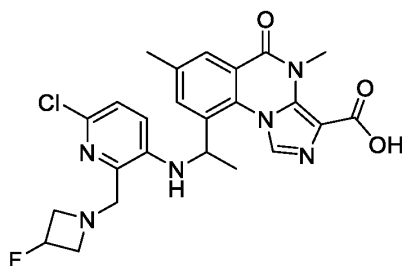
10 *Step 1: tert-butyl 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate*



15 The titled compound was prepared using similar procedures as described in Example 91 with tert-butyl 9-(1-bromoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (Example 1, step 9) replacing 9-(1-bromoethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide in step 2. LCMS calculated for $\text{C}_{36}\text{H}_{41}\text{ClFN}_6\text{O}_4$ ($\text{M}+\text{H}$)⁺ $m/z = 675.3$; found 675.3.

20

Step 2: 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid

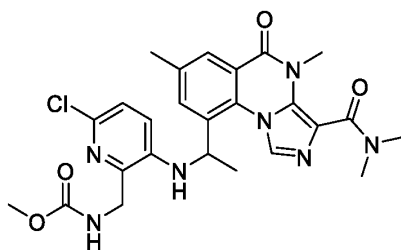


tert-Butyl 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (530 mg, 0.78 mmol) was treated with TFA (1.5 mL) at
 5 rt. The resulting mixture was stirred at rt for 4 h, then the solvent was removed under reduced pressure. The residue was azeotrope with toluene 3 times. The resulting crude was used in the next step directly. LCMS calculated for $C_{24}H_{25}ClFN_6O_3$ ($M+H$)⁺ m/z = 499.2; found 499.2.

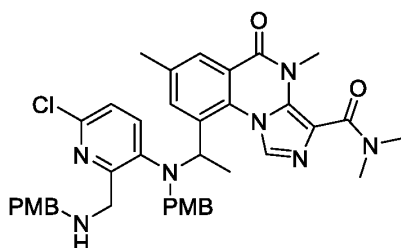
10 *Step 3: 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N-(2-hydroxyethyl)-N,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide*

To the solution of 9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-
 15 carboxylic acid (40 mg, 0.08 mmol) in DMF (0.8 mL) was added HATU (39 mg, 0.10 mmol), *N*-ethyl-*N*-isopropyl-propan-2-amine (139 μ L, 0.80 mmol), and 2-(methylamino)ethanol (8 μ L, 0.10 mmol) at rt. The resulting mixture was stirred for 1 hour before diluted with methanol and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B:
 20 acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product LCMS calculated for $C_{27}H_{32}ClFN_7O_3$ ($M+H$)⁺ m/z = 556.2; found 556.2.

Example 93. Methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)methyl)carbamate
 25



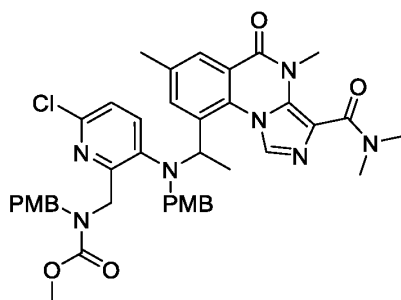
Step 1: 9-(1-((6-chloro-2-(((4-methoxybenzyl)amino)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



5

The titled compound was prepared using similar procedures as described in Example 91 with 4-methoxybenzylamine replacing 3-fluoroazetidine hydrochloride in step 5. LCMS calculated for $C_{39}H_{43}ClN_7O_4$ ($M+H$)⁺ m/z = 708.3; found 708.3.

Step 2: methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)(4-methoxybenzyl)amino)pyridin-2-yl)methyl)(4-methoxybenzyl)carbamate



To the solution of 9-(1-((6-chloro-2-(((4-methoxybenzyl)amino)methyl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (30 mg, 0.04 mmol) in dichloromethane (1 mL) was added methyl chloroformate (4 μ L, 0.05 mmol) at 0 °C dropwise. After stirring for 30 min, the resulting mixture was

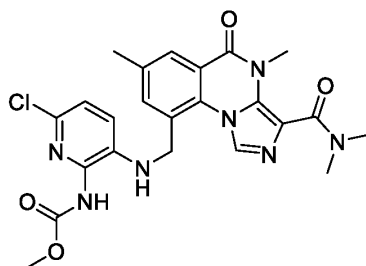
concentrated under reduced pressure. The residue was used in the next step directly.

LCMS calculated for $C_{41}H_{45}ClN_7O_6$ (M+H)⁺ m/z = 766.3; found 766.3.

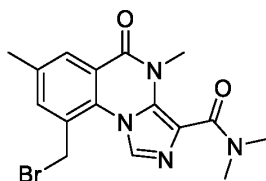
Step 3: methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)methyl)carbamate

To the crude of methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)(4-methoxybenzyl)amino)pyridin-2-yl)methyl)(4-methoxybenzyl)carbamate from last step was added 5 to 1 mixture of trifluoroacetic acid and triflic acid at 0 °C dropwise. Upon completion, the mixture was diluted with methanol, purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product. LCMS calculated for $C_{25}H_{29}ClN_7O_4$ (M+H)⁺ m/z = 526.2; found 526.2.

Example 94. Methyl (6-chloro-3-(((3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)pyridin-2-yl)carbamate



Step 1: 9-(bromomethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



The titled compound was prepared using similar procedures as described in Example 1 with 9-formyl-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (Intermediate 14) replacing tert-butyl 9-acetyl-4,7-

dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate in step 8.

LCMS calculated for $C_{16}H_{18}BrN_4O_2$ (M+H)⁺ m/z = 377.1; found 377.1.

Step 2: methyl (6-chloro-3-(((3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)pyridin-2-yl)carbamate

To the solution of 9-(bromomethyl)-N,N,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide (15 mg, 0.04 mmol) in DMF (0.1 mL) was added methyl N-(3-amino-6-chloro-2-pyridyl)carbamate (Intermediate 5) (10 mg, 0.05 mmol) at rt. The resulting mixture was heated at 80 °C for 1 h. The mixture was then diluted with methanol purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product. LCMS calculated for $C_{23}H_{25}ClN_7O_4$ (M+H)⁺ m/z = 498.2; found 498.2.

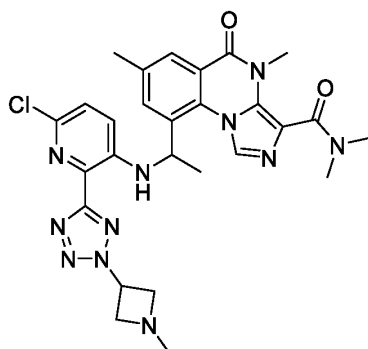
Examples 95-96.

The following compounds in Table 9 were prepared similarly according to the procedures described for Example 94 using appropriate intermediates.

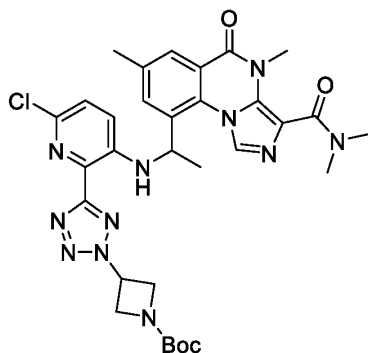
Table 9.

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
95	9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-N,N,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide		467.2
96	9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-4,7-dimethyl-5-oxo-N,N-bis(trideuteriomethyl)imidazo[1,5-a]quinazoline-3-carboxamide		473.2

Example 97. 9-(1-((6-Chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide



Step 1: *tert*-butyl 3-(5-(6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)-2H-tetrazol-2-yl)azetidine-1-carboxylate



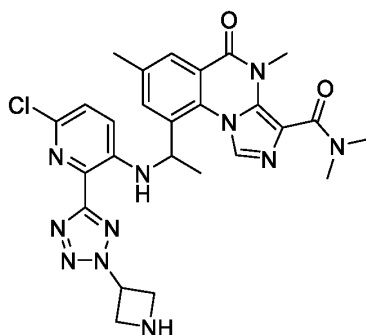
5

The titled compound was prepared using similar procedures as described in Example 48 with *tert*-butyl 3-(5-(3-amino-6-chloropyridin-2-yl)-2H-tetrazol-2-yl)azetidine-1-carboxylate (Intermediate 8) replacing 3-amino-6-chloropicolinamide in step 2. The resulting mixture was concentrated under reduced pressure. The residue was used in the next step directly. LCMS calculated for $C_{31}H_{37}ClN_{11}O_4$ ($M+H$)⁺ m/z = 662.3; found 662.3.

10

Step 2: 9-(1-((2-(2-(azetidin-3-yl)-2H-tetrazol-5-yl)-6-chloropyridin-3-yl)amino)ethyl)-*N,N*,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

15



To the crude of tert-butyl 3-(5-(6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)-2H-tetrazol-2-yl)azetidine-1-carboxylate from last step was added neat trifluoroacetic acid at 0 °C. After stirring for 20 min, the mixture was diluted with methanol, purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product. LCMS calculated for C₂₆H₂₉ClN₁₁O₂ (M+H)⁺ m/z = 562.2; found 562.2.

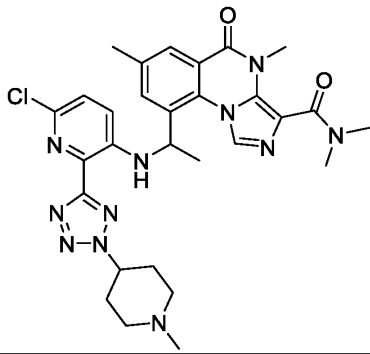
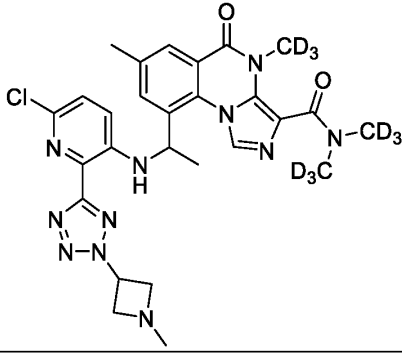
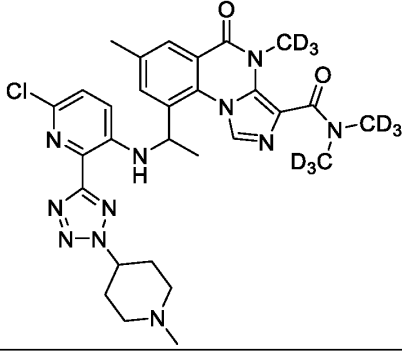
Step 3: 9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide

To the solution of 9-(1-((2-(2-(azetidin-3-yl)-2H-tetrazol-5-yl)-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide TFA salt (10 mg, 0.018 mmol) in DCM (0.5 mL) was added formaldehyde (37% water solution) (10 uL), DIEA (20 uL) and sodium triacetoxyborohydride (12 mg, 0.06 mmol) at rt successively. The resulting mixture was stirred at rt for 1 h. The reaction was then diluted with methanol, purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product. LCMS calculated for C₂₇H₃₁ClN₁₁O₂ (M+H)⁺ m/z = 576.2; found 576.2.

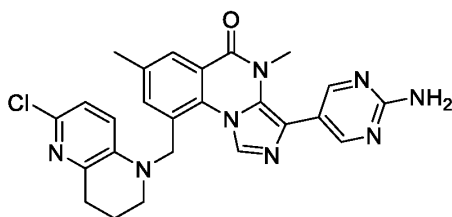
Examples 98-100.

The following compounds in Table 10 were prepared similarly according to the procedures described for Example 97 using appropriate intermediates.

Table 10.

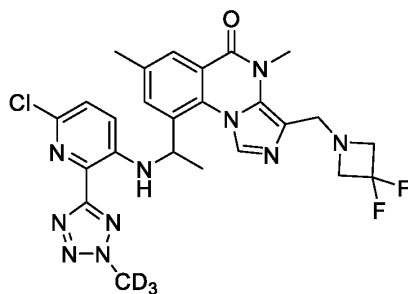
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
98	9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		604.3
99	9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		585.3
100	9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide		613.3

- 5 **Example 101.** 3-(2-Aminopyrimidin-5-yl)-9-((6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

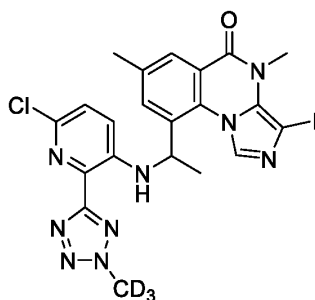


The titled compound was prepared using similar procedures as described for *Example 87* with 6-chloro-1,2,3,4-tetrahydro-1,5-naphthyridine (Intermediate 10) replacing 6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine in step 1, and 5-
 5 (4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine replacing (6-amino-3-pyridyl)boronic acid in step 3. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired
 10 product as a white solid. LCMS calculated for C₂₅H₂₄ClN₈O (M+H)⁺ m/z = 487.2; found 487.2.

**Example 102. 9-(1-((6-Chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-((3,3-difluoroazetidin-1-yl)methyl)-4,7-dimethylimidazo[1,5-
 15 a]quinazolin-5(4H)-one**

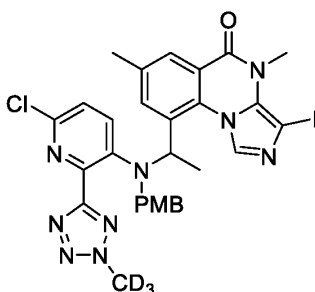


Step 1: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7 dimethylimidazo[1,5-a]quinazolin-5(4H)-one



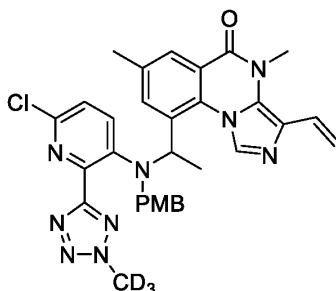
The titled compound was prepared using similar procedures as described for Example 8, Step 7.

- 5 *Step 2: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one*



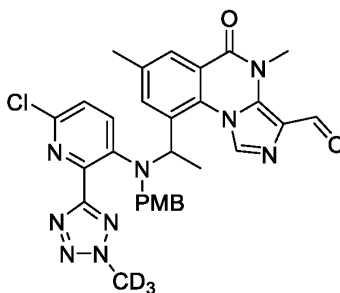
- To the solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7 dimethylimidazo[1,5-a]quinazolin-5(4H)-one (150 mg, 0.26 mmol) in DMF (5 mL) at 0 °C was added sodium hydride (60% dispersion in mineral oil, 20.7 mg, 0.52 mmol). The resulting solution was warmed to room temperature and stirred for 30 min. Then 4-methoxybenzyl bromide (74.4 uL, 0.52 mmol) was added and the reaction was stirred for 4 h. The mixture was then quenched with sat. NH₄Cl solution and extracted with EA (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and EA (0 to 95%) to provide the desired product as a white solid (85 mg, 47%). LCMS calculated for C₂₉H₂₅D₃ClIN₉O₂ (M+H)⁺ m/z = 699.1; found 699.1.

Step 3: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-3-vinylimidazo[1,5-a]quinazolin-5(4H)-one



To the mixture of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (85 mg, 0.12 mmol), bis(triphenylphosphine)palladium(II) dichloride (8.5 mg, 0.01 mmol) and tributyl(vinyl)tin (46 μ L, 0.16 mmol) was added dioxane (3 mL). The resulting mixture was stirred at 100 °C under nitrogen atmosphere for 8 h. Upon cooling to rt, the mixture was then quenched with water and extracted with EA (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and EA (0 to 95%) to provide the desired product as a white solid (55 mg, 76%). LCMS calculated for C₃₁H₂₈D₃ClN₉O₂ (M+H)⁺ m/z = 599.2; found 599.2.

Step 4: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carbaldehyde



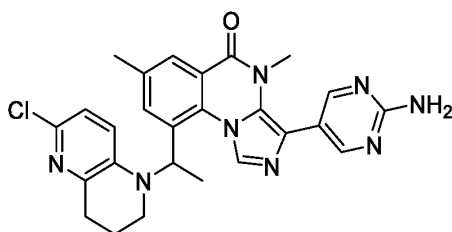
To a solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-3-vinylimidazo[1,5-a]quinazolin-

5(4H)-one (55 mg, 0.09 mmol) in THF (4 mL) and water (1 mL) was added 2,6-lutidine (21.4 μ L, 0.18 mmol), osmium tetroxide solution (4 wt. % in H₂O, 29.2 μ L, 0.0045 mmol) and sodium periodate (78.5 mg, 0.37 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for 4 h. The mixture was then quenched with water and extracted with EA (2x). The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM and EA (0 to 95%) to provide the desired product as a white solid (34 mg, 62%). LCMS calculated for C₃₀H₂₆D₃ClN₉O₃ (M+H)⁺ m/z = 601.2; found 601.2.

Step 5: 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-((3,3-difluoroazetidin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

To the solution of 9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)(4-methoxybenzyl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carbaldehyde (10 mg, 0.01 mmol) in DCM (1 mL) was added 3,3-difluoroazetidine hydrochloride (4.3 mg, 0.03 mmol). The reaction was stirred at room temperature for 2 hours. Then sodium triacetoxyborohydride (7.0 mmol, 0.03 mmol) was added and the reaction was stirred for 30 min. Then trifluoroacetic acid (2 mL) was added and the reaction was stirred for additional 2 hours. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₅H₂₃D₃ClF₂N₁₀O (M+H)⁺ m/z = 558.2; found 558.2.

Example 103: 3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



The titled compound was prepared using similar procedures as described in Example 8 with 6-chloro-1,2,3,4-tetrahydro-1,5-naphthyridine (Intermediate 10) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in step 5. The crude product was purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₆ClN₈O (M+H)⁺ m/z = 501.2; found 501.2.

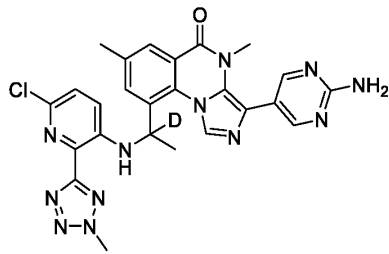
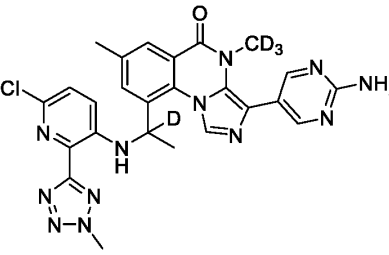
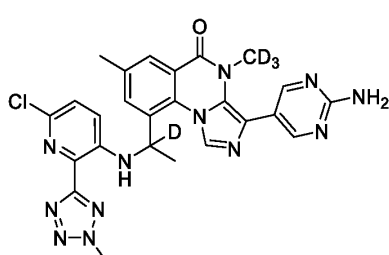
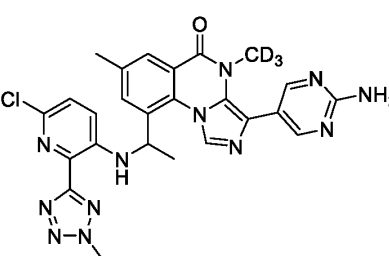
Examples 104-125.

Selected racemic compounds of the Examples can be resolved by chiral HPLC to afford enantiopure compounds provided in Table 11.

Table 11.

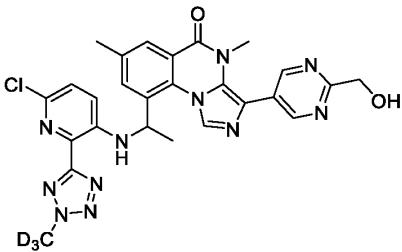
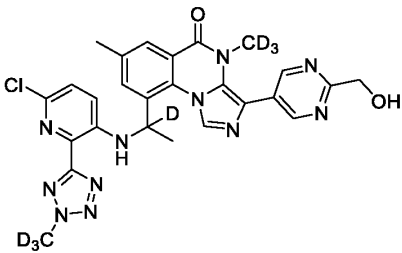
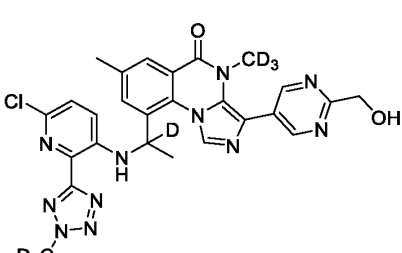
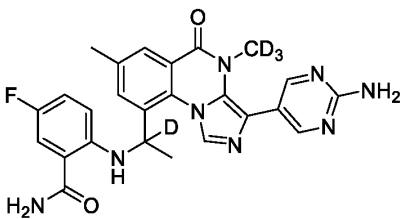
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
104	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		543.2

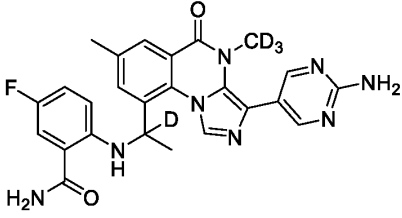
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
105	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		543.2
106	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		547.2
107	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		547.2
108	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		544.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
109	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		544.2
110	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		547.2
111	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		547.2
112	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		546.2

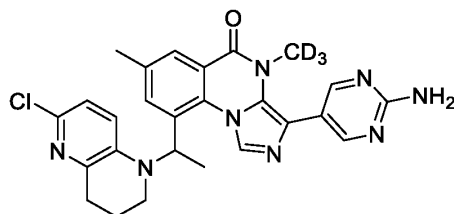
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
113	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		546.2
114	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		549.2
115	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		549.2
116	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		550.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
117	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		550.2
118	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (enantiomer 1)		527.2
119	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide (enantiomer 2)		527.2
120	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		561.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
121	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		561.2
122	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 1)		565.2
123	9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one (enantiomer 2)		565.2
124	2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide (enantiomer 1)		491.2

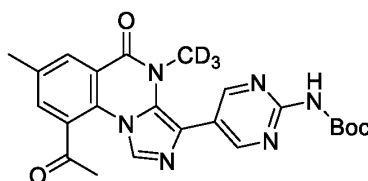
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
125	2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d-amino)-5-fluorobenzamide (enantiomer 2)		491.2

Example 126. 3-(2-Aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one



5

Step 1: tert-butyl (5-(9-acetyl-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate

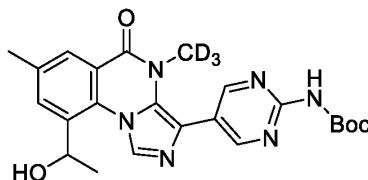


A mixture of 9-acetyl-3-iodo-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one (Example 20, step 3) (1.0 g, 2.6 mmol), tert-butyl (5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-yl)carbamate (963 mg, 3 mmol), K₃PO₄ (0.96 g, 4.5 mmol) and Xphos-PdG2 (204 mg, 0.26 mmol) in dioxane (10 mL) and water (1 mL) was heated at 100 °C for 1h under nitrogen atmosphere. After cooling to rt, the reaction mixture was diluted with water and extracted with ethyl acetate (3X). The combined organics were washed with water, sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to provide the desired

15

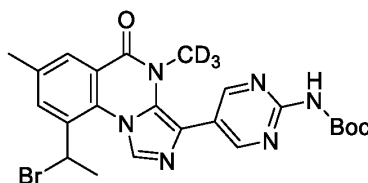
product as a light yellow solid (891 mg, 76%). LCMS calculated for $C_{23}H_{22}D_3N_6O_4$ $(M+H)^+$ $m/z = 452.2$; found 452.2.

Step 2: *tert-butyl (5-(9-(1-hydroxyethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-*
 5 *dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate*



tert-Butyl (5-(9-(1-hydroxyethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-
 a]quinazolin-3-yl)pyrimidin-2-yl)carbamate (891 mg, 1.97 mmol) was dissolved in
 MeOH (10 mL) and DCM (10 mL) then $NaBH_4$ (94 mg, 2.4 mmol) was added at 0 °C
 10 in three portions under nitrogen. The resulting mixture was stirred at same
 temperature for 10 min before quenched with sat. NH_4Cl . The mixture was diluted
 with water and extracted with DCM. The combined organics were washed with sat.
 $NaCl$, and dried with anhydrous sodium sulfate, filtered, and concentrated under
 reduced pressure. The residue was purified by silica gel column chromatography,
 15 eluted with DCM and MeOH (0 to 4%) to provide the desired product as a light
 brown solid (687 mg 77%). LCMS calculated for $C_{23}H_{24}D_3N_6O_4$ $(M+H)^+$ $m/z =$
 454.2; found 454.2.

Step 3: *tert-butyl (5-(9-(1-bromoethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-*
 20 *dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate*



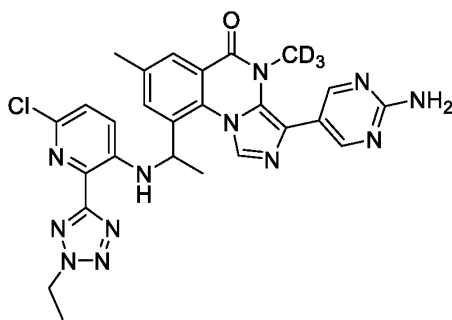
To a mixture of *tert-butyl (5-(9-(1-hydroxyethyl)-7-methyl-4-(methyl-d₃)-5-*
 oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate (687 mg,
 1.51 mmol) in DCM (100 mL) was added pyridine (134 mg, 1.7 mmol) and PBr_3
 25 (0.16 mL, 1.6 mmol) at 0 °C. The resulting mixture was warmed to rt and stirred for
 2 h. The mixture was then quenched with sat. $NaHCO_3$ and extracted with DCM (2x).

The combined organics were washed with sat. NaCl, and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was used directly in the next step without further purification.

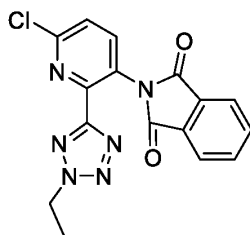
5 *Step 4: 3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one*

To the solution of tert-butyl (5-(9-(1-bromoethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate (20 mg, 0.04 mmol) in DMF (0.5 mL) was added 6-chloro-1,2,3,4-tetrahydro-1,5-naphthyridine (20 mg, 0.12 mmol). The mixture was heated at 80 °C for 2 h. Upon
10 cooling to rt, the solvent was removed, and the residue was dissolved in TFA (0.5 mL). The resulting mixture was stirred for 30 min before diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min);
15 eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₃D₃ClN₈O (M+H)⁺ m/z = 504.2; found 504.3.

20 **Example 127. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one**

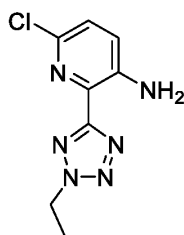


Step 1: 2-(6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione



To a solution of 2-[6-chloro-2-(1H-tetrazol-5-yl)-3-pyridyl]isoindoline-1,3-dione (Example 8, step 2) (1.55 g, 4.74 mmol) in 10 mL DMF was added iodoethane (0.57 mL, 7.12 mmol) and potassium carbonate (1.97 g, 14.2 mmol). The reaction mixture was stirred at r.t. for 2h, then diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography, eluted with hexanes and ethyl acetate to provide the desired product as a yellow solid (0.46 g, 27.3%) and another regioisomer as a yellow solid (0.19 g, 11.3 %). LCMS calculated for C₁₆H₁₂ClN₆O₂ (M+H)⁺ m/z = 355.1; found 355.1.

Step 2: 6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-amine



The mixture of 2-(6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)isoindoline-1,3-dione (0.46 g, 1.30 mmol) in 2 mL of hydrazine monohydrate was stirred at 45 °C for 2 h, then the reaction mixture was cooled to rt and the resulting precipitate was collected by filtration and washed with water to give the desired product as a white solid (160 mg, 55 %). LCMS calculated for C₈H₁₀ClN₆ (M+H)⁺ m/z = 225.1; found 225.1.

Step 3: 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one

To the solution of tert-butyl (5-(9-(1-bromoethyl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-yl)pyrimidin-2-yl)carbamate (Example 126, Step 3: 30 mg, 0.06 mmol) in DMF (0.5 mL) was added 6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-amine (17 mg, 0.08 mmol). The mixture was heated at 80 °C for 2 h. Upon cooling to rt, the solvent was removed, and the residue was dissolved in TFA (0.5 mL). The resulting mixture was stirred for 30 min before diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5µm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₃D₃ClN₁₂O (M+H)⁺ m/z = 560.2; found 560.3.

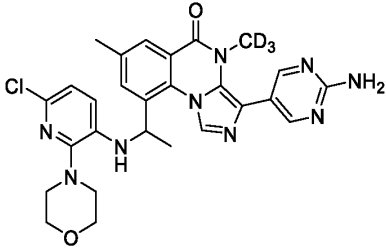
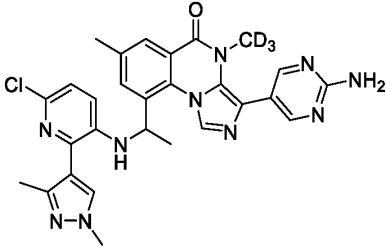
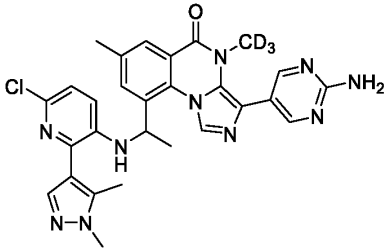
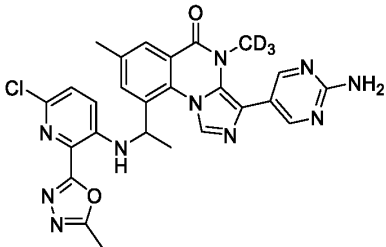
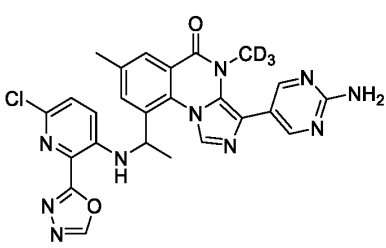
Example 128-141.

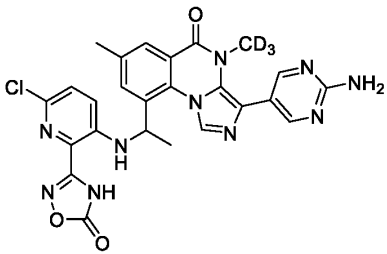
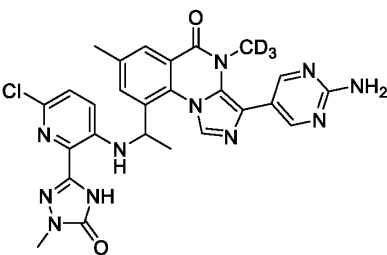
The following compounds in Table 12 were prepared similarly as described for Example 126 using appropriate intermediates.

Table 12.

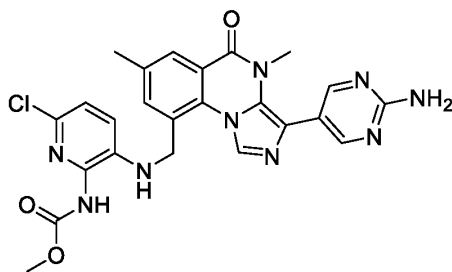
Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
128	methyl (3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)carbamate		537.2
129	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		544.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
130	3-(2-aminopyrimidin-5-yl)-9-(1-((6-fluoro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		528.2
131	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		570.2
132	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		586.2
133	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(pyrimidin-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		542.2
134	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(4-hydroxypiperidin-1-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		563.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
135	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-morpholinopyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		549.2
136	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		558.2
137	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,5-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		558.2
138	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(5-methyl-1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		546.2
139	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		532.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
140	3-(3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d ₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one		548.2
141	3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d ₃)imidazo[1,5-a]quinazolin-5(4H)-one		561.2

Example 142. Methyl (3-(((3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)-6-chloropyridin-2-yl)carbamate



5

The titled compound was prepared using similar procedures as described for Example 87 with methyl (3-amino-6-chloropyridin-2-yl)carbamate (Intermediate 5) replacing 6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine in step 1, and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine replacing (6-amino-3-pyridyl)boronic acid in step 2. The crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired

10

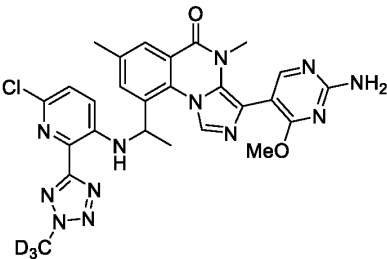
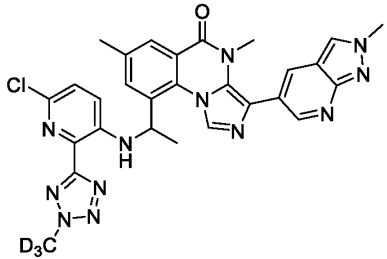
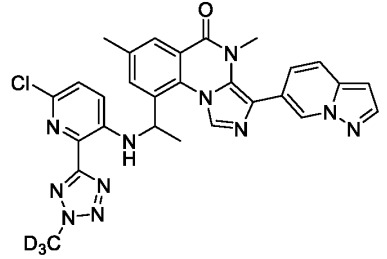
product as a white solid. LCMS calculated for $C_{24}H_{23}ClN_9O_3$ ($M+H$)⁺ m/z = 520.2; found 520.2.

Example 143-149.

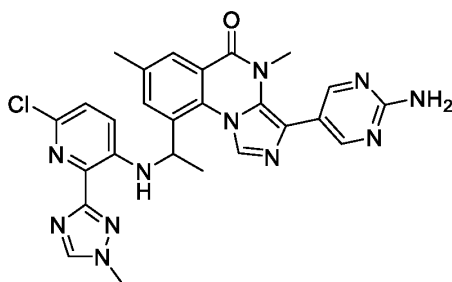
5 The following compounds in Table 13 were prepared similarly as described for Example 8 using appropriate intermediates.

Table 13.

Example #	Chemical name	Structure	LCMS m/z ($M+H$) ⁺
143	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one		519.2
144	3-(6-amino-5-chloropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		579.2
145	3-(6-amino-5-methylpyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		559.2
146	3-(6-amino-5-methoxypyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		575.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
147	3-(2-amino-4-methoxypyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one		576.2
148	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(2-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one		584.2
149	9-(1-((6-chloro-2-(2-(methyl-d ₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyridin-6-yl)imidazo[1,5-a]quinazolin-5(4H)-one		569.2

Example 150. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

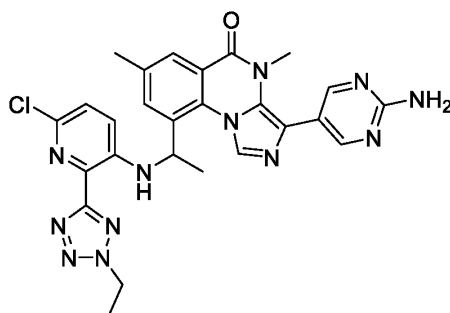


5

The titled compound was prepared using similar procedures as described for Example 8 with 6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-amine (Intermediate 27) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in

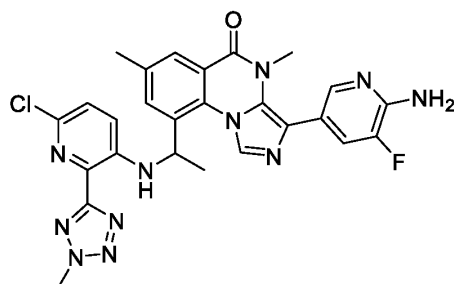
step 5. The final crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₅ClN₁₁O (M+H)⁺ m/z = 542.2; found 542.2.

Example 151. 3-(2-Aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

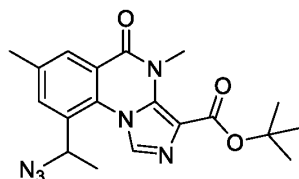


The titled compound was prepared using similar procedures as described for Example 8 with 6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-amine (Example 127, step 2) replacing 6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine in step 5. The final crude product was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5 μ m; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a white solid. LCMS calculated for C₂₆H₂₆ClN₁₂O (M+H)⁺ m/z = 557.2; found 557.2.

Example 152. 3-(6-Amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

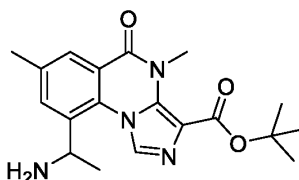


Step 1: *tert*-butyl 9-(1-azidoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate



5 To a solution of the *tert*-butyl 9-(1-hydroxyethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate (Example 1, step 8) (12.40 g, 34.7 mmol) in toluene (125 mL) was added diphenyl phosphorazidate (8.95 mL, 11.46 g, 41.63 mmol) dropwise for 10 min, followed by dropwise addition of 2,3,4,6,7,8,9,10-octahydropyrimido[1,2-*a*]azepine (6.21 mL, 6.34 g, 41.63 mmol) over 30 min. The
10 resulting cloudy mixture was warmed to 80 °C and continued to stir at 80 °C for 4 h. The resulting red slurry was allowed to cool to rt, and the solvent was evaporated under vacuum. The residue was treated with H₂O (200 mL), and the resulting mixture was extracted with EtOAc (5x50 mL). The combined organic layers were then washed with 10 wt% aqueous citric acid (50 mL) and then 10 wt% aqueous NaHCO₃
15 (50 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum to give the title compound (12.50 g, 94.2 %).

Step 2: *tert*-butyl 9-(1-aminoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-*a*]quinazoline-3-carboxylate

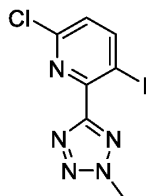


20

A round bottom flask was charged with *tert*-butyl 9-(1-azidoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (12.50 g, 32.69 mmol) and palladium on activated carbon (10%, 50% wet with water) (1.74 g, 1.63 mmol), purged with hydrogen, then added MeOH. A hydrogen balloon was then
5 attached to the flask and the reaction mixture was stirred at rt for 12h. The reaction mixture was filtered through a bed of celite and the filtrate was dried over Na₂SO₄, filtered, and concentrated under vacuum to afford the title compound (9.50 g, 81.5 %). LCMS calculated for C₁₉H₂₅N₄O₃ (M+H)⁺ m/z = 357.2; found 357.2.

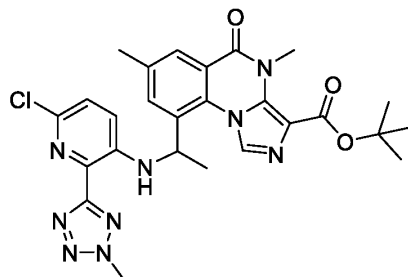
The racemic material was separated using chiral SFC, the first peak was used
10 in the next steps.

Step 3: 6-chloro-3-iodo-2-(2-methyl-2H-tetrazol-5-yl)pyridine



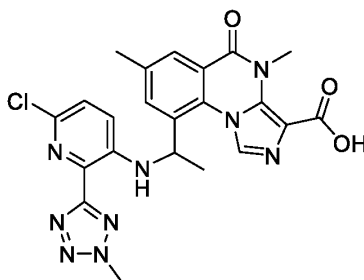
6-Chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-amine (Example 8, step 4)
15 (2.37 g, 11.25 mmol) was suspended in water (11 mL) while stirring. The mixture was cooled in an ice bath and sulfuric acid (10.92 mL, 19.98 g, 203.67 mmol) was added slowly (yellow suspension turned into yellow solution). A solution of sodium nitrite (1.40 g, 20.25 mmol) in water (11 mL) was added dropwise (brown color fume generated). The reaction mixture was stirred for an additional 15 min at 0-5°C. The
20 mixture was poured into a well-stirred solution of potassium iodide (2.80 g, 16.88 mmol) in water (23 mL). The resulting mixture was stirred at rt for 30 min. Upon completion of reaction, the solid was collected by filtration. The collected solid was dissolved in ethyl acetate, washed with 20% sodium bisulfite in water. The organic layer was separated, washed with saturated brine, dried with sodium sulfate, and
25 concentrated under reduced pressure to give orange residue. The residue was purified with silica gel chromatography, eluted with 0-50% EtOAc/DCM, to give desired product (3.00 g, 82.9 %) as a light-yellow solid.

Step 4: *tert*-butyl 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate



5 The mixture of *tert*-butyl 9-(1-aminoethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (peak 1 from step 2) (1.00 g, 2.81 mmol), 6-chloro-3-iodo-2-(2-methyl-2H-tetrazol-5-yl)pyridine (1.08 g, 3.37 mmol), Cs₂CO₃ (1.83 g, 5.61 mmol), and XantPhos-Pd-G2 (0.50 g, 0.56 mmol) in dioxane (3.0 mL) was purged with N₂ then heated at 100 °C for 18 h under nitrogen
10 atmosphere. Upon cooling to rt, the reaction was diluted with water and extracted with EtOAc. The combined organics were washed with brine and dried with anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography, eluted with DCM and ethyl acetate to provide the desired product as a solid (850 mg, 55 %).
15 LCMS calculated for C₂₆H₂₉ClN₉O₃ (M+H)⁺ m/z = 550.2; found 550.2.

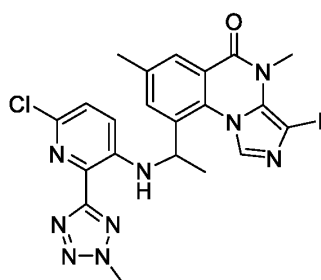
Step 5: 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylic acid



20 *tert*-Butyl 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxylate (850 mg, 1.54 mmol) was dissolved in TFA (10 mL). The mixture was

stirred for 3 h at rt. After completion, TFA was removed under vacuum. EtOAc (20 mL) and hexanes (20 mL) were added to the reaction residue while stirring. After stirring for 20 min, the resulting solid was collected to afford a white solid, which was washed with hexanes/EtOAc (1:1). The solid was dried under vacuum to provide the pure product (607 mg, 80%). LCMS calculated for $C_{22}H_{21}ClN_9O_3$ (M+H)⁺ m/z = 494.1; found 494.2.

Step 6: 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one



10

To a mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-3-carboxylic acid (607 mg, 1.23 mmol) in DMF (10 mL) under nitrogen was added NaHCO₃ (252 mg, 3 mmol) at 0 °C, after stirring for 5 min, NIS (281 mg, 1.23 mmol) was added in one portion. The resulting mixture was warmed to rt and stirred for 2 h under vacuum. After completion, the reaction mixture was quenched with sat. Na₂S₂O₃ and diluted with water. The resulting solid was collected as a brown solid by filtration which was purified by silica gel column chromatography, eluted with DCM and EtOAc to provide the desired product as a white solid (337 mg, 72%). LCMS calculated for $C_{21}H_{20}ClIN_9O$ (M+H)⁺ m/z = 576.1; found 576.1.

20

Step 7: 3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one

The mixture of 9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-iodo-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (10 mg, 0.017 mmol), 3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-amine (7 mg, 0.03 mmol), K₃PO₄ (5 mg, 0.024 mmol) and Pd(amphos)Cl₂ (2 mg,

25

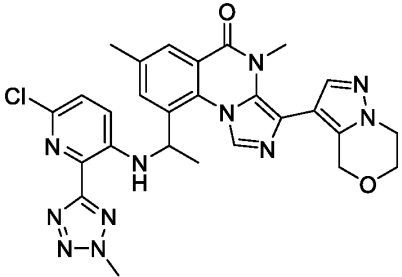
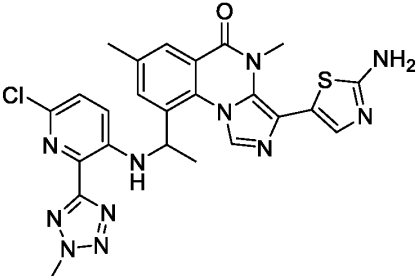
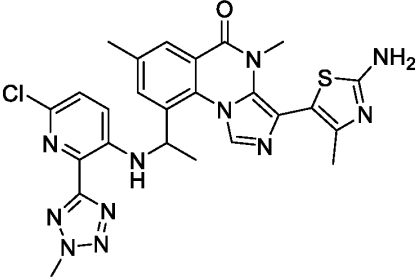
0.003 mmol) in dioxane (1.0 mL) and water (0.2 mL) was heated at 80 °C for 4h under nitrogen atmosphere. The reaction was diluted with MeOH and purified by prep-HPLC (column: Sunfire prep C18 column, 30*150 mm, 5μm; mobile phase A: water (0.1% TFA), mobile phase B: acetonitrile; flow rate: 60 mL/min); eluted fractions were collected and lyophilized to provide the TFA salt of the desired product as a light yellow. LCMS calculated for C₂₆H₂₄ClFN₁₁O (M+H)⁺ m/z = 560.2; found 560.2.

Example 153-157.

The following compounds in Table 14 were prepared similarly as described for Example 152 using appropriate intermediates.

Table 14.

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
153	3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (intermediate from Example 152, step 6)		557.2
154	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-imidazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one (intermediate from Example 152, step 6)		530.2

Example #	Chemical name	Structure	LCMS m/z (M+H) ⁺
155	9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (intermediate from Example 8, step 7)		572.2
156	3-(2-aminothiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (intermediate from Example 8, step 7)		548.1
157	3-(2-amino-4-methylthiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one (intermediate from Example 8, step 7)		562.2

Example A. pS473 AKT Assay Protocol

T47D (PIK3CA H1047R) cells were cultured using 10-cm petri dishes with recommended medium plus 10% fetal bovine serum. One day before the assay, cells were seeded in 96-well plates. After overnight incubation, the medium was changed to DMEM with 2.5% fetal bovine serum (FBS) and the cells were treated with different concentrations of the compounds for 2 h. Cells were then fixed using 4%

paraformaldehyde at room temperature for 20 min. Aspirate 4% paraformaldehyde, and wash cells using 1X regular phosphate buffered saline 3 times, 5 min each. Aspirate any residual phosphate buffered saline and block cells using 10% goat serum containing 1% bovine serum albumin and 0.3% Triton X-100 at room temperature for 1 h. Without any additional washing, primary antibodies (rabbit anti-pSer473 AKT) were diluted using blocking buffer and added at a final volume of 50 microliter per well. Keep assay plates with primary antibodies overnight at 4°C. Wash cells using 1X regular phosphate buffered saline 3 times, 5 min each. After the final wash, incubate cells with horseradish peroxidase-conjugated secondary antibodies (goat Anti-rabbit IgG) diluted using the same blocking buffer at room temperature for 1 h. Wash cells thoroughly using 1X regular phosphate buffered saline 3 times, 5 min each. Aspirate any residual phosphate buffered saline. Add Super-Signal ELISA Pico Chemiluminescent Substrate at a final volume of 100 microliter per well. Read plates on i3x Multi-Mode Microplate Reader and calculate IC₅₀ values using GraphPad Prism software.

Results of the assay described above are presented in Table A. “+” indicates an IC₅₀ less than 100 nM; “++” indicates an IC₅₀ greater than or equal to 100 nM but less than 500 nM; “+++” indicates an IC₅₀ greater than or equal to 500 nM but less than 1000 nM; and “++++” indicates an IC₅₀ greater than or equal to 1000 nM.

20

Table A.

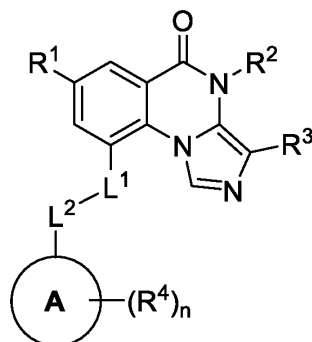
Example	T47D_IC ₅₀ (nM)	Example	T47D_IC ₅₀ (nM)	Example	T47D_IC ₅₀ (nM)
1	+	2	++++	3	+
4	+	5	+	6	+
7	+	8	+	9	+
10	+	11	+	12	+
13	+	14	+	15	+
16	++++	17	+	18	+
19	+	20	+	21	+
22	+	23	+	24	+
25	+	26	+	27	+
28	++	29	+	30	+
31	+	32	+	33	+
34	+	35	+	36	+
37	+	38	+	39	+
40	+	41	+	42	+
43	+	44	+	45	+
46	++	47	+	48	+

Example	T47D_IC ₅₀ (nM)	Example	T47D_IC ₅₀ (nM)	Example	T47D_IC ₅₀ (nM)
49	+	50	+	51	++
52	+	53	++	54	+
55	+	56	++	57	+
58	+	59	++	60	+
61	+	62	+	63	+
64	+	65	+	66	+
67	+	68	+	69	+
70	+	71	+	72	+
73	+	74	+	75	+
76	++	77	+	78	++
79	++	80	+	81	+
82	+	83	+	84	+
85	+	86	+	87	+
88	+	89	+	90	+
91	+	92	++	93	++
94	+	95	++	96	++
97	++	98	++	99	++
100	++	101	+	102	+
127	+	128	+	129	+
130	+	131	+	132	+
133	+	134	+	150	+
151	+	152	+	153	+
154	+	155	+	156	+
157	+				

Various modifications of the invention, in addition to those described herein, will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims. Each reference, including all patent, patent applications, and publications, cited in the present application is incorporated herein by reference in its entirety.

WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

n is 0, 1, 2, 3, 4, 5, or 6;

Ring A is C₃₋₁₄ cycloalkyl, C₆₋₁₀ aryl, 4-14 membered heterocycloalkyl, or 5-10 membered heteroaryl;

L¹ is C₁₋₄ alkylene, wherein the C₁₋₄ alkylene is optionally substituted with 1, 2, 3, or 4 independently selected R^G substituents;

L² is selected from bond, -O-, and -N(R^L)-;

R^L is selected from H, C₁₋₆ alkyl, and C₁₋₆ haloalkyl;

R¹ is selected from H, halo, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, and -CN;

R² is selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₇ cycloalkyl, and C₃₋₇ cycloalkyl-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₇ cycloalkyl, and C₃₋₇ cycloalkyl-C₁₋₄ alkyl of R² are each optionally substituted with 1, 2, 3, or 4 independently selected R^G substituents;

R³ is selected from H, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a3}, -SR^{a3}, -NR^{c3}R^{d3}, -NO₂, -C(O)R^{a3}, -C(O)OR^{a3}, -C(O)NR^{c3}R^{d3}, -C(O)NR^{c3}(OR^{a3}), -OC(O)R^{a3}, -OC(O)NR^{c3}R^{d3}, -OC(O)OR^{a3}, -OS(O)₂R^{b3}, -OS(O)₂NR^{c3}R^{d3}, -NR^{c3}C(O)R^{a3}, -NR^{c3}C(O)OR^{a3}, -NR^{c3}C(O)NR^{c3}R^{d3}, -NR^{c3}S(O)₂R^{b3},

-NR^{c3}S(O)₂NR^{c3}R^{d3}, -NR^{c3}OR^{a3}, -NR^{c3}S(O)R^{b3}, -NR^{c3}S(O)NR^{c3}R^{d3}, -S(O)R^{b3}, -S(O)₂R^{b3}, -S(O)NR^{c3}R^{d3}, -S(O)₂NR^{c3}R^{d3}, -C(=NR^{e3})R^{a3}, -C(=NR^{e3})NR^{c3}R^{d3}, -NR^{c3}C(=NR^{e3})R^{a3}, -NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}, -NR^{c3}S(O)(=NR^{e3})R^{b3}, -NR^{c3}S(O)(=NR^{e3})NR^{c3}R^{d3}, -OS(O)(=NR^{e3})R^{b3}, -S(O)(=NR^{e3})R^{b3}, -S(O)(=NR^{e3})NR^{c3}R^{d3}, -C(O)NR^{c3}S(O)₂R^{b3}, -C(O)NR^{c3}S(O)₂NR^{c3}R^{d3}, -S(O)₂NR^{c3}C(O)R^{b3}, -NR^{c3}S(O)NR^{c3}C(O)R^{b3}, and -P(O)R^{f3}R^{g3}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R³ are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{a3}, R^{c3}, and R^{d3} is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{a3}, R^{c3}, and R^{d3} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

or, any R^{c3} and R^{d3} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{b3} is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-

10 membered heteroaryl)-C₁₋₄ alkyl of R^{b3} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{3A} substituents;

each R^{e3} is independently selected from H, OH, CN, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{f3} and R^{g3} are independently selected from H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{3A} is independently selected from oxo, H, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a3A}, -SR^{a3A}, -NR^{c3A}R^{d3A}, -NO₂, -C(O)R^{a3A}, -C(O)OR^{a3A}, -C(O)NR^{c3A}R^{d3A}, -C(O)NR^{c3A}(OR^{a3A}), -OC(O)R^{a3A}, -OC(O)NR^{c3A}R^{d3A}, -OC(O)OR^{a3A}, -OS(O)₂R^{b3A}, -OS(O)₂NR^{c3A}R^{d3A}, -NR^{c3A}C(O)R^{a3A}, -NR^{c3A}C(O)OR^{a3A}, -NR^{c3A}C(O)NR^{c3A}R^{d3A}, -NR^{c3A}S(O)₂R^{b3A}, -NR^{c3A}S(O)₂NR^{c3A}R^{d3A}, -NR^{c3A}OR^{a3A}, -NR^{c3A}S(O)R^{b3A}, -NR^{c3A}S(O)NR^{c3A}R^{d3A}, -S(O)R^{b3A}, -S(O)₂R^{b3A}, -S(O)NR^{c3A}R^{d3A}, -S(O)₂NR^{c3A}R^{d3A}, -C(=NR^{e3A})R^{a3A}, -C(=NR^{e3A})NR^{c3A}R^{d3A}, -NR^{c3A}C(=NR^{e3A})R^{a3A}, -NR^{c3A}C(=NR^{e3A})NR^{c3A}R^{d3A}, -NR^{c3A}S(O)(=NR^{e3A})R^{b3A}, -NR^{c3A}S(O)(=NR^{e3A})NR^{c3A}R^{d3A}, -OS(O)(=NR^{e3A})R^{b3A}, -S(O)(=NR^{e3A})R^{b3A}, -S(O)(=NR^{e3A})NR^{c3A}R^{d3A}, -C(O)NR^{c3A}S(O)₂R^{b3A}, -C(O)NR^{c3A}S(O)₂NR^{c3A}R^{d3A}, -S(O)₂NR^{c3A}C(O)R^{b3A}, -NR^{c3A}S(O)NR^{c3A}C(O)R^{b3A}, and -P(O)R^{f3A}R^{g3A}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{3A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{a3A} , R^{c3A} , and R^{d3A} is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{a3A} , R^{c3A} , and R^{d3A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

or, any R^{c3A} and R^{d3A} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{b3A} is independently selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl, wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl of R^{b3A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{e3A} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^{f3A} and R^{g3A} are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4}

alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

R⁴ is selected from oxo, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a4}, -SR^{a4}, -NR^{c4}R^{d4}, -NO₂, -C(O)R^{a4}, -C(O)OR^{a4}, -C(O)NR^{c4}R^{d4}, -C(O)NR^{c4}(OR^{a4}), -OC(O)R^{a4}, -OC(O)NR^{c4}R^{d4}, -OC(O)OR^{a4}, -OS(O)₂R^{b4}, -OS(O)₂NR^{c4}R^{d4}, -NR^{c4}C(O)R^{a4}, -NR^{c4}C(O)OR^{a4}, -NR^{c4}C(O)NR^{c4}R^{d4}, -NR^{c4}S(O)₂R^{b4}, -NR^{c4}S(O)₂NR^{c4}R^{d4}, -NR^{c4}OR^{a4}, -NR^{c4}S(O)R^{b4}, -NR^{c4}S(O)NR^{c4}R^{d4}, -S(O)R^{b4}, -S(O)₂R^{b4}, -S(O)NR^{c4}R^{d4}, -S(O)₂NR^{c4}R^{d4}, -C(=NR^{e4})R^{a4}, -C(=NR^{e4})NR^{c4}R^{d4}, -NR^{c4}C(=NR^{e4})R^{a4}, -NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}, -NR^{c4}S(O)(=NR^{e4})R^{b4}, -NR^{c4}S(O)(=NR^{e4})NR^{c4}R^{d4}, -OS(O)(=NR^{e4})R^{b4}, -S(O)(=NR^{e4})R^{b4}, -S(O)(=NR^{e4})NR^{c4}R^{d4}, -C(O)NR^{c4}S(O)₂R^{b4}, -C(O)NR^{c4}S(O)₂NR^{c4}R^{d4}, -S(O)₂NR^{c4}C(O)R^{b4}, -NR^{c4}S(O)NR^{c4}C(O)R^{b4}, and -P(O)R^{f4}R^{g4}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R⁴ are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{a4}, R^{c4}, and R^{d4} is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{a4}, R^{c4}, and R^{d4} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

or, any R^{c4} and R^{d4} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the

4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{b4} is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{b4} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^{4A} substituents;

each R^{e4} is independently selected from H, OH, CN, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{f4} and R^{g4} are independently selected from H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl;

each R^{4A} is independently selected from oxo, H, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, (5-10 membered heteroaryl)-C₁₋₄ alkyl, -CN, -OR^{a4A}, -SR^{a4A}, -NR^{c4A}R^{d4A}, -NO₂, -C(O)R^{a4A}, -C(O)OR^{a4A}, -C(O)NR^{c4A}R^{d4A}, -C(O)NR^{c4A}(OR^{a4A}), -OC(O)R^{a4A}, -OC(O)NR^{c4A}R^{d4A}, -OC(O)OR^{a4A}, -OS(O)₂R^{b4A}, -OS(O)₂NR^{c4A}R^{d4A}, -NR^{c4A}C(O)R^{a4A}, -NR^{c4A}C(O)OR^{a4A}, -NR^{c4A}C(O)NR^{c4A}R^{d4A}, -NR^{c4A}S(O)₂R^{b4A}, -NR^{c4A}S(O)₂NR^{c4A}R^{d4A}, -NR^{c4A}OR^{a4A}, -NR^{c4A}S(O)R^{b4A}, -NR^{c4A}S(O)NR^{c4A}R^{d4A}, -S(O)R^{b4A}, -S(O)₂R^{b4A}, -S(O)NR^{c4A}R^{d4A}, -S(O)₂NR^{c4A}R^{d4A}, -C(=NR^{e4A})R^{a4A}, -C(=NR^{e4A})NR^{c4A}R^{d4A}, -NR^{c4A}C(=NR^{e4A})R^{a4A}, -NR^{c4A}C(=NR^{e4A})NR^{c4A}R^{d4A}, -NR^{c4A}S(O)(=NR^{e4A})R^{b4A}, -

NR^{c4A}S(O)(=NR^{e4A})NR^{c4A}R^{d4A}, -OS(O)(=NR^{e4A})R^{b4A}, -S(O)(=NR^{e4A})R^{b4A}, -S(O)(=NR^{e4A})NR^{c4A}R^{d4A}, -C(O)NR^{c4A}S(O)₂R^{b4A}, -C(O)NR^{c4A}S(O)₂NR^{c4A}R^{d4A}, -S(O)₂NR^{c4A}C(O)R^{b4A}, -NR^{c4A}S(O)NR^{c4A}C(O)R^{b4A}, and -P(O)R^{f4A}R^{g4A}, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{a4A}, R^{c4A}, and R^{d4A} is independently selected from H, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{a4A}, R^{c4A}, and R^{d4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

or, any R^{c4A} and R^{d4A} attached to the same N atom, together with the N atom to which they are attached, form a 4-10 membered heterocycloalkyl group, wherein the 4-10 membered heterocycloalkyl group is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

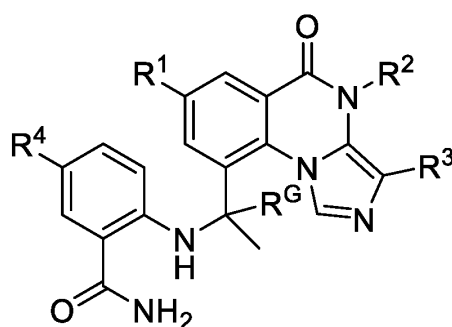
each R^{b4A} is independently selected from C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl, wherein the C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₀ aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C₃₋₁₀ cycloalkyl-C₁₋₄ alkyl, C₆₋₁₀ aryl-C₁₋₄ alkyl, (4-10 membered heterocycloalkyl)-C₁₋₄ alkyl, and (5-10 membered heteroaryl)-C₁₋₄ alkyl of R^{b4A} are each optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^G substituents;

each R^{e4A} is independently selected from H, OH, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^{f4A} and R^{g4A} are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-10} aryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl- C_{1-4} alkyl, (4-10 membered heterocycloalkyl)- C_{1-4} alkyl, and (5-10 membered heteroaryl)- C_{1-4} alkyl;

each R^G is independently selected from H, D, OH, CN, halo, oxo, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} haloalkyl, cyano- C_{1-4} alkyl, HO- C_{1-4} alkyl, C_{1-4} alkoxy- C_{1-4} alkyl, C_{3-7} cycloalkyl, 4-7 membered heterocycloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-3} alkylamino, di(C_{1-3} alkyl)amino, thio, C_{1-3} alkylthio, C_{1-3} alkylsulfinyl, C_{1-3} alkylsulfonyl, carbamyl, C_{1-3} alkylcarbamyl, di(C_{1-3} alkyl)carbamyl, carboxy, C_{1-3} alkylcarbonyl, C_{1-3} alkoxy carbonyl, C_{1-3} alkylcarbonyloxy, C_{1-3} alkylcarbonylamino, C_{1-3} alkoxy carbonylamino, aminocarbonyloxy, C_{1-3} alkylaminocarbonyloxy, di(C_{1-3} alkyl)aminocarbonyloxy, C_{1-3} alkylsulfonylamino, aminosulfonyl, C_{1-3} alkylaminosulfonyl, di(C_{1-3} alkyl)aminosulfonyl, aminosulfonylamino, C_{1-3} alkylaminosulfonylamino, di(C_{1-3} alkyl)aminosulfonylamino, aminocarbonylamino, C_{1-3} alkylaminocarbonylamino, and di(C_{1-3} alkyl)aminocarbonylamino.

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



II

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from halo, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^2 is C_{1-3} alkyl;

R^3 is selected from pyrazolyl, pyrimidinyl, piperidinyl, and $C(O)NR^{c3}R^{d3}$,

wherein the pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from C_{1-3} alkyl, amino, and $-C(O)C_{1-3}$ alkyl;

each R^{c3} and R^{d3} is independently selected from C_{1-3} alkyl and C_{1-3} haloalkyl;

R^4 is halo; and

R^G is H or D.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from chloro, methyl, and trifluoromethyl.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein R^2 is selected from methyl and trideuteromethyl.

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^3 is $C(O)NR^{c3}R^{d3}$.

6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl.

7. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each methyl.

8. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each trideuteromethyl.

9. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from pyrazolyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from C_{1-3} alkyl, amino, and $-C(O)C_{1-3}$ alkyl.
10. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from pyrazolyl, pyridinyl, pyrimidinyl, and piperidinyl, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each optionally substituted with one R^{3A} substituent selected from methyl, amino, and methylcarbonyl.
11. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^3 is selected from methylpyrazolyl, aminopyrimidinyl, and (methylcarbonyl)piperidinyl.
12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^4 is fluoro or chloro.
13. The compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein R^G is H.
14. The compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein R^G is D.
15. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein:
- R^1 is selected from chloro, methyl, and trifluoromethyl;
 - R^2 is selected from methyl and trideuteromethyl;
 - R^3 is selected from pyrazolyl, pyridinyl, pyrimidinyl, piperidinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrazolyl, pyrimidinyl, and piperidinyl of R^3 are each

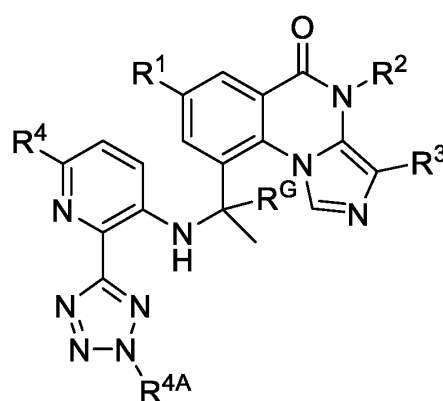
optionally substituted with one R^{3A} substituent selected from methyl, amino, and methylcarbonyl;

R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

R^4 is fluoro or chloro; and

R^G is H or D.

16. The compound of claim 1, wherein the compound of Formula I is a compound of Formula III:



III

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is halo or C_{1-3} alkyl;

R^2 is C_{1-3} alkyl;

R^3 is selected from pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidinyl, azetidylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from halo, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} alkoxy, oxetanyl, amino, C_{1-3} alkylamino, di(C_{1-3} alkyl)amino, $-C(O)C_{1-3}$ alkyl, $-C(O)C_{1-3}$ hydroxyalkyl, $-C(O)C_{3-6}$ cycloalkyl, and $-S(O)_2C_{1-3}$ alkyl;

R⁴ is selected from H, halo, C₁₋₃ alkyl, and C₁₋₃ alkoxy;

R^{4A} is selected from C₁₋₃ alkyl, azetidiny, and piperidiny, wherein the azetidiny and piperidiny of R⁴ are each optionally substituted with C₁₋₃ alkyl; and R^G is H or D.

17. The compound of claim 1 or 16, or a pharmaceutically acceptable salt thereof, wherein R¹ is chloro or methyl.

18. The compound of any one of claims 1, 16, and 17, or a pharmaceutically acceptable salt thereof, wherein R² is methyl or trideuteromethyl.

19. The compound of any one of claims 1 and 16 to 18, or a pharmaceutically acceptable salt thereof, wherein R³ is selected from pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny, wherein the pyrimidiny, azetidinylmethyl, pyrazolyl, pyridiny, piperidiny, 2H-pyrazolo[3,4-b]pyridiny, pyrazolo[1,5-a]pyridiny, pyrazolo[1,5-a]pyrimidiny, and imidazo[1,5-a]pyridiny of R³ are each optionally substituted with 1 or 2 R^{3A} substituents.

20. The compound of any one of claims 1 and 16 to 19, or a pharmaceutically acceptable salt thereof, wherein each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl.

21. The compound of any one of claims 1 and 16 to 18, or a pharmaceutically acceptable salt thereof, wherein R³ is selected from (difluoroazetidiny)methyl, oxetanylpiperidiny, (methylcarbonyl)piperidiny, (isopropylcarbonyl)piperidiny, (hydroxymethylcarbonyl)piperidiny, (cyclopropylcarbonyl)piperidiny, (methylsulfonyl)piperidiny, (isopropylsulfonyl)piperidiny, (cyclopropylsulfonyl)piperidiny, pyrazolyl, methylpyrazolyl, (hydroxyethyl)pyrazolyl, pyridiny, (hydroxymethyl)pyridiny, aminopyridiny,

(amino)(chloro)pyridinyl, (methylamino)pyridinyl, (dimethylamino)pyridinyl, aminopyrimidinyl, (hydroxymethyl)pyrimidinyl, (amino)(fluoro)pyrimidinyl, (amino)(methyl)pyrimidinyl, (amino)(methoxy)pyrimidinyl, methyl-2H-pyrazolo[3,4-b]pyridine, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, (amino)(fluoro)pyridinyl, methylimidazolyl, aminothiazolyl, (amino)(methyl)thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl.

22. The compound of any one of claims 1 and 16 to 18, or a pharmaceutically acceptable salt thereof, wherein R^3 is $C(O)NR^{c3}R^{d3}$.

23. The compound of any one of claims 1, 16 to 18, and 22, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl.

24. The compound of any one of claims 1, 16 to 18, and 22, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each methyl.

25. The compound of any one of claims 1, 16 to 18, and 22, or a pharmaceutically acceptable salt thereof, wherein R^{c3} and R^{d3} are each trideuteromethyl.

26. The compound of any one of claims 1 and 16 to 25, or a pharmaceutically acceptable salt thereof, wherein R^4 is selected from H, fluoro, chloro, methyl, and methoxy.

27. The compound of any one of claims 1 and 16 to 26, or a pharmaceutically acceptable salt thereof, wherein R^{4A} is selected from methyl, trideuteromethyl, ethyl, azetidiny, and piperidinyl, wherein the azetidiny and piperidinyl of R^{4A} are each optionally substituted with methyl.

28. The compound of any one of claims 1 and 16 to 26, or a pharmaceutically acceptable salt thereof, wherein R^{4A} is selected from methyl, trideuteromethyl, ethyl, methylazetidiny, and methylpiperidinyl.

29. The compound of any one of claims 1 and 16 to 28, or a pharmaceutically acceptable salt thereof, wherein R^G is H.

30. The compound of any one of claims 1 and 16 to 28, or a pharmaceutically acceptable salt thereof, wherein R^G is D.

31. The compound of claim 1 or 16, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is chloro or methyl;

R^2 is methyl or trideuteromethyl;

R^3 is selected from pyrimidinyl, azetidinylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl, and $C(O)NR^{c3}R^{d3}$, wherein the pyrimidinyl, azetidinylmethyl, pyrazolyl, pyridinyl, piperidinyl, 2H-pyrazolo[3,4-b]pyridinyl, pyrazolo[1,5-a]pyridinyl, pyrazolo[1,5-a]pyrimidinyl, imidazo[1,5-a]pyridinyl, imidazolyl, thiazolyl, and 6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazinyl of R^3 are each optionally substituted with 1 or 2 R^{3A} substituents;

each R^{3A} is independently selected from methyl, fluoro, chloro, methoxy, amino, methylamino, dimethylamino, hydroxymethyl, hydroxyethyl, oxetanyl, methylcarbonyl, isopropylcarbonyl, hydroxymethylcarbonyl, cyclopropylcarbonyl, methylsulfonyl, isopropylsulfonyl, and cyclopropylsulfonyl;

R^{c3} and R^{d3} are each independently selected from methyl and trideuteromethyl;

R^4 is selected from H, fluoro, chloro, methyl, and methoxy;

R^{4A} is selected from methyl, ethyl, trideuteromethyl, azetidinyl, and piperidinyl, wherein the azetidinyl and piperidinyl of R^{4A} are each optionally substituted with methyl; and

R^G is H or D.

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

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*R*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*S*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

2-((1-(3-(1-acetylpiperidin-4-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-7-chloro-4-methyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,7-trimethyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl-1-d)-4-methyl-N,N-bis(methyl-d₃)-5-oxo-7-(trifluoromethyl)-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(6-(hydroxymethyl)pyridin-3-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(6-(methylamino)pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6-(dimethylamino)pyridin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyethyl)-1H-pyrazol-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyrimidin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(imidazo[1,5-a]pyridin-6-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-6-chloropyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-N,N,4-tris(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

methyl 3-((1-(3-(bis(methyl-d3)carbamoyl)-7-methyl-4-(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-6-chloropyridin-2-yl)carbamate;

9-(1-((2-carbamoyl-4-chlorophenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
methyl (6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)carbamate;
9-(1-((4-fluoro-2-sulfamoylphenyl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
9-(1-((5-chloroquinolin-8-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
N,N,4,7-tetramethyl-9-(1-((6-methyl-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;
2-((1-(3-(1-acetylpiperidin-4-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;
2-((1-(4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
5-fluoro-2-((1-(7-methyl-4-(methyl-d₃)-3-(1-methyl-1H-pyrazol-5-yl)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)benzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-5-fluorobenzamide;
2-((1-(3-(2-aminopyrimidin-5-yl)-7-chloro-4-methyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(oxetan-3-yl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;
3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(1-acetylpiperidin-4-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-isobutyrylpiperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropanecarbonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-(methylsulfonyl)piperidin-4-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(isopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(1-(cyclopropylsulfonyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-methoxy-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((6-methyl-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-9-(1-((2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-methoxy-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((4-fluoro-2-(1-(methyl-d₃)-1H-tetrazol-5-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(pyridin-3-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((4-fluoro-2-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((4-fluoro-2-(1-methyl-1H-1,2,3-triazol-4-yl)phenyl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-3-pyridyl)-9-[1-[4-fluoro-2-(1-methyltriazol-4-yl)anilino]ethyl]-4,7-dimethyl-imidazo[1,5-a]quinazolin-5-one;

3-(1-acetylpiperidin-4-yl)-9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-(6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)ethyl)-3-(1-(2-hydroxyacetyl)piperidin-4-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-aminopyridin-3-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-4,7-dimethyl-3-(1-methyl-1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-((6-chloro-2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazin-1-yl)methyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-((3-fluoroazetidin-1-yl)methyl)pyridin-3-yl)amino)ethyl)-N-(2-hydroxyethyl)-N,4,7-trimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

methyl ((6-chloro-3-((1-(3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)pyridin-2-yl)methyl)carbamate;

methyl (6-chloro-3-(((3-(dimethylcarbamoyl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)pyridin-2-yl)carbamate;

9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-N,N,4,7-tetramethyl-5-oxo-imidazo[1,5-a]quinazoline-3-carboxamide;

9-[(6-chloro-2,3-dihydropyrido[2,3-b][1,4]oxazin-1-yl)methyl]-4,7-dimethyl-5-oxo-N,N-bis(trideuteriomethyl)imidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-N,N,4,7-tetramethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylazetidin-3-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

9-(1-((6-chloro-2-(2-(1-methylpiperidin-4-yl)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-N,N,4-tris(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

3-(2-aminopyrimidin-5-yl)-9-((6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-((3,3-difluoroazetidin-1-yl)methyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d3)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-7-methyl-4-(methyl-d3)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*R*)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-N,N-bis(methyl-d3)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide;

(*S*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-d)-3-(2-(hydroxymethyl)pyrimidin-5-yl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

(*R*)-2-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl-1-d)amino)-5-fluorobenzamide;

3-(2-aminopyrimidin-5-yl)-9-(1-(6-chloro-3,4-dihydro-1,5-naphthyridin-1(2H)-yl)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

methyl 3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)carbamate;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-fluoro-2-(1-methyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-cyclopropyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(pyrimidin-5-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(4-hydroxypiperidin-1-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-morpholinopyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,5-dimethyl-1H-pyrazol-4-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(5-methyl-1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1,3,4-oxadiazol-2-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(3-((1-(3-(2-aminopyrimidin-5-yl)-7-methyl-4-(methyl-d₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)ethyl)amino)-6-chloropyridin-2-yl)-1,2,4-oxadiazol-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-7-methyl-4-(methyl-d₃)imidazo[1,5-a]quinazolin-5(4H)-one;

methyl 3-(((3-(2-aminopyrimidin-5-yl)-4,7-dimethyl-5-oxo-4,5-dihydroimidazo[1,5-a]quinazolin-9-yl)methyl)amino)-6-chloropyridin-2-yl)carbamate;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1H-pyrazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-chloropyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-methylpyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(6-amino-5-methoxypyridin-3-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methoxypyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(2-methyl-2H-pyrazolo[3,4-b]pyridin-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-(methyl-d₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(pyrazolo[1,5-a]pyridin-6-yl)imidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(1-methyl-1H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one; and

3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-ethyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

or a pharmaceutically acceptable salt thereof.

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

3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*R*)-3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

(*S*)-3-(6-amino-5-fluoropyridin-3-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

3-(2-amino-4-methylpyrimidin-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;

9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethyl-3-(1-methyl-1H-imidazol-5-yl)imidazo[1,5-a]quinazolin-5(4H)-one;
9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-3-(6,7-dihydro-4H-pyrazolo[5,1-c][1,4]oxazin-3-yl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
3-(2-aminothiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one; and
3-(2-amino-4-methylthiazol-5-yl)-9-(1-((6-chloro-2-(2-methyl-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl)-4,7-dimethylimidazo[1,5-a]quinazolin-5(4H)-one;
or a pharmaceutically acceptable salt thereof.

34. The compound of claim 1 or 2, which is (*R*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-*N,N*-bis(methyl-*d*₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide, or a pharmaceutically acceptable salt thereof.

35. The compound of claim 1 or 2, which is (*S*)-9-(1-((2-carbamoyl-4-fluorophenyl)amino)ethyl)-4,7-dimethyl-*N,N*-bis(methyl-*d*₃)-5-oxo-4,5-dihydroimidazo[1,5-a]quinazoline-3-carboxamide, or a pharmaceutically acceptable salt thereof.

36. The compound of claim 1 or 16, which is 3-(2-aminopyrimidin-5-yl)-9-(1-((6-chloro-2-(2-(methyl-*d*₃)-2H-tetrazol-5-yl)pyridin-3-yl)amino)ethyl-1-*d*)-7-methyl-4-(methyl-*d*₃)imidazo[1,5-a]quinazolin-5(4H)-one, or a pharmaceutically acceptable salt thereof.

37. A pharmaceutical composition, comprising a compound of any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

38. A method of inhibiting an activity of PI3K α kinase, comprising contacting the kinase with a compound of any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof.
39. A method of treating a PI3K α -mediated disease or disorder in a patient, comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof.
40. The method of claim 39, wherein the disease or disorder is a cancer.
41. The method of claim 40, wherein the cancer is selected from breast cancer, brain cancer, prostate cancer, endometrial cancer, gastric cancer, leukemia, lymphoma, sarcoma, colorectal cancer, lung cancer, ovarian cancer, skin cancer, and head and neck cancer.
42. The method of claim 39, wherein the disease or disorder is CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome), or PIK3CA-related overgrowth syndrome (PROS).